Polymers in Nanotechnology

History of Nanotechnology

Knowing the History and Facts

From Brown to Green

1886. Shiny copper color

1906~1920. Blue-green

Frédéric-Auguste Bartholdi: "This thing will live to eternity, when we shall have passed away, and everything living with us has moldered away."

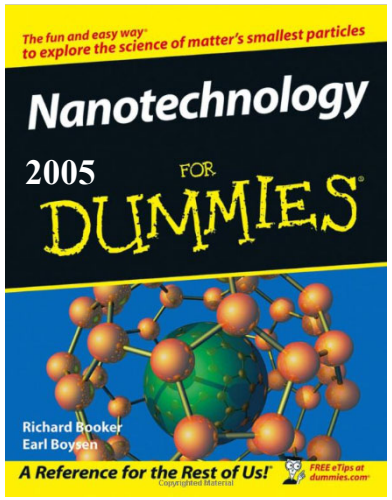
https://www.nyhistory.org/community/when-did-the-statue-of-liberty-turn-green
https://www.dailymail.co.uk/sciencetech/article-4652254/The-Statue-Liberty-RED-turned-green.html
https://www.nps.gov/stli/learn/historyculture/frederic-auguste-bartholdi.htm

The Big Picture on Nanotechnology

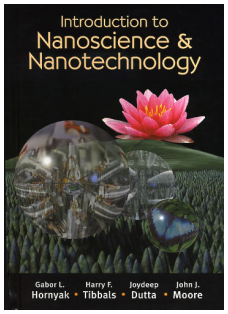
The Beginning

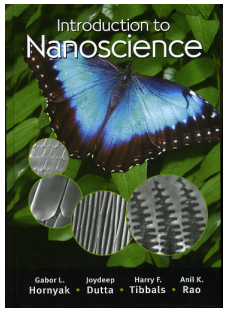
Gerd Binnig & Heinrich Rohrer
Inventors of the Scanning
tunneling microscope (STM)

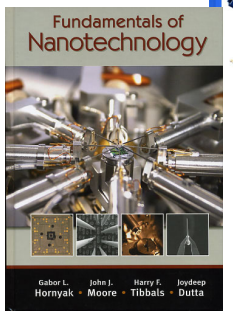
The Trending

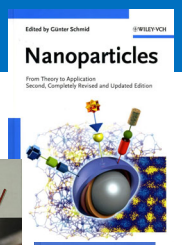


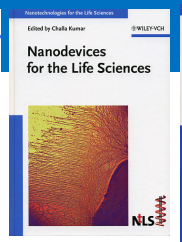
The Boom

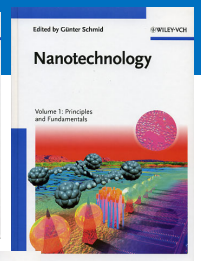


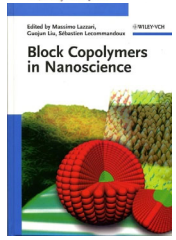


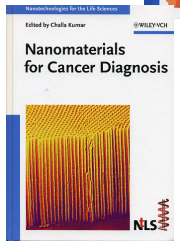


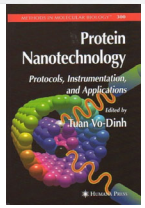


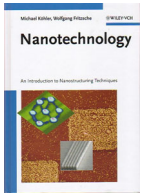


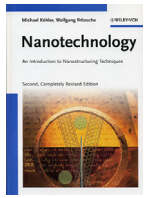


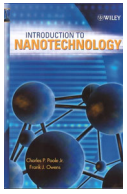


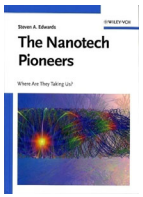


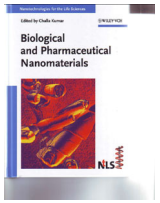


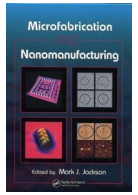


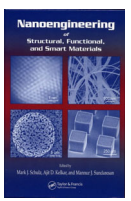


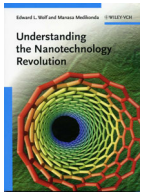


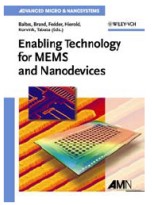


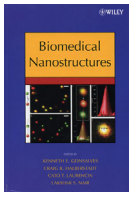


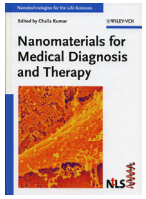


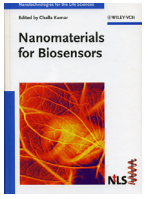


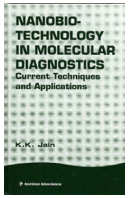


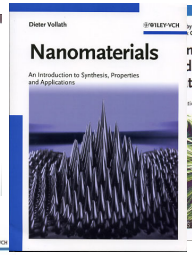


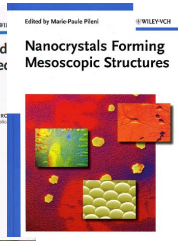


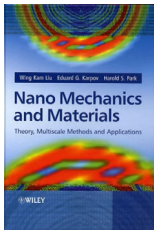


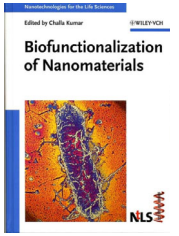


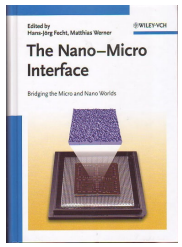


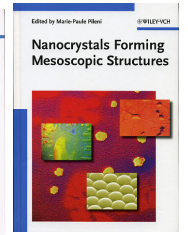


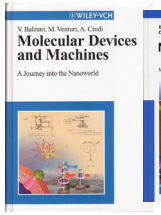


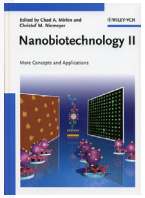


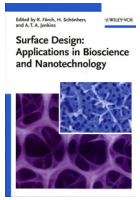


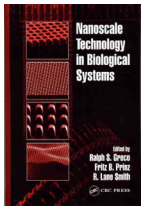


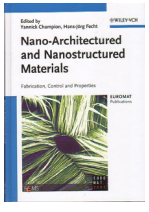


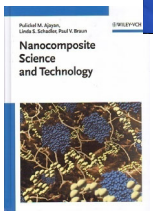


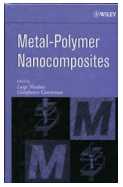


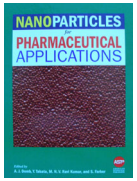






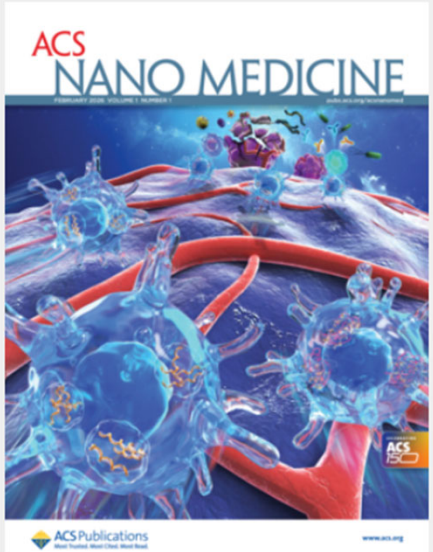






Scientific Journals on Nano

ACS Nano
ACS Nanomedicine
Beilstein Journal of Nanotechnology
IEEE Transactions on Nanotechnology
International Journal of Applied Nanotechnology
International Journal of Nanomaterials and Nanostructures
International Journal of Nanomedicine
Bionanoscience
Journal of Biomedical Nanotechnology
Journal of Nanoparticle Research
Journal of Nanophotonics
Materials Today Nano
Microfluidics and Nanofluidics
Nano-Horizons
Nano Communication Networks
Nano Convergence
Nano Energy
Nano Letters
Nano Research
Nano Today
Nanomedicine: Nanotechnology, Biology, and Medicine
Nanoscale
Nanoscale Horizons
Nanotechnology (IOP Science)
Nature Nanotechnology
Nano Trends-A Journal of Nano Technology & Its
Small (Covers micro/nanoscale)



February 11, 2026
Volume 1, Issue 1
Pages 1-297

Sample This sample issue provides free access to the full text of all articles. (Subscription Information)

About the Cover:

mRNA vaccines are designed and developed using advanced delivery technologies. Efficient mRNA vaccine delivery enables activation of immune responses to elicit protective effects against specific pathogens, demonstrating substantial potential for preventing and treating a wide range of diseases.

View the article.

Download Cover

ACS Nano Medicine

Welcome to *ACS Nano Medicine*: From Nanoscale Innovation to Clinical Impact

Cite This: *ACS Nano Med.* 2026, 1, 1–2

Paul Ehrlich's early 20th century "magic bullet" (Zauberkugel) concept articulated a transformative vision for medicine, i.e., therapies that precisely target disease while minimizing collateral damage. A century later, nanomedicine has emerged as a powerful realization of this idea, harnessing nanoscale carriers to deliver potent drugs and/or contrast probes selectively to pathological cells. The field has matured from a largely exploratory discipline into a translational engine that is reshaping how we diagnose, monitor, and treat disease. What began as an effort to exploit size-dependent physicochemical phenomena has evolved into a sophisticated convergence of materials science, chemistry, biology, engineering, and clinical medicine. As we enter the next phase of growth, the field faces both unprecedented opportunity and necessary recalibration.

ACS Nano Medicine, the newly launched journal from the American Chemical Society, sits at this technological inflection point charged with capturing foundational advances while setting a clear vision for clinical translation. The journal welcomes studies that not only advance nanoscale science but also illuminate the biological, engineering, and regulatory parameters essential for real-world impact. By embracing work

Over the past year, the field has confronted hard realities as many elegant nanomaterials have struggled to progress beyond proof-of-concept. Challenges related to reproducibility and quality control, product manufacturing and scalability, biological complexity, regulatory pathways, and integration into real-world clinical workflows and care pathways have slowed translation. Rather than signaling failure, these realities mark a long-anticipated transition from a predominantly discovery-driven enterprise to a more mature translation-focused phase. The future of nanomedicine will be defined not by novelty of nanomaterials alone, but by mechanistic clarity, robustness, and clinical relevance.

Looking forward, several themes are poised to define the next decade of nanomedicine. First, a deep mechanistic understanding of nanobio interactions must take center stage. High-impact nanomedicine research must rigorously connect nanoscale structure, morphology, dynamics, and interfacial chemistry to biological function. This includes quantitative understanding of nanobio interactions, transport phenomena, pharmacokinetics and pharmacodynamics, immune engagement, metabolic processes, and degradation pathways across tissues and cellular compartments. Studies

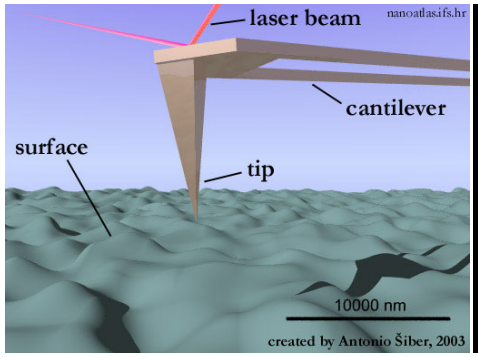
Nanotechnology: Introduction

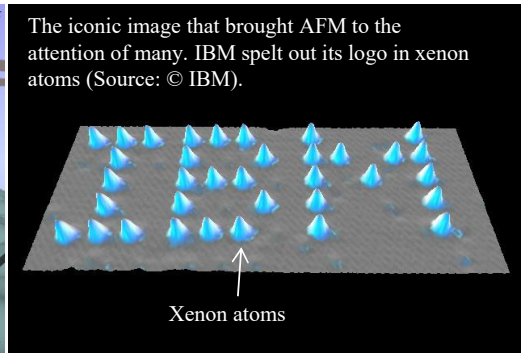
It is debatable when nanotechnology, as we now know it, began. Perhaps, we can trace the beginnings to the invention of the scanning tunneling microscope in 1980, as it and the subsequently developed atomic force microscope enabled manipulation of individual atoms and molecules.

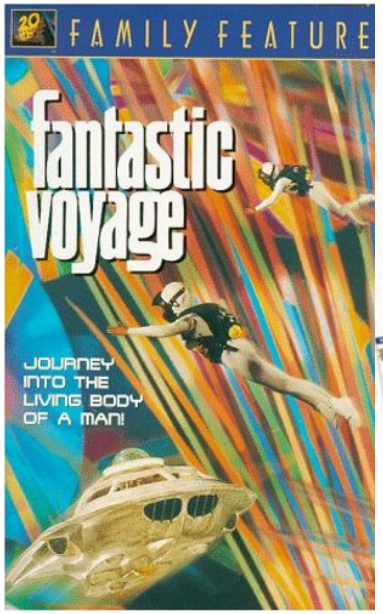
The nanotechnology fever began when the United States launched the National Nanotechnology Initiative (https://www.nano.gov/), the world's first program of its kind, in 2000. Since then, we have been bombarded with dazzling images and cartoons about nanotechnology, such as nanorobots killing cancer cells, which resemble the plot of Fantastic Voyage. Tens of thousands of articles have been published on nanotechnology, and the press feeds the public a steady diet of potential advances enabled by it.

Park 2013, Facing the truth about nanotechnology in drug delivery

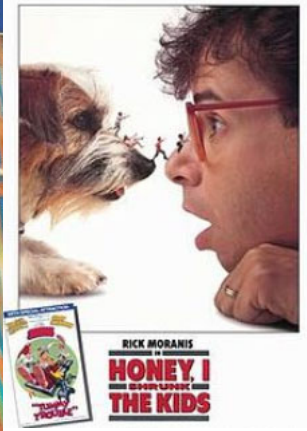
Scanning tunneling microscope → atomic force microscope



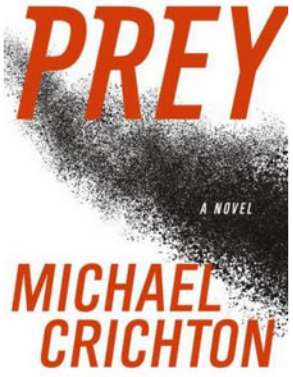




1966



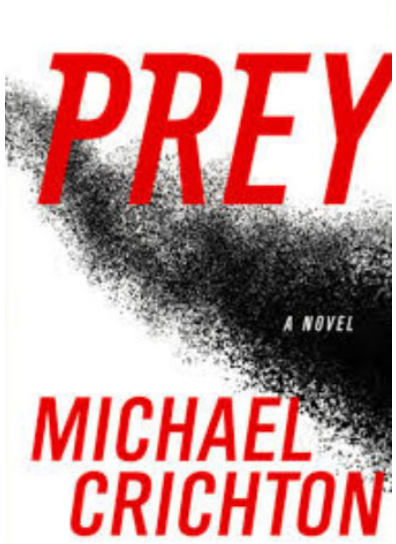
1989



2002

Hollywood versions of nanotechnology

Nanotechnology Future: Fiction and Fact



MAKING PREHISTORY Michael Crichton at the Natural History Museum of Los Angeles County, in 2004. BY BLAKE LITTLE/CONTOUR/GETTY IMAGES.

2002

https://www.spaghettibookclub.org/review.php?reviewId=4396
https://www.goodreads.com/review/show/203477000

Prey- Written by Michael Crichton
Illustrated by Will Staehle, Reviewed by Matthew W. (age 10, 4th Grader))

Have you ever heard of a nano particle? Well Prey is about a company called Xmos that develops nano technology and creates nano particles. Nano particles are micro super computer robots capable of intelligent life. Jack (a father of three kids who had been working at Xmos but was fired several weeks ago) has been asked to come back to Xmos by his best friend, Ricky. Ricky says that they have a runaway swarm of nano particles. After several days at Xmos, Jack gets suspicious of his wife, Julia, who is working to solve the mystery as well. She is acting very strangely toward him and Jack wants to know what's wrong. What Jack doesn't know is that the answer could get him killed!

I highly recommend this book. The plot was fantastic and exiting. I was never bored because the book moved fast and there was always an adventure going on. Jack was very interesting. His brightness and curiosity helped solve the mystery. He knows a lot about computers and he saves many lives. The book was scary and strange. I do not recommend this book for all ages. Unless you are a good reader and your parents will let you read it you should not read this book. If you read it, I hope you like it.

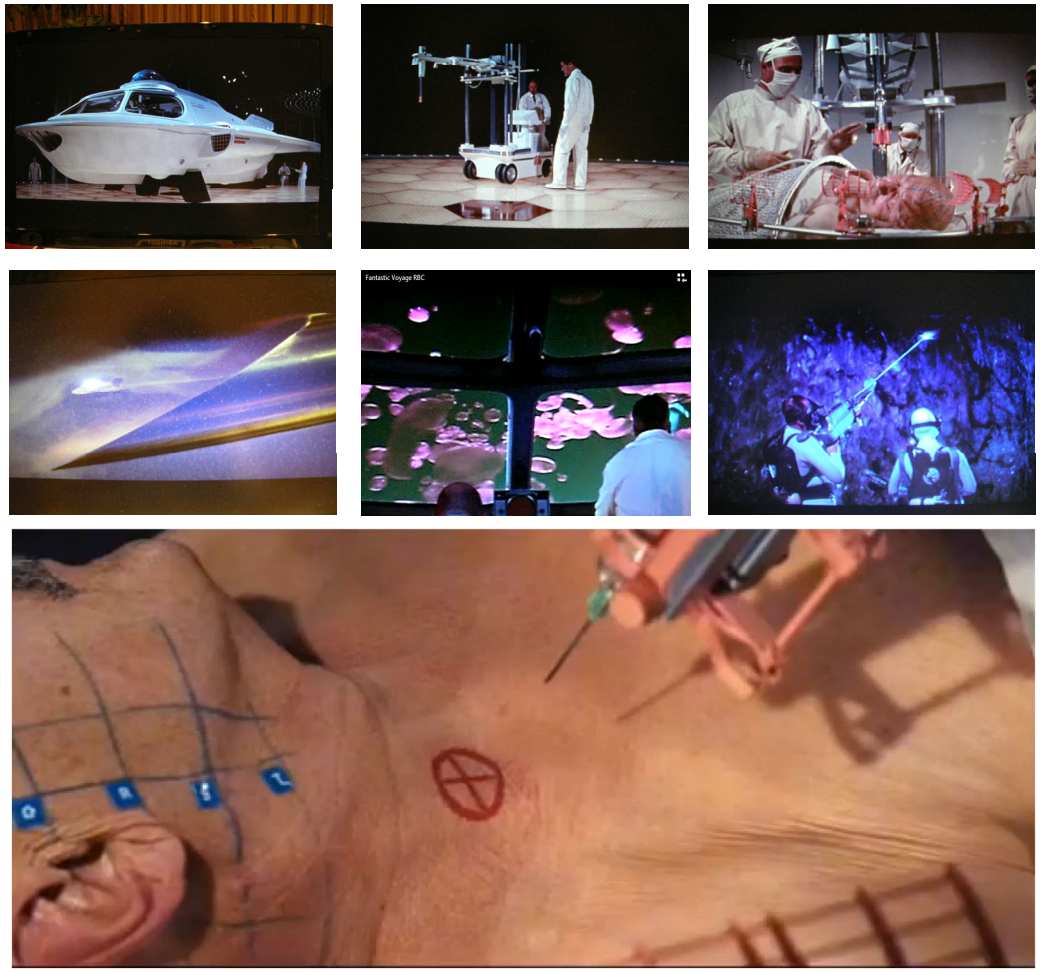
I recommend this book to boys who like scary and weird books. You can find this book at your local library. I hope you like it!

https://www.spaghettibookclub.com/review.php?reviewId=4396

Nanoparticles in the Blood

Blood is "infinitely" more complicated than birds in the air.

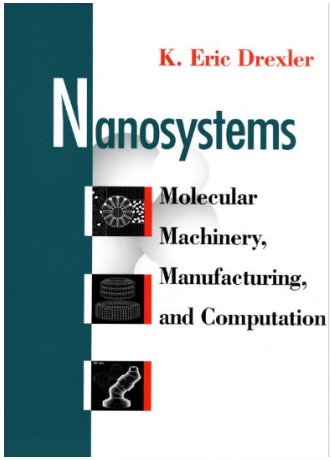
Fantastic Voyage (1966)



US Airways Flight 1549 in the Hudson River, New York, USA (January 15, 2009)

https://simpleflying.com/the-miracle-on-the-hudson/
https://www.sciencephoto.com/media/852378/view/us-airways-flight-1549-incident-illustration

Nanotechnology: Chip to Machine



1992

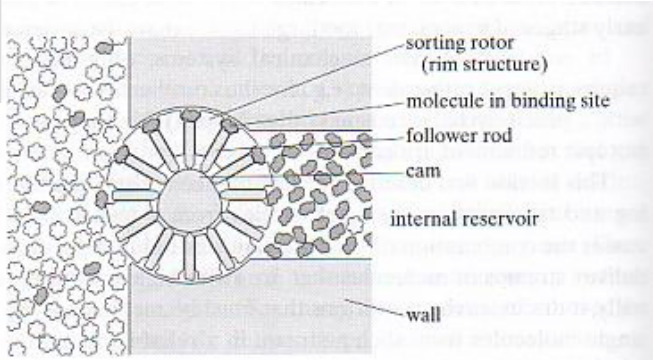


Figure 13.1. A sorting rotor based on modulated receptors. In this approach (illustrated schematically), a cam surface modulates the position of a set of radial rods. In the binding position (mapping the illustration onto a 12-hour clock dial, 10:00), the rods form the bottom of a site adapted to bind molecules of the desired type. Between 10:00 and 2:00, the receptors undergo transport to the interior, driven by shaft power (coupling not shown). Between 2:00 and 4:00, the molecules are forcibly ejected by the rods, which are thrust outward by the cam surface. Between 4:00 and 8:00, the sites, now blocked and incapable of transporting molecules, undergo transport to the exterior. Between 8:00 and 10:00, the rods retract, regenerating an active receptor. Section 13.2.1c discusses receptor properties; Section 13.2.1e discusses energy dissipation.

By K. Eric Drexler

Machine-Phase Nanotechnology

A molecular nanotechnology pioneer predicts that the tiniest robots will revolutionize manufacturing and transform society

IN 1959 PHYSICIST Richard Feynman gave an after-dinner talk exploring the limits of miniaturization. He set out from known technology (at a time when an adding machine could barely fit in your pocket), surveyed the limits set by physical law and ended by arguing the possibility—even inevitability—of "atom by atom" construction.

What at the time seemed absurdly ambitious, even bizarre, has recently become a widely shared goal. Decades of technological progress have shrunk microelectronics to the threshold of the molecular scale, while scientific progress at the molecular level—especially on the molecular machinery of living systems—has now made clear to many what was envisioned by a sole genius so long ago.

Inspired by molecular biology, studies of advanced nanotechnologies have focused on bottom-up construction, in which molecular machines assemble molecular building blocks to form products, including new molecular machines. Biology shows us that molecular machine systems and their products can be made cheaply and in vast quantities.

Stepping beyond the biological analogy, it would be a natural goal to be able to put every atom in a selected place (where it would serve as part of some active or structural component) with no extra molecules on the loose to jam the works. Such a system would not be a liquid or gas, as no molecules would move randomly, nor would it be a solid, in which molecules are fixed in place. Instead this new machine-phase matter would exhibit the molecular movement seen today only in liquids and gases as well as the mechanical strength typically associated with solids. Its volume would be filled with active machinery.

The ability to construct objects with molecular precision will revolutionize manufacturing, permitting materials properties and device performance to be greatly improved. In addition, when a production process maintains control of each atom, there is no reason to dump toxic leftovers into the air or water. Improved manufacturing would also drive down the cost of solar cells and energy storage systems, cutting demand for coal and petroleum, further reducing pollution. Such advances raise hope that those in the developing world will be able to reach First World living standards without causing environmental disaster.

Low-cost, lightweight, extremely strong materials would make transportation far more energy efficient and—finally—make space transportation economical. The old dreams of expanding the biosphere beyond our one vulnerable planet suddenly look feasible once more.

Perhaps the most exciting goal is the molecular repair of the human body. Medical nanorobots are envisioned that could destroy viruses and cancer cells, repair damaged structures, remove accumulated wastes from the brain and bring the body back to a state of youthful health.

Another surprising medical application would be the eventual ability to repair and revive those few pioneers now in suspended animation (currently regarded as legally deceased), even those who have been preserved using the crude cryogenic storage technology available since the 1960s. Today's vitrification techniques—which prevent the formation of damaging ice crystals—should make repair easier, but even the original process appears to preserve brain structure well enough to enable restoration.

Those researchers most familiar with the field of molecular nanotechnology see the technology base underpinning such capabilities as perhaps one to three decades off. At the moment, work focuses on the earliest stages: finding out how to build larger structures with atomic precision, learning to design molecular machines and identifying intermediate goals with high payoff.

To understand the potential of molecular manufacturing technology, it helps to look at the macroscale machine systems used now in industry. Picture a robotic arm that reaches over to a conveyor belt, picks up a loaded tool, applies the tool to a workpiece under construction, replaces the empty tool on the belt, picks up the next loaded tool, and so on—as in today's automated factories.

In principle, Drexler says, a molecular construction system called an assembler could build almost anything, including copies of itself.

Now mentally shrink this entire mechanism, including the conveyor belt, to the molecular level to form an image of a nanoscale construction system. Given a sufficient variety of tools, this system would be a general-purpose building device, nicknamed an assembler. In principle, it could build almost anything, including copies of itself.

Molecular nanotechnology as a field does not depend on the feasibility of this particular proposal—a collection of less general building devices could carry out the functions mentioned above. But because the assembler concept is still controversial, it's worth mentioning the objections being raised.

One prominent chemist speaking at a recent event sponsored by the American Association for the Advancement of Science asked how one could power and direct an assembler and whether it could really break and re-form strong molecular bonds. These are reasonable questions that can be answered only by describing designs and calculations too bulky to fit in this essay. Fortunately, technical literature providing seemingly adequate answers has been available since at least 1992, when my book *Nanosystems* was published.

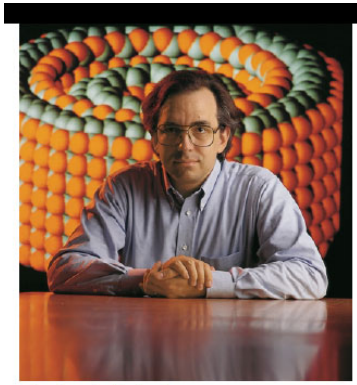
Another well-known chemist objects that an assembler would need 10 robotic "fingers" to carry out its operations and that there isn't room for them all. The need for such a large number of manipulators, however, has never been established or even seriously argued. In contrast, the designs that have received (and survived) the most peer review use one tool at a time and grip their tools without using any fingers at all.

These examples point to the difficulty of finding appropriate critiques of nanotechnology designs. Many researchers whose work seems relevant are actually the wrong experts—they are excellent in their discipline but have little expertise in systems engineering. The shortage of molecular systems engineers will probably be a limiting factor in the speed with which nanotechnology can be developed.

It is important that critiques of nanotechnology are well executed, because vital societal decisions depend on them. If molecular nanotechnology as described here is correct, policy issues can look quite different from what is generally expected. Today most people believe that global warming will be hard to correct—with nanotechnology, excess greenhouse gases could be inexpensively removed from the atmosphere. Current Social Security projections assume increasing numbers of aged citizens in poor health. With advanced medical nanotechnology, tomorrow's seniors could be more active and healthy than they are now, bringing new meaning to the "golden years."

Likewise, we need to focus now on avoiding accidents and preventing abuse of this powerful technology. Solid work has been done on the problem of heading off major nanotechnology accidents. The Foresight Guidelines, available on the World Wide Web, sketch out proposed safety rules *[see below]*.

But the challenge of preventing abuse—the exploitation of this technology by aggressive governments, terrorist groups or even individuals for their own purposes—still looms large. The closest analogy to this problem these days is the difficulty of controlling the proliferation of chemical and biological weapons. The advance toward molecular nanotechnology highlights the urgency in finding effective ways to manage emerging technologies that are powerful, valuable and open to misuse.



NANOSCRIBE K. Eric Drexler conceived the concept of molecular machine systems (a component of one is shown in the background).

ABOUT THE AUTHOR

K. ERIC DREXLER is chairman of the Foresight Institute, research fellow of the Institute for Molecular Manufacturing, and author of *Engines of Creation* and *Nanosystems: Molecular Machinery, Manufacturing, and Computation*.

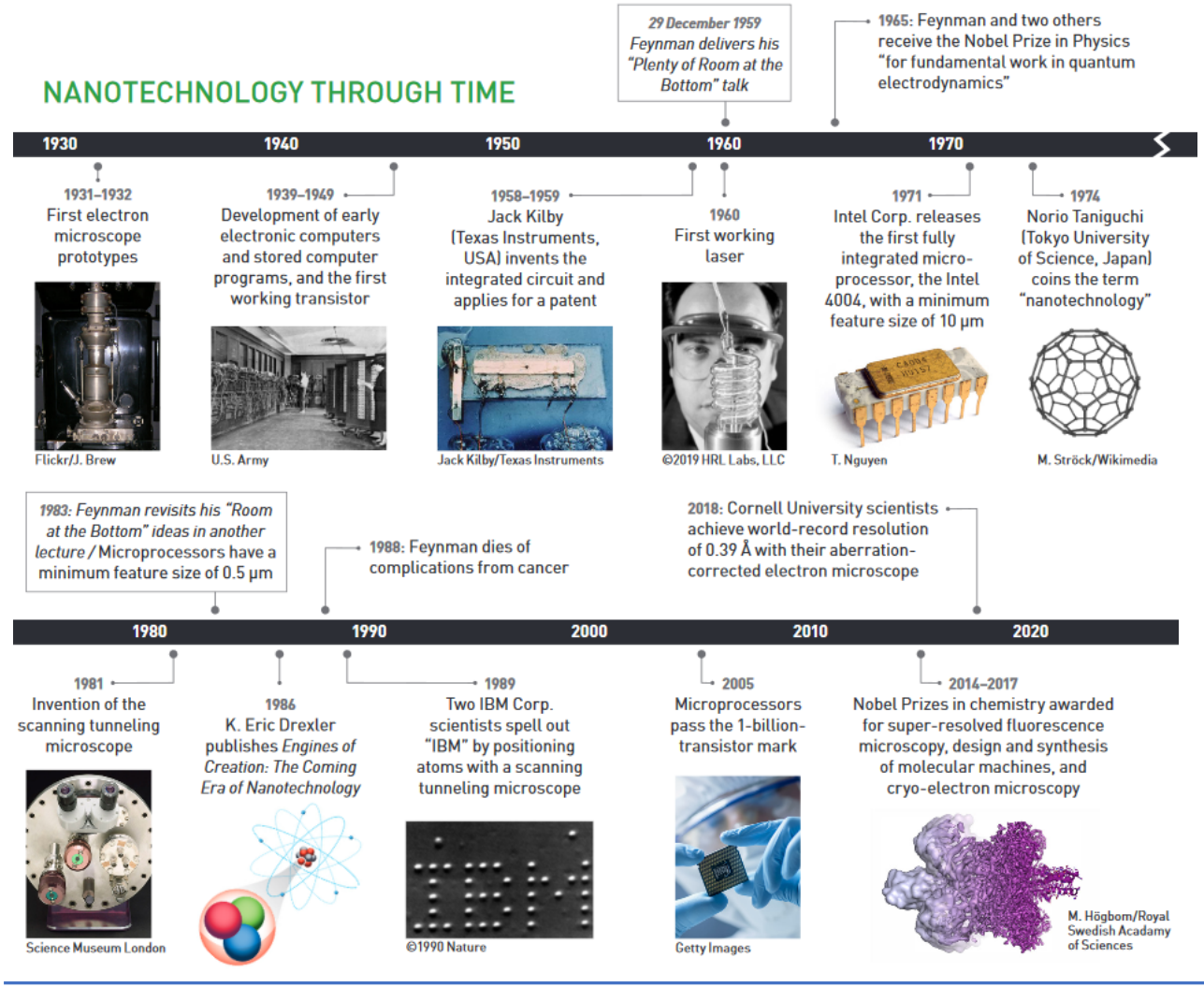
MORE TO EXPLORE

Engines of Creation: The Coming Era of Nanotechnology. K. E. Drexler. Fourth Estate, 1990.
Nanosystems: Molecular Machinery, Manufacturing, and Computation. K. E. Drexler. John Wiley & Sons, 1992.
The Foresight Institute and the Foresight Guidelines: **www.foresight.org**
Richard Feynman's lecture "There's Plenty of Room at the Bottom" can be found at **www.zyvex.com/nanotech/feynman.html**

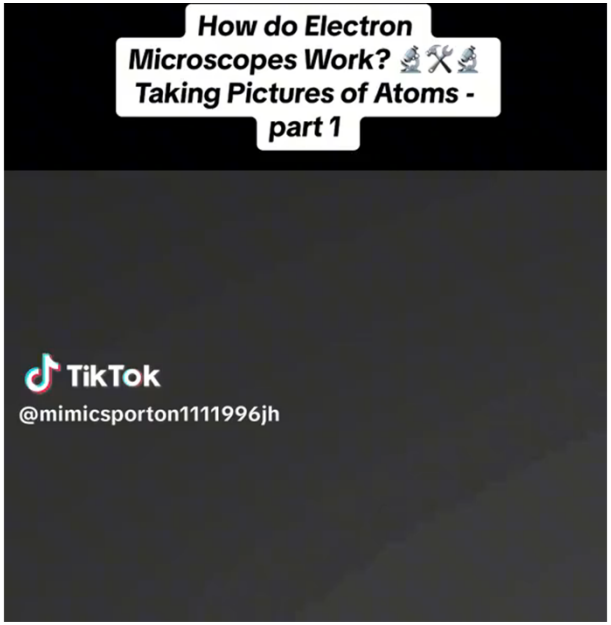
Theory vs. Practice

Nanotechnology through Time

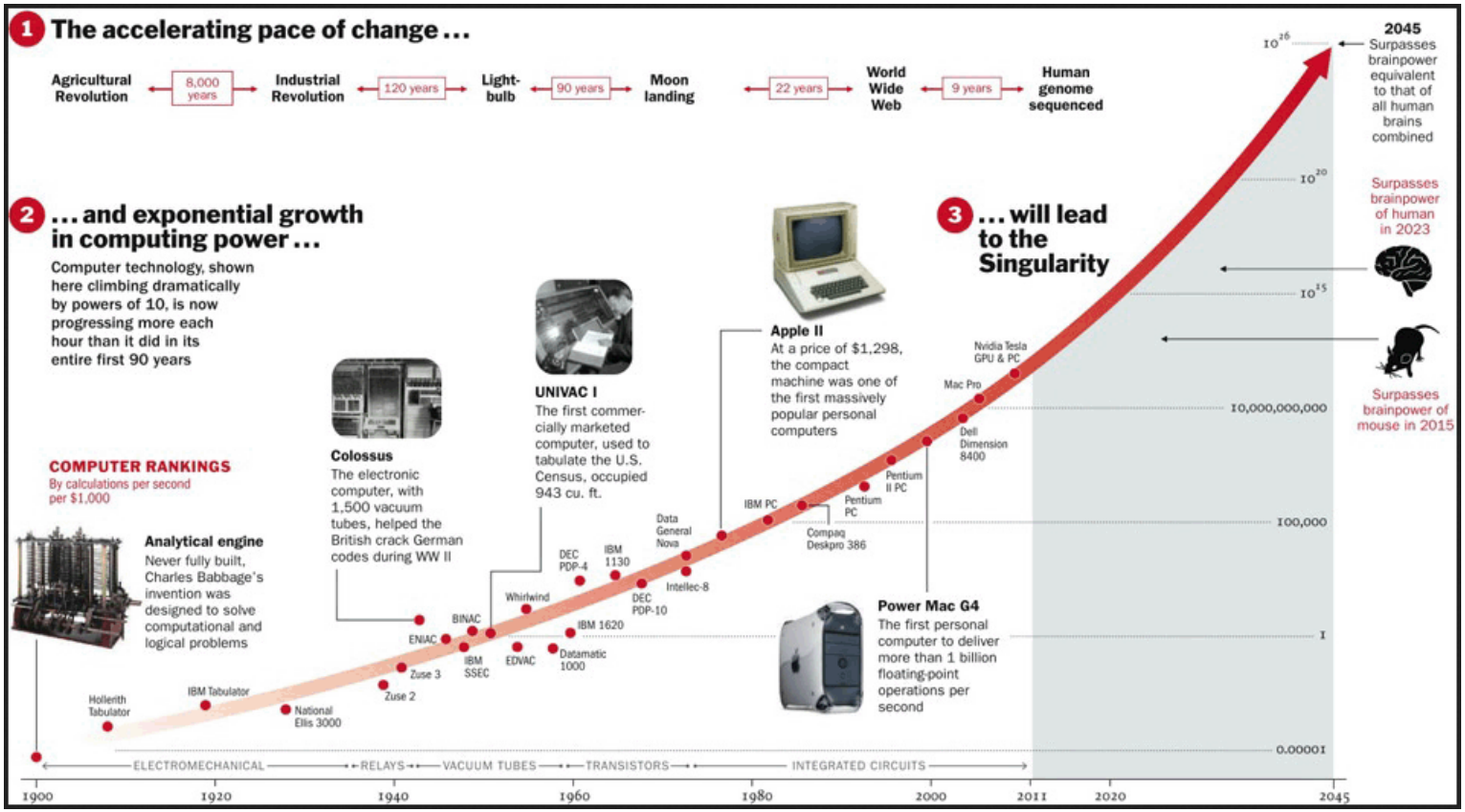
https://www.osa-opn.org/opn/media/Images/PDF/2019/07_0819/24-31_OPN_07_08_19.pdf?ext=.pdf



Patricia Daukantas: Still plenty of room at the bottom, Optics & Photonics News, July/August, 25-31, 2019.



The Accelerating Pace of Change & Growth



Whatever has been done can be outdone.
Gordon Moore

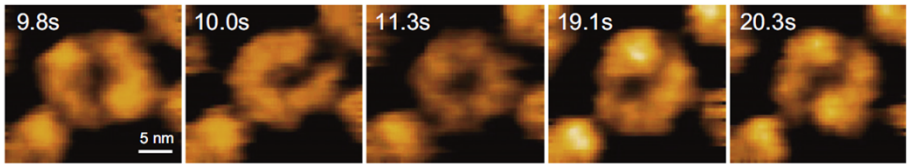
In 1965, Gordon Moore made a prediction that would set the pace for our modern digital revolution. From careful observation of an emerging trend, Moore extrapolated that computing would dramatically increase in power, and decrease in relative cost, at an exponential pace. The insight, known as Moore's Law (the number of transistors in a dense integrated circuit (IC) doubles about every two years), became the golden rule for the electronics industry, and a springboard for innovation. As a co-founder, Gordon paved the path for Intel to make the ever faster, smaller, more affordable transistors that drive our modern tools and toys. Even over 50 years later, the lasting impact and benefits are felt in many ways.

https://www.intel.com/content/www/us/en/silicon-innovations/moores-law-technology.html

https://ourworldindata.org/technological-progress

https://external-preview.redd.it/IHdaR-B3P5UvLf0n520AVuKE_qQhbBuIjB44JA7GZRM.png?auto=webp&s=9ce56fd8924ba75aee566c1dc53d417938831c0b

High-Speed Atomic Force Microscopy (AFM)



HS-AFM images showing massive conformational changes of DN-ClpB during the ATPase reaction. Different structures appeared, including a twisted-half-spiral ring (9.8 s, 20.3 s), a round ring (11.3 s), a spiral ring (10.0 s), and an intermediate between spiral and twisted-half spiral rings (19.1 s). Imaging rate, 10 fps.

HS-AFM for biomolecular imaging was established in 2008. The feed- back bandwidth (FB) of our system, which determines the system's speed performance, is about 110 kHz when it is used together with a short cantilever with resonant frequency of 1.2 MHz in water. HS-AFM has been used for not only imaging proteins but also live cell imaging [8,9], chemically oriented studies on DNA/RNA, mechanical measurements of cells and biopolymers, and others. However, in this mini review I focus on HS-AFM imaging of proteins (other than transmembrane proteins).

The advent of high-speed atomic force microscopy (HS-AFM) has changed the field of biology considerably. Unlike conventional AFM, which has a slow scanning rate, HS-AFM can scan a biological molecule (100 nm size) in 100 ms or less. The feedback bandwidth and short cantilever in HS-AFM allow high spatiotemporal resolution scanning without affecting the integrity of biomolecules. The greatest advantage of HS-AFM is the real-time imaging of biomolecules. In addition, sample preparation, for example, crystallization or fixation, is unnecessary for HS-AFM scanning to observe native or transformed conformations of target biomolecules. Therefore, this advantage overcomes the technical limitations that exist in the aforementioned techniques. By using HS-AFM, we have achieved several remarkable breakthroughs in biomolecular imaging, including structural characterization, visualization of conformational dynamics, and revealing the dynamic interactions of biomolecules and organelles. Recently, we have successfully conducted a pilot study regarding realtime visualization of the native structure and conformational dynamics of the hemagglutinin precursor (HA0) of H5N1 in the physiological buffer.

Ando 2019, High-speed atomic force microscopy
Lim 2020, High-speed AFM reveals molecular dynamics of human influenza a hemagglutinin and its interaction with exosomes
Lim 2023, Nanoscopic assessment of anti-SARS-CoV-2 spike neutralizing antibody using high-speed AFM

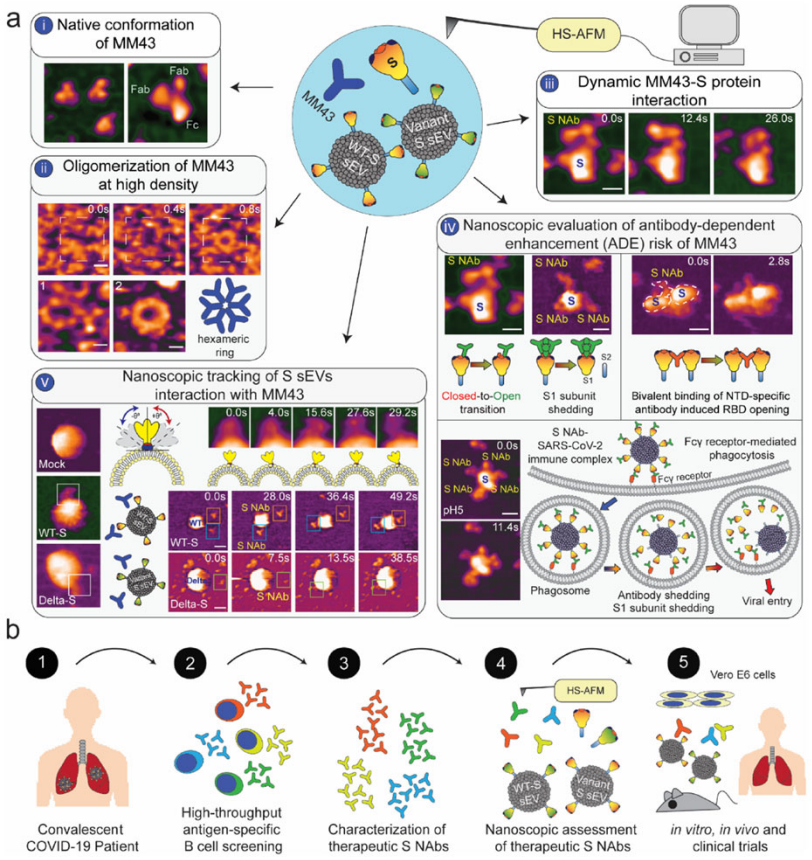


Figure 5. A nanoscopic perspective of S NAb and S protein interaction is essential for the assessment of S NAb therapeutic potential. (a) Nanoscopic observation of MM43 using HS-AFM reveals its native conformation (i) and intrinsic properties (ii), oligomerization for example. High spatiotemporal resolution enables HS-AFM to capture the dynamic MM43-S protein interaction and its binding pattern (iii). Direct visualization of S protein conformation in an immune complex at either neutral or acidic pH could provide important information related to antibody-dependent enhancement (ADE) such as RBD "Closed"-to-"Open" transition,[8,10] S1 subunit shedding,[8] and antibody shedding[34] (iv). S sEVs are safe alternative materials for nanoscopic tracking of the MM43 and SARS-CoV-2 interaction (v). Topology of S sEV and dynamic movement of S protein on sEV surface resemble SARS-CoV-2 virus. (b) Our results as summarized in (a) demonstrate that HS-AFM is feasible for nanoscopic assessment of potential therapeutic S NAbs. Patients recovered from COVID-19 have acquired immunity against SARS-CoV-2 (1). High-throughput screening of antigenic-specific B cells (2) is performed to isolate S NAbs for further evaluation of their therapeutic values (3). Nanoscopic assessment of these candidates using HS-AFM could provide essential information for better selection of S NAbs (4). Finally, the selected S NAbs will be used for downstream *in vitro* and *in vivo* experiments as well as clinical trials to validate their therapeutic efficacies (5).

Single-Molecule Optical Biosensing

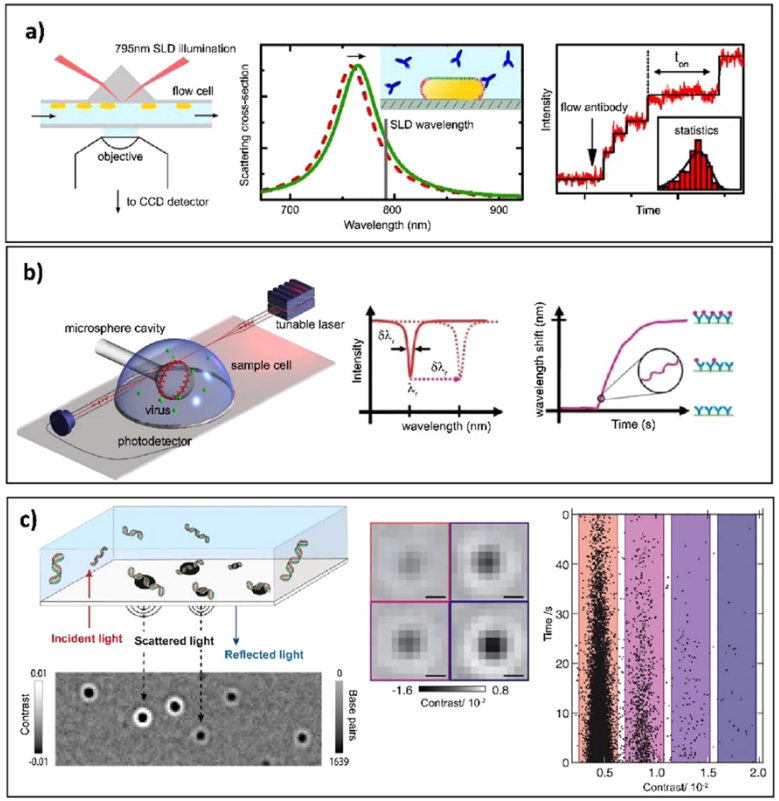


Figure 2. Examples of single-molecule direct assays. (a) Left: Schematic of the optical setup for monitoring stochastic protein interactions using plasmon sensing. Middle: Illustration of detection principle; gold nanorods are functionalized with receptors (depicted in red), whereas the sides are blocked with tetra ethylene glycol (depicted in green). The binding of individual antibodies results in a red shift of the plasmon resonance. Right: Time trace of the normalized scattered intensity of a single gold nanorod. Stepwise changes in the signal indicate stochastic binding of single antibodies. The distribution of waiting times between events is used to determine the antibody concentration. Reproduced with permission from 23. Copyright 2015 American Chemical Society. (b) Left: Experimental design of a Whispering Gallery Mode (WGM) based sensing platform showing detection of single virus particles. Middle: The resonance is identified at a specific wavelength from a dip in the transmission spectrum acquired with a tunable laser. A resonance shift associated with molecular binding; $\Delta\lambda_r$ is indicated by the dashed arrow. Bottom panel: Binding of analyte is identified from a shift $\Delta\lambda_r$ of resonance wavelength. Reproduced with permission from 28. Copyright 2008 Proceedings of the National Academy of Sciences. (c) Left: Concept of interferometric scattering mass spectrometry (iSCAMS) and working principle of label-free DNA detection employing iSCAMS. Individual DNA molecules diffusing in solution bind to an appropriately charged glass surface. Middle: Binding events cause changes to the reflectivity of the interface, visualized by a contrast-enhanced interferometric scattering microscope through the interference between scattered and reflected light. Right: Statistics of the image contrast provide a single-molecule readout of molecular mass. Adapted with permission from ref 33. Copyright 2020 Oxford University Press. Adapted with permission from 36. Copyright 2018 American Association for the Advancement of Science.

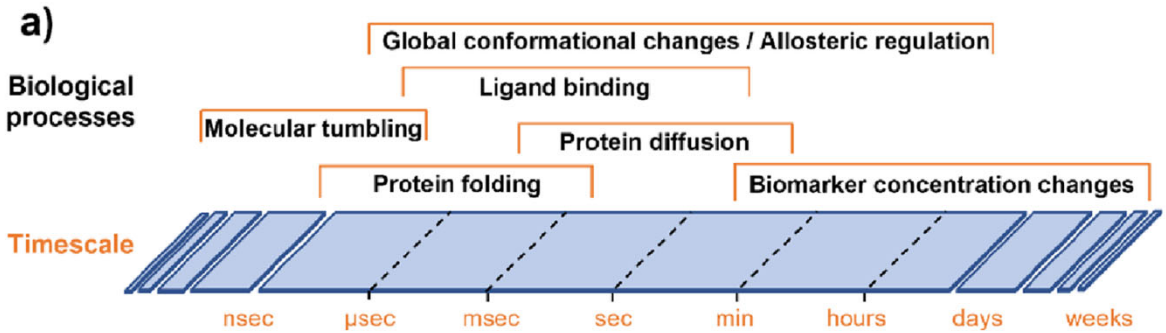


Figure 5. (a) Characteristic time scales for various biomolecular processes.

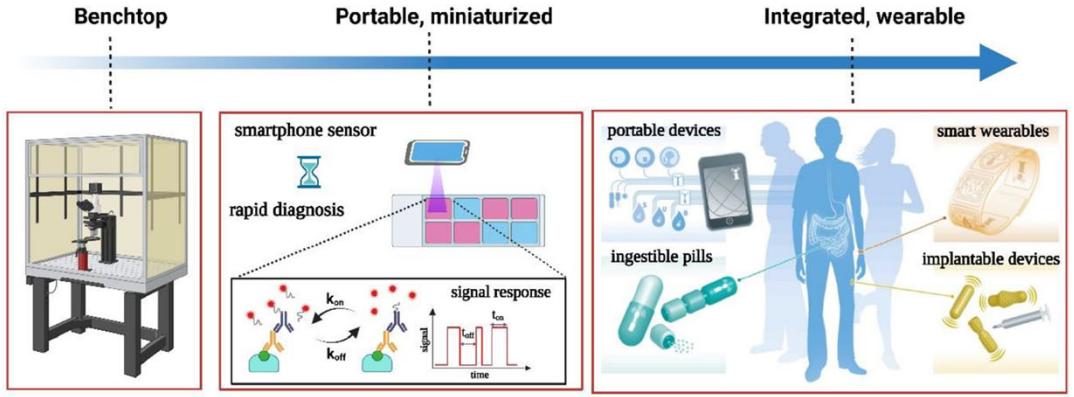


Figure 8. Timeline depicting the evolution of optical biosensors (left, benchtop detection ; middle, rapid, diagnostic field testing kits and portable smartphone based sensors; right, integrated smart biosensors for personalized health monitoring. Reprinted with permission from ref 102. Copyright 2016 Nature Publishing Group.

Dey 2023, Single-molecule optical biosensing-Recent advances and future challenges

Surface Plasmon Resonance (SPR) Biosensors

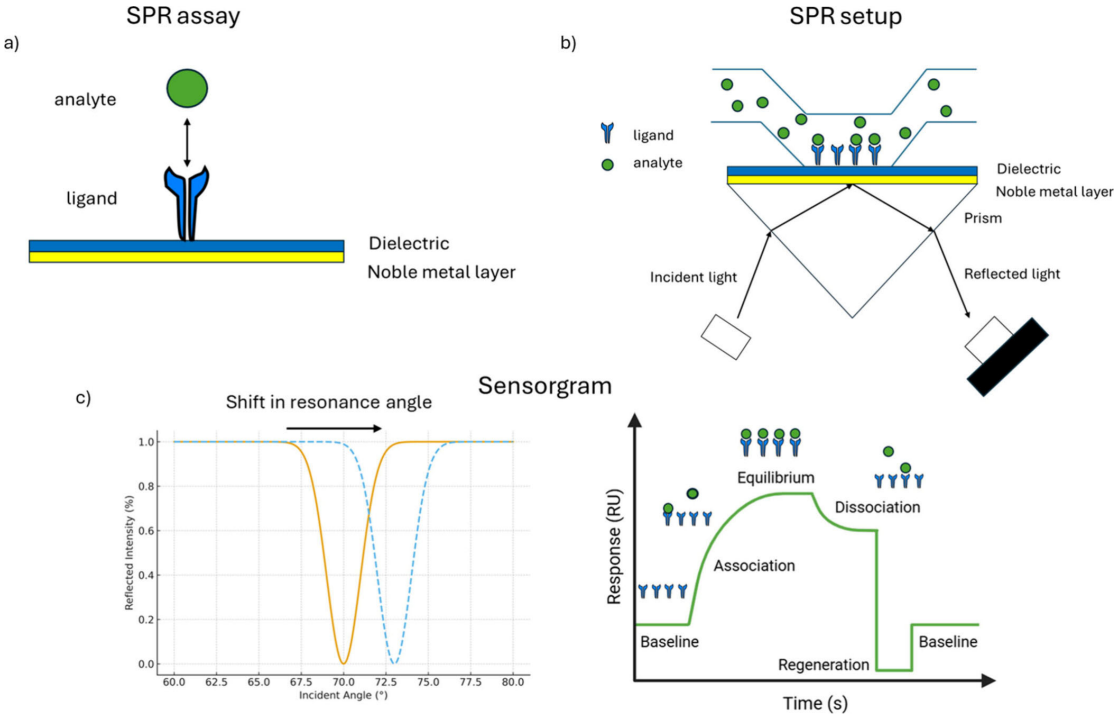


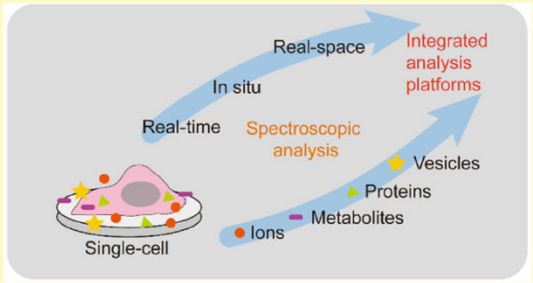
Figure 1. Schematic representation of the SPR setup. a) In a standard SPR assay, one molecule, termed the ligand, is immobilized on the sensor surface. The sensor is prefunctionalized with specific surface chemistries to facilitate ligand attachment, enabling optimal interaction with its binding partner, the analyte. b) A solution containing the analyte is then passed over the functionalized sensor surface, where ligand–analyte binding occurs through specific molecular recognition. c) The minimum in reflected light intensity shifts as the angle of incidence changes, corresponding to variations in the refractive index caused by mass accumulation on the sensor surface. This shift is recorded in a sensorgram that depicts the real-time association and dissociation kinetics of the analyte–ligand interaction as a function of time.

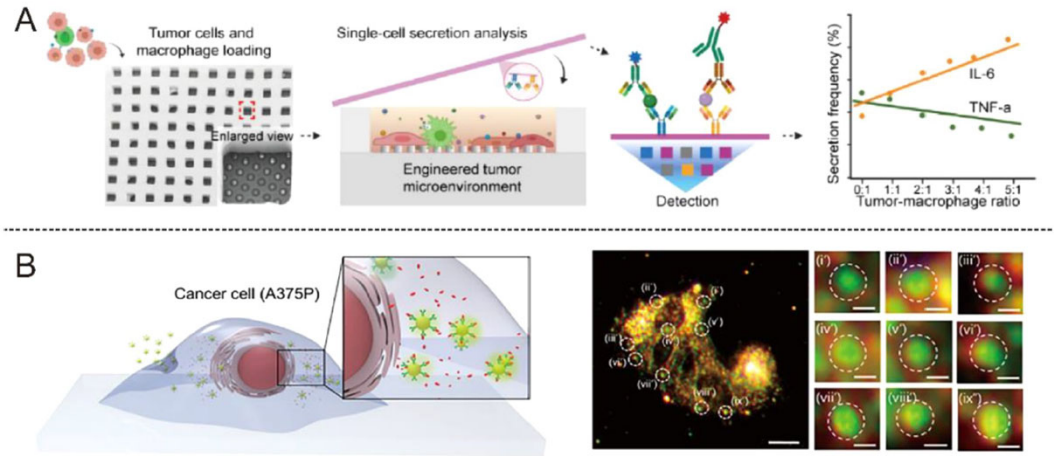
Since its introduction in the 1980s, SPR has emerged as one of the most powerful label-free analytical techniques for studying macromolecular interactions, offering exceptional specificity, sensitivity, and the ability to determine kinetic parameters. This optical sensing method detects subtle variations in the refractive index that occur near the surface of thin metallic films, typically composed of gold, silver, aluminum, or similar materials, when biomolecular interactions take place. The principle of SPR is rooted in the phenomenon of Attenuated Total Reflection (ATR). Under this condition, the free electrons in a noble metal resonate collectively with an incident electromagnetic field, producing a characteristic decrease in reflectivity at a specific incidence angle known as the resonance angle. This angle varies depending on the wavelength of the incident light and the optical properties of the surrounding medium. In an SPR experiment, biorecognition elements, such as antibodies, enzymes, peptides, or DNA strands, are immobilized onto the metallic surface of the sensor chip. When a solution containing the target analyte flows across the surface, binding interactions between the analyte and immobilized receptors induce a change in the local refractive index. This results in a shift of the resonance angle, which can be detected by monitoring the reflected light intensity as a function of the angle of incidence during the receptor–ligand binding process (Figure 1).

Chirco 2025, A tutorial review on surface plasmon resonance biosensors-Applications in biomedicine

Optical Sensing of Single Cell Secretion

ABSTRACT: Measuring cell secretion events is crucial to understand the fundamental cell biology that underlies cell−cell communication, migration, proliferation, and differentiation. Although strategies targeting cell populations have provided significant information about live cell secretion, they yield ensemble profiles that obscure intrinsic cell-to-cell variations. Innovation in single-cell analysis has made breakthroughs allowing accurate sensing of a wide variety of secretions and their release dynamics with high spatiotemporal resolution. This perspective focuses on the power of single-cell protocols to revolutionize cell-secretion analysis by allowing real-time and real-space measurements on single live cell resolution. We begin by discussing recent progress on single-cell bioanalytical techniques, specifically optical sensing strategies such as fluorescence-, surface plasmon resonance-, and surface-enhanced Raman scattering-based strategies, capable of in situ real-time monitoring of single-cell released ions, metabolites, proteins, and vesicles. Single-cell sensing platforms which allow for high-throughput high-resolution analysis with enough accuracy are highlighted. Furthermore, we discuss remaining challenges that should be addressed to get a more comprehensive understanding of secretion biology. Finally, future opportunities and potential breakthroughs in secretome analysis that will arise as a result of further development of single-cell sensing approaches are discussed.





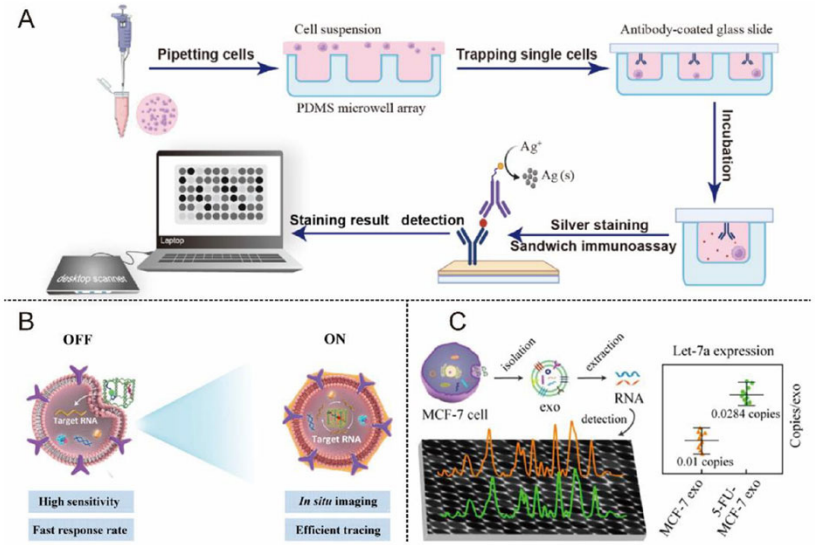


Figure 4. (A) Workflow illustration of trapping of single cells and using gold nanoparticle-enhanced silver staining to enable detection with the desktop scanner for the single-cell EV secretion assay. Reprinted with permission from ref 102. Copyright 2021 American Chemical Society. (B) In situ monitoring of exosomal miRNAs with double-accelerated DNA cascade amplifier nanocubes. Reprinted with permission from ref 106. Copyright 2022 American Chemical Society. (C) Schematic illustration of the SERS sensing exosomal microRNAs. Reprinted with permission from ref 111. Copyright 2021 American Chemical Society.

Figure 3. (A) Engineering and characterization of single-cell secretion analysis platform. A fluorescent immunoassay-based single cell analysis platform has been developed for investigating the differential modulation effect in cytokine secretions by the tumor microenvironment (B) Immunoplasmonic approach for transforming growth factor-β. The method used antibody-conjugated single gold nanoparticles as optical detection probes.

Zhong 2022, Optical Sensing Strategies for Probing Single-Cell Secretion

Extracellular vesicles (EVs)

Extracellular vesicles (EVs) are released by all living cells and are formed from bilayer lipid membranes. EVs consist of a variety of subtypes, including exosomes, microvesicles (MVs), ectosomes, oncosomes, and apoptotic bodies; EV is understood to be a generic term that refers to secreted vesicles. EVs are not just a simple lipid bilayer membrane structure; they are an important cargo carrier of various bioactive molecules, and these components of EVs can reflect the characteristics of the originating cells. EVs carry various cell-derived bioactive molecules, including proteins, nucleic acids, lipids, and metabolites, and circulate in extracellular spaces in biofluids such as blood, ascites, urine, and saliva. A major historical turning point in this research field was the discovery of novel EV functions as the mediators of cell-to-cell interactions where EVs can deliver functional molecules to recipient cells resulting in the alteration of their physiological and pathological functions.

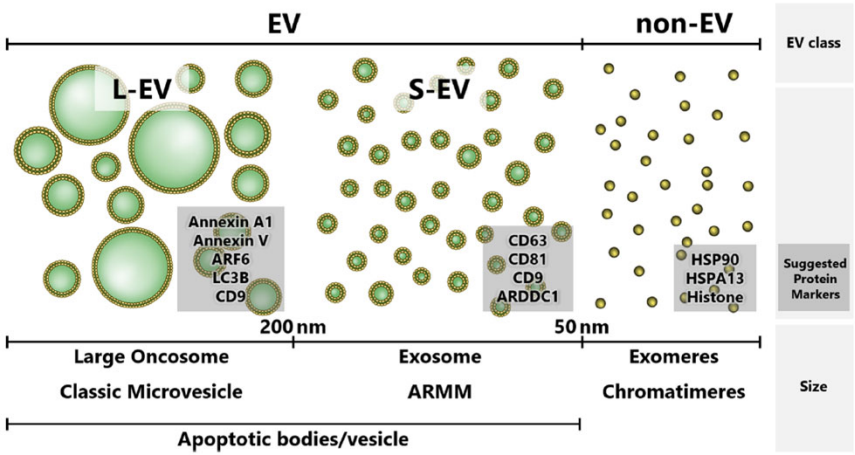


Fig. 2. Heterogeneity of extracellular vesicle. Diverse subtypes of EVs and non-EV populations. Currently, small-EVs (S-EV) are defined as being < 200 nm in diameter and large-EVs (L-EV) are over 200 nm.

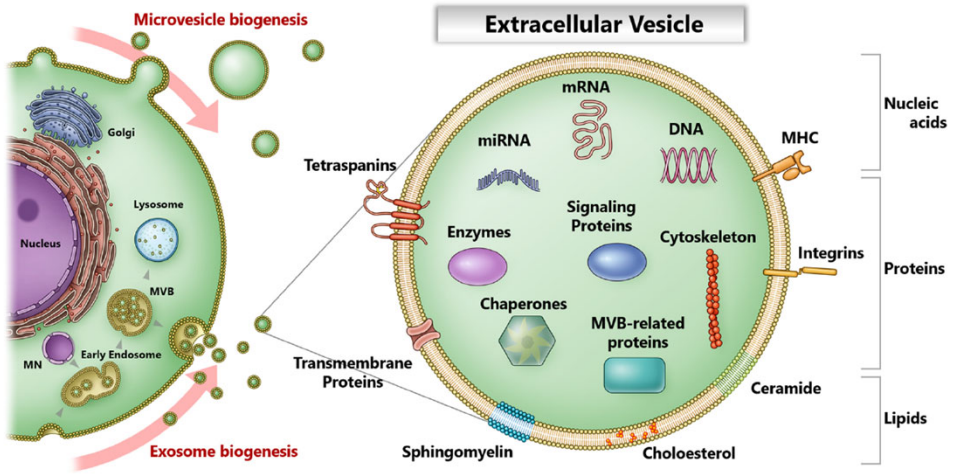
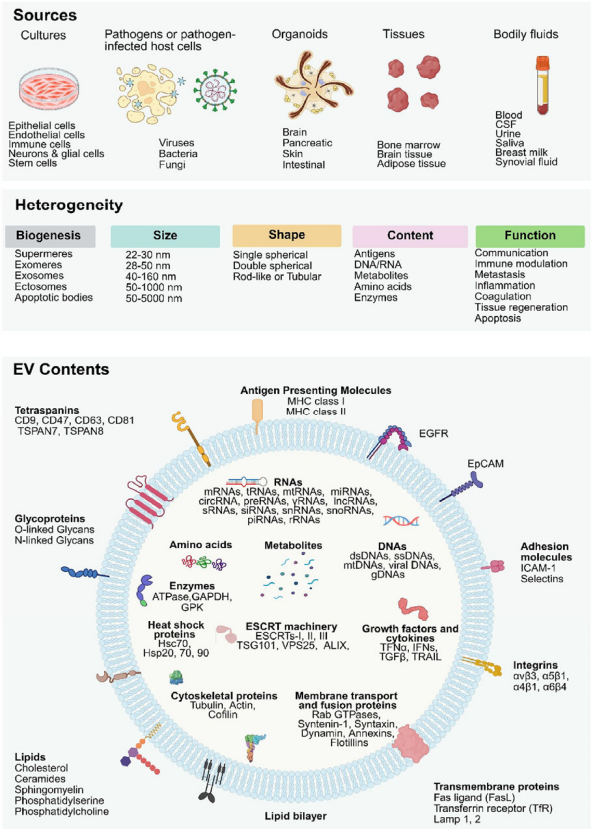


Fig. 1. Extracellular vesicle biogenesis and components. A. Microvesicle (MV) biogenesis comprises several steps, including plasma membrane reorganization, redistribution of phospholipids, outward repositioning of phosphatidylserine, disassembly of the cytoskeleton network, and actomyosin basal abscission. B. Exosome biogenesis starts inward of the plasma membrane to form early endosomes. Intraluminal vesicles (ILVs) are formed, and the endosomes mature to multivesicular bodies (MVBs). MVBs fuse with the plasma membrane to release ILVs into the extracellular space, where they are then referred to as exosomes. Alternatively, the MVBs can fuse with lysosomes, resulting in the degradation of ILVs. C. EVs can contain nucleic acids (DNA and/or RNA), membrane anchored-proteins, cytosolic proteins, and lipids; these contents can vary depending on the releasing cell types and their conditions.

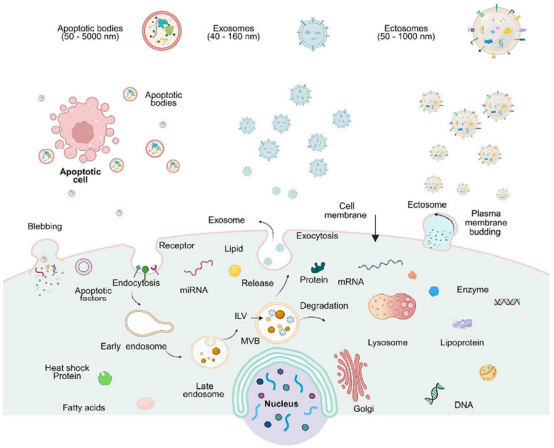
Yakoi 2021, Exosomes and extracellular vesicles- Rethinking the essential values in cancer biology

Extracellular Vesicles for Clinical Diagnostics



Heterogeneity of Extracellular Vesicles. EVs collected from different sources (cell cultures, pathogens or pathogen-infected host cells, organoids, tissues, or bodily fluids; top) exhibit significant heterogeneity in their biogenesis, size, shape, content, and function (middle), and their molecular content (bottom), reflecting the characteristics of the cells from which they originated. The contents of EVs are varied, encompassing both surface components (such as membrane proteins, glycoproteins, and lipids) and internal cargo (including RNAs, amino acids, metabolites, DNAs, enzymes, and proteins). These biomolecules contribute to EVs' roles in intercellular communication, immune modulation, metastasis, inflammation, coagulation, tissue regeneration, and apoptosis. The figure emphasizes the complexity of individual EVs and their ability to transport biologically active molecules, influencing various biological processes across different tissues and organs. Figure created with Biorender.com.

From Bulk Measurements to Single-Vesicle Analysis



Biogenesis and secretion of EVs. EVs can be broadly classified into three major subtypes: exosomes, ectosomes (also known as microvesicles), and apoptotic bodies. Exosomes originate from the endosomal pathway, in which early endosomes mature into late endosomes. Late endosomes develop intraluminal vesicles (ILVs), becoming multivesicular bodies (MVBs), which then follow either a degradative pathway or a secretory pathway. In the latter, MVBs fuse with the plasma membrane and release their ILVs as exosomes. Ectosomes are generated by budding from the cell membrane. Apoptotic bodies are released during apoptosis, when cells undergo programmed cell death and fragmentation. Figure created with Biorender.com.

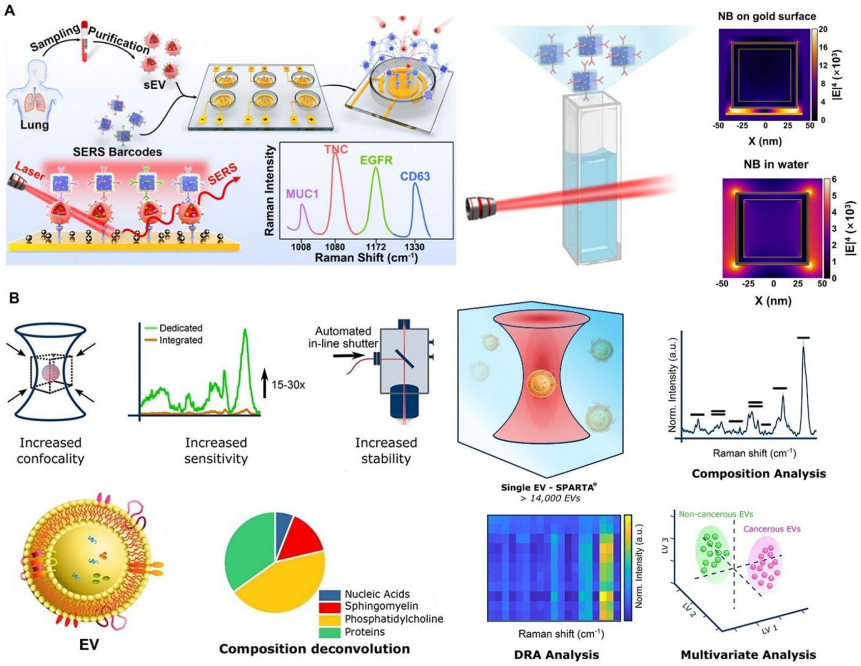


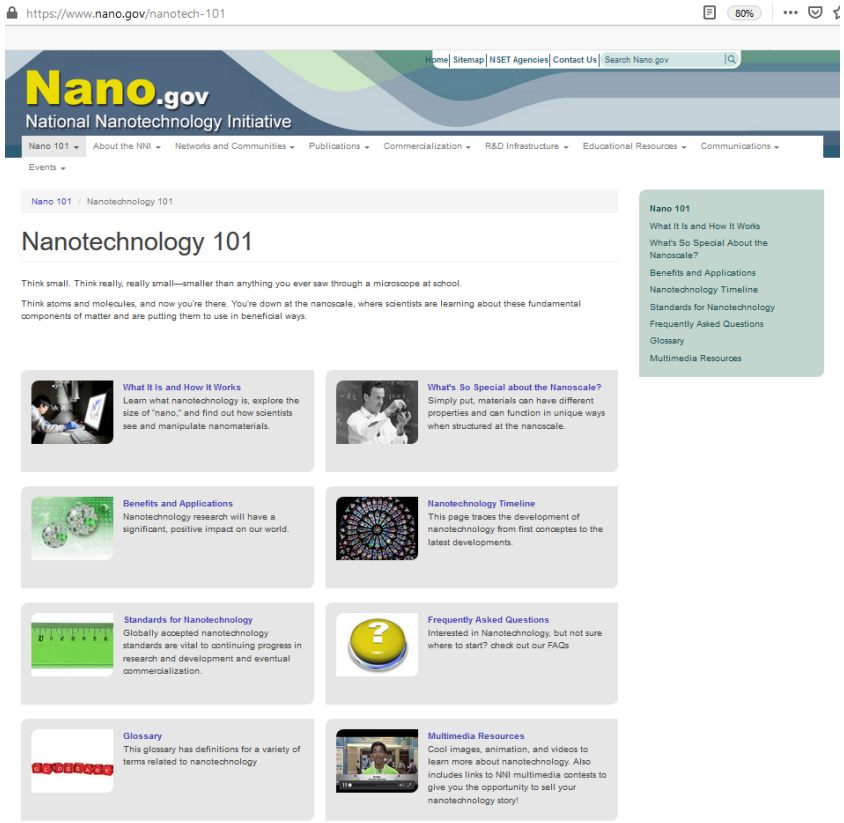
Figure 12. Advanced Raman techniques for BuEV to SiEV analysis. (A) Surface-enhanced Raman scattering (SERS) barcode-based gold microelectrode for BuEV detection. BuEVs purified from human blood are captured and identified using nanobox-based SERS barcodes under alternating current. Upon laser excitation, BuEVs bridge the gold microelectrode and the SERS barcode, forming a nanocavity that detects Raman signals corresponding to specific protein expression levels. Copyright 2024, American Chemical Society. Reprinted with permission from ref 611. (B) Single-particle automated Raman trapping analysis (SPARTA) platform. SPARTA uses surface plasmon resonance microscopy (SPRM) for automated SiEV analysis, generating detailed compositional Raman spectra for over 14,000 individual SiEVs.

Tran 2025, Extracellular vesicles for clinical diagnostics- From bulk measurements to single-vesicle analysis

Definitions of Nanotechnology

National Nanotechnology Initiative

2000. A very good place to learn the basic of nanotechnology is the National Nanotechnology Initiative (NNI) (https://www.nano.gov/).



Learning from Nature and mimicking natural materials!

Nanomedicine: What are the Fundamental Concepts?

Nanotechnology has been considered as an enabling technology. If nanotechnology is such an enabling technology, however, why have nanoformulations been used only for targeted delivery to tumors? Why has none of the nanotechnology been used to treat other important diseases? Even for tumor targeting, no nanoformulations have been effective. The main problem is that nanoparticles have been simply assumed to have a targeting property. It was just an assumption based on in vitro cell culture studies.

NIH Nanomedicine website (https://commonfund.nih.gov/nanomedicine/overview) does not provide any scientific reasons or evidence why nanomedicine will be better in treating various diseases. The National Nanotechnology Initiative does not provide any scientific evidence either.

Under the section of "Fundamental concepts in nanoscience and nanotechnology", the National Nanotechnology Initiative says, "Although modern nanoscience and nanotechnology are quite new, nanoscale materials were used for centuries. Alternate-sized gold and silver particles created colors in the stained glass windows of medieval churches hundreds of years ago. The artists back then just didn't know that the process they used to create these beautiful works of art actually led to changes in the composition of the materials they were working with".

It is well known that Michael Faraday was fascinated by the ruby color of colloidal gold (https://link.springer.com/content/pdf/10.1007/BF03215598.pdf). The size of colloidal gold particles ranges from a few nanometers to micrometers. Does this mean that the current nanotechnology is simply a rehash of the hundreds-year old technology? Then, what does nanotechnology really mean? The National Nanotechnology Initiative further describes, **"Nanotechnology is not simply working at ever smaller dimensions; rather, working at the nanoscale enables scientists to utilize the unique physical, chemical, mechanical, and optical properties of materials that naturally occur at that scale"** (https://www.nano.gov/nanotech-101/special). It continues, "Nanoscale materials have far larger surface areas than similar masses of larger-scale materials. As surface area per mass of a material increases, a greater amount of the material can come into contact with surrounding materials, thus affecting reactivity". The larger surface area of nanoscale materials has a few advantages in drug delivery, but it still does not explain how nanotechnology, or nanomedicine, brings new properties that traditional drug delivery systems do not have, and thus improved treatment.

Definitions of Nanotechnology and Nanomedicine

The term "nanotechnology" was defined as "science, engineering, and technology conducted at the nanoscale, which is **about 1 to 100 nanometers**" (https://www.nano.gov/nanotech-101/what/definition).

The term "**nanomedicine**" refers to "highly specific medical intervention at the molecular scale for curing disease or repairing damaged tissues, such as bone, muscle, or nerve". It is further explained that "**It is at this size scale - about 100 nanometers or less - that biological molecules and structures operate in living cells**" (https://commonfund.nih.gov/nanomedicine/overview).

These definitions sound magnificent and futuristic, but a closer examination to better understand them leaves us confused. First, if the matter we are dealing with is larger than 100 nm, is it not not considered nanotechnology? **What are the scientific criteria that set the boundary at 100 nm?** Would it make sense to limit the size to 200 nm, 300 nm, or larger?
Second, the description of nanomedicine is so generic that the term "nanomedicine" can be easily named by others, e.g., "molecular medicine". After all, if medical interventions are made at the molecular scale, isn't it better to call it "molecular medicine"? If engineering occurs at the molecular level, isn't it what we call chemistry, biochemistry, and molecular biology? The prefix "nano" has dominated science worldwide with no particular rationale, just as the prefix "i" has dominated the market since the successful introduction of the iPod. It is these arbitrary, generic definitions of nanotechnology and nanomedicine that set the stage for a decades-long stray from the otherwise more productive, useful, and practical path. Even today, many scientists, engineers, and clinicians who are not familiar with drug delivery think that nanotechnology or nanomedicine will solve their research problems regardless of the nature of those problems.

In drug delivery systems, there are few truly sub-100 nm systems. Drug delivery systems exist to deliver a drug, and a system smaller than 100 nm lacks sufficient reservoir space for effective drug delivery. Most polymer micelles, a major class of nanomedicines, are typically larger than 100 nm, especially after drug loading. Drug delivery systems are usually larger than 100 nm by necessity, but they are not considered nanosystems according to the definition provided by the National Nanotechnology Initiative [14]. What nonsense! More correctly, what nano-nonsense!

For the drug delivery field **the definition of nanomedicine described by the FDA** may be more relevant. According to the FDA Guidance for Industry regarding nanotechnology products, nanomaterials are defined as **materials that have at least one dimension in the size range of approximately 1 nm to 100 nm** (https://www.fda.gov/regulatory-information/search-fda-guidance-documents/considering-whether-fda-regulated-product-involves-application-nanotechnology). This follows the definition by the National Nanotechnology Initiative. The FDA, however, chose to include a much broader meaning of nanomaterials by asking "Whether a material or end product is engineered to exhibit properties or phenomena, including physical or chemical properties or biological effects, that are attributable to its dimension(s), even if these dimensions fall outside the nanoscale range, up to **one micrometer (1,000 nm)**". This definition is very forgiving regarding size limitations, and indeed, many products can fall within the definition of a nanotechnology product. This is why, when drug products in the U.S. were analyzed, more than 350 were found to contain nanomaterials (https://www.nature.com/articles/nnano.2017.67). This number, however, is misleading because it is based mostly on traditional formulations, such as liposomes, emulsions, and drug crystals, which were introduced several decades ago.

Look at the Data, Nothing Else

To understand why and how we ended up where we are now, we need an "independent" examination. The term "independent" here means an impartial approach between "confirmation bias" and "negativity bias". A mind with a confirmation bias seeks out data that support the preconceived idea, while a mind with a negativity bias does the same with the opposite goal.

Talking about the truth and criticizing something that most believe is difficult. Quite often, those who criticize the mainstream idea are labeled as pessimistic or politically motivated, as if science has to rely on the majority opinion or blind optimism. Accurate data interpretation has nothing to do with one's feeling. If the data point to a different direction from the expected, a new direction should be explored. This is of course assuming that the data are not fake. In his book "Only the Paranoid Survive", Andy Grove pointed out that an industry going through a strategic inflection point follows a sequence of denial, anger, bargaining, depression, and ultimately, acceptance (Only the Paranoid Survive). Going through an unknown future requires an accurate grasp of the reality, identification of the source of the problems, and preparation for the future. Only those with an independent mindset can go through such due diligent work, because they are not biased and not influenced by internal and external factors.

Park 2017, The drug delivery field at the inflection point- Time to fight its way out of the egg

Think, Think, and Think

Then, You Will Become Better than Most.

Do Not Fall into the Nanotechnology Trap

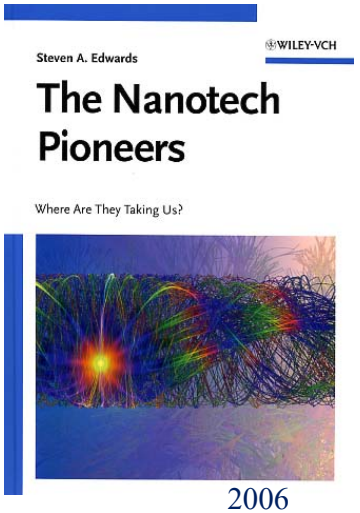
Table 2 The proliferation of "Nano" as a Prefix.

nanoage	nanocrystals	nanomagnetic	nanoscale
nanoarray	nanocube	nanomanipulator	nanoscience
nanoassembly	nanodevice	nanomaterial	nanoscope
nanobacteria	nanodivide	nanomedicine	nanosecond
nanobiologist	nanodomain	nanometer	nanoshell
nanobiomedicine	nanoelectromechanical	nanomicelle	nanostructured
nanobiotechnology	nanoelectronics	nanoparticle	nanostructures
nanobot	nanoencapsulation	nanoparticulate	nanoswarm
nanocapsule	nanofabrication	nanophase	nanosystems
nanocassette	nanofibers	nanoplatelates	nanotechnology
nanocatalyst	nanofilter	nanoporous	nanotool
nanocomponent	nanofluidics	nanopowder	nanotube
nanocomposite	nanolayer	nanoproduct	nanotweezers
nanoconnections	nanoliter	nanoreactor	nanowire
nanocosm	nanolithography	nanoreplicator	nanoworks
nanocrystalline	nanomachine	nanorobotics	nanoworld

Table 2 is hardly an exhaustive list, particularly if you start including the names of companies – NanoInk, NanoSphere, Nano-Opto, Nanoproprietary, Nanoset, Nanosys, etc. – or the names of products – Nano-fur, NanoReader, NanoSolve, Nanobac.

Scientists are supposed to have a clear, open mind just following the data, and should not fall into the populism and the fashion. At the height of the nanofashion, many started adding the prefix 'nano' to almost all words in the dictionary.

Does anybody know what 'nanoage' means? Or 'nanoworld'? Isn't nanocomponent called atom or molecule?



2006

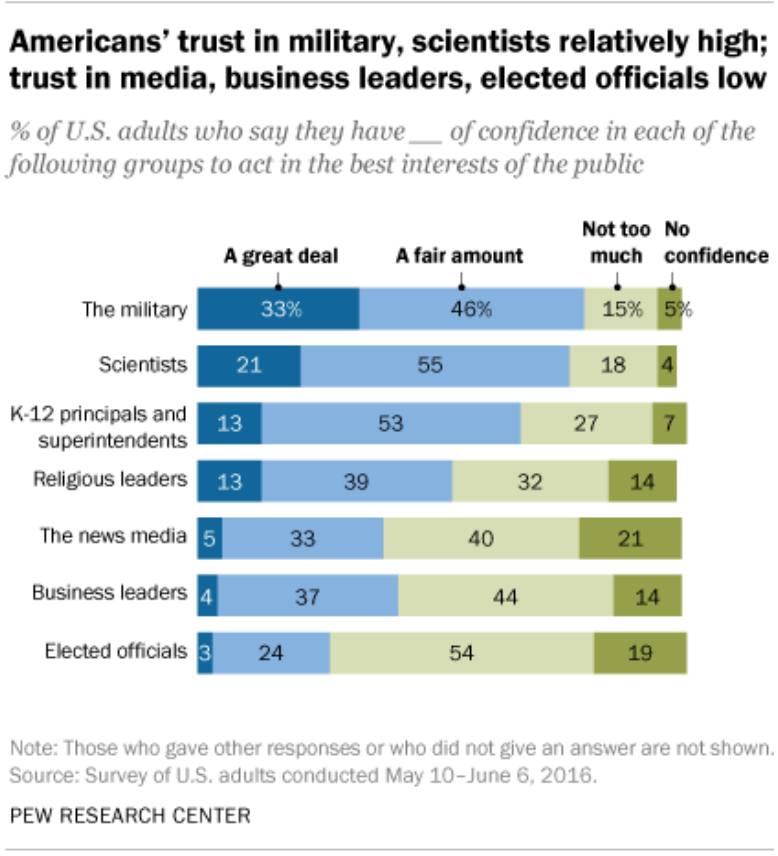
When iPod was first introduced and became hugely popular, almost all product names in Walmart began with 'i', such as iFlower, iChair, etc.

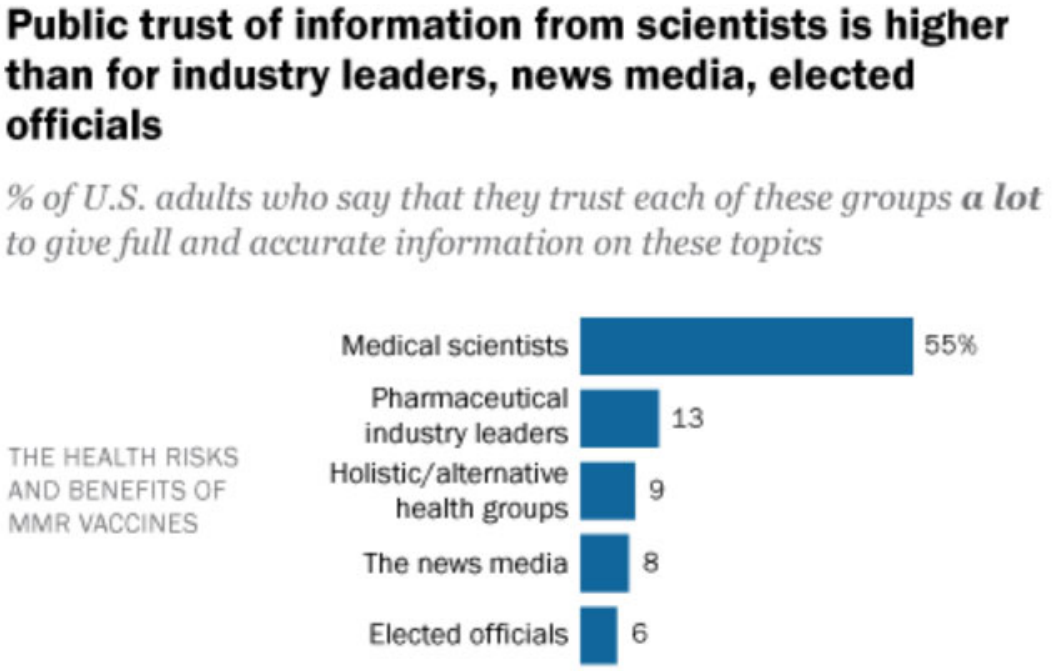
Simply changing the name to more fancy names, like including "i' or 'nano', does make things better.

How about "*i*NanoBoilermaker"?

Trust Scientists? Earn the Trust

America and many countries around the world have systematically downplayed the importance of science for the special interest groups who increase their political power through dismissing science and promoting their agendas. Even then, the trust in scientists is as high as that in the military. It is not surprising that the trusts in business leaders and politicians are very low. Scientists need to work hard to tell the truth and improve the public's trust to close to 100%. Telling the truth based on accurate data is the best weapon scientists have.





https://www.pewresearch.org/science/2017/12/08/mixed-messages-about-public-trust-in-science/

Why We Must Rebuild Trust in Science

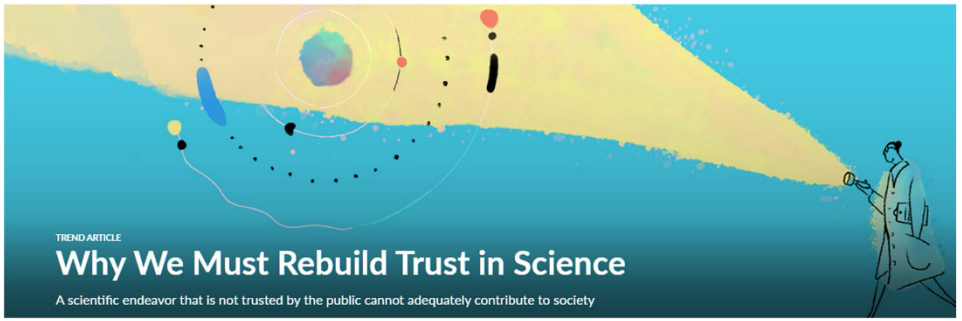
A scientific endeavor that is not trusted by the public cannot adequately contribute to society (February 9, 2021, BySudip Parikh)

Despite failures in our public health response to the pandemic, the biomedical research enterprise has never worked more quickly than during its quest to understand and address COVID-19. While basic researchers work around-the-clock to answer fundamental questions about the coronavirus' structure, transmission, and impacts, clinicians and physician scientists are testing therapeutics and vaccines.

One element is absolutely critical to the success of our mission to improve the human condition: trust. It's a foundational element of any relationship, but for the mutual benefit of the scientific enterprise and the people who support it, trust is essential. Simply put, a scientific endeavor that is not trusted by the public cannot adequately contribute to society and will be diminished as a result. The COVID-19 pandemic presents us with just such an example. Late last year two of the vaccine candidates in clinical trials demonstrated safety and effectiveness in preventing infection of the virus that causes COVID-19. Although this was a remarkable accomplishment on its own, manufacturing and delivering these vaccines to the world's population will be an enormous challenge. To further complicate this situation, a public that is generally trusting of scientists and health professionals is receiving vastly different information, guidance, and recommendations based on its news consumption, political leaders, and geography. A September 2020 Pew Research Center survey found that Americans were evenly divided as to whether they would get a vaccine to prevent COVID-19 if one were available now.

Importantly, it is not enough to say the public should trust scientists because we know better or because we know more. Trust must be earned. Unfortunately, science and scientists have not consistently earned and nurtured this trust. In some respects, this is the result of the advancement of the scientific enterprise. Science in the 21st century is much more removed from daily life because of the necessity of speaking with precision by using technical terms and jargon.

https://www.pewtrusts.org/en/trend/archive/winter-2021/why-we-must-rebuild-trust-in-science



The COVID-19 pandemic will not be the last time that science will be essential to society's triumph over existential threats.

The practice of science is messy. Hypotheses are put forward and tested. Understanding evolves and comes in fits and starts. The trial and error in research methodology and the repetitive testing in laboratories are often hidden behind the end products of scientific research - a new treatment, a new piece of technology, a new or revised piece of public health guidance - without the public seeing the puts and takes that are required along the way. When that process is then seen in real time, as we're all experiencing during the COVID-19 pandemic, **the public has little context for updates in public health guidance, such as the change to recommending wearing face masks to limit and prevent infection**.

More disturbingly, science has sometimes lost the trust of the public through researchers' own painful missteps and blatant violations of that trust. Science, engineering, and medicine are not immune to the discrimination, subjugation, and silencing of marginalized people and voices. We have too often been unwitting perpetuators of the status quo, and the reasons are deeply ingrained in the systems that govern our society.

At the same time, increased political polarization and an outspoken faction of Americans who distrust experts, including scientists who develop evidence-based findings that may challenge closely held opinions, have also widened the gap between Americans' trust in science and scientists. **Science is not just for the few. It is for everyone and can be used by anyone.**

Why are Americans so slow to get booster shots?

The New York Times (February 7, 2022, By David Leonhardt)

The enemy of the good

The United States has a vaccination problem. And it is not just about the relatively large share of Americans who have refused to get a shot. The U.S. also trails many other countries in the share of vaccinated people who have received a booster shot.

In Canada, Australia and much of Europe, the recent administering of Covid-19 booster shots has been rapid. In the U.S., it has been much slower. The booster shortfall is one reason the U.S. has suffered more deaths over the past two months than many other countries

Two explanations

What explains the American booster shortfall? I think there are two main answers, both related to problems with the American health system.

First, medical care in the U.S. is notoriously fragmented. There is neither a centralized record system, as in Taiwan, nor a universal insurance system, as in Canada and Scandinavia, to remind people to get another shot. Many Americans also do not have a regular contact point for their health care.

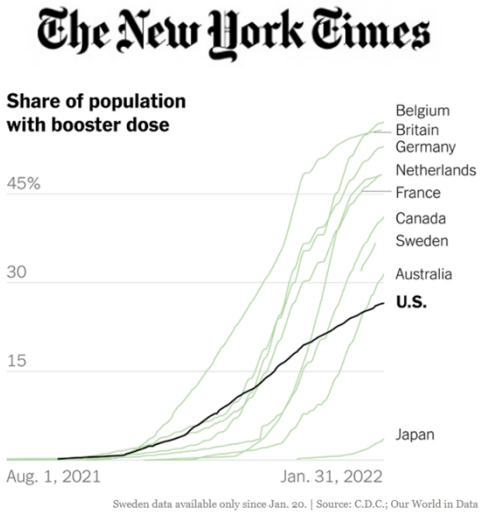
The second problem is one that has also bedeviled other aspects of U.S. Covid response: Government health officials, as well as some experts, struggle to communicate effectively with the hundreds of millions of us who are not experts. **They speak in the language of academia, without recognizing how it confuses people**. **Rather than clearly explaining the big picture, they emphasize small amounts of uncertainty that are important to scientific research but can be counterproductive during a global emergency**. They are cautious to the point of hampering public health. As an analogy, imagine if a group of engineers surrounded firefighters outside a burning building and started questioning whether they were using the most powerful hoses on the market. The questions might be reasonable in another setting — and pointless if not damaging during a blaze. A version of this happened early in the pandemic, when experts, including the C.D.C. and the World Health Organization, discouraged widespread mask wearing. They based that stance partly on the absence of research specifically showing that masks reduced the spread of Covid. But obviously there had not been much research on a brand-new virus. Multiple sources of scientific information did suggest that masks would probably reduce Covid's spread, much as they reduced the spread of other viruses. Health officials cast aside this evidence.

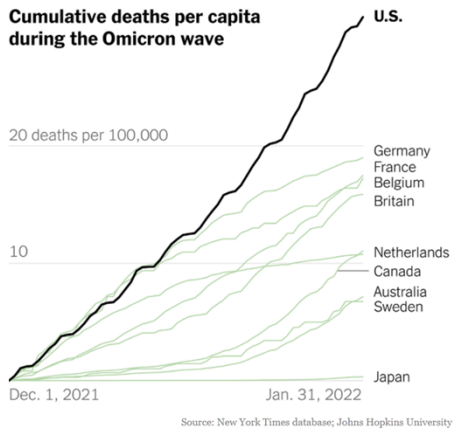
Tests, vaccines, boosters

Similar problems have occurred since then, especially in the U.S.: (1) slow to give formal approval to the Covid vaccines, (2) slow to approve rapid tests, and (3) slow to tell people who had received the Johnson & Johnson vaccine to get a follow-up shot.

In the U.S., some officials and experts continue to raise questions about whether the evidence is strong enough to encourage boosters for younger adults. Two top F.D.A. officials quit partly over the Biden administration's recommendation of universal boosters. The skeptics say they want to wait for more evidence.

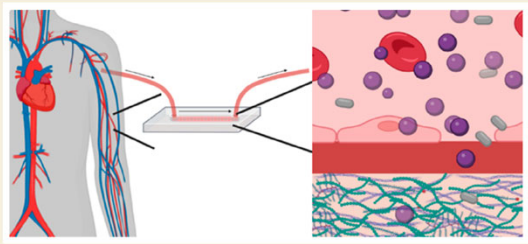
I don't fully understand why statistical precision seems to be a particularly American obsession.



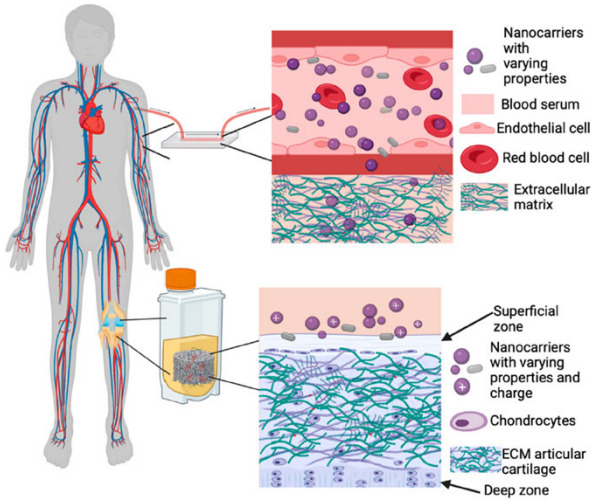


Precision Healthcare through Nanomedicine

ABSTRACT: The ability to customize medical choices according to an individual's genetic makeup and biomarker patterns marks a significant advancement toward overall improved healthcare for both individuals and society at large. By transitioning from the conventional one-size-fits-all approach to tailored treatments that can account for predispositions of different patient populations, nanomedicines can be customized to target the specific molecular underpinnings of a patient's disease, thus mitigating the risk of collateral damage. However, for these systems to reach their full potential, our understanding of how nano-based therapeutics behave within the intricate human body is necessary. Effective drug administration to the targeted organ or pathological niche is dictated by properties such as nanocarrier (NC) size, shape, and targeting abilities, where understanding how NCs change their properties when they encounter biomolecules and phenomena such as shear stress in flow remains a major challenge. This Review specifically focuses on vessel-on-a-chip technology that can provide increased understanding of NC behavior in blood and summarizes the specialized environment of the joint to showcase advanced tissue models as approaches to address translational challenges. Compared to conventional cell studies or animal models, these advanced models can integrate patient material for full customization. Combining such models with nanomedicine can contribute to making personalized medicine achievable.



KEYWORDS: *Personalized Medicine, Precision Medicine, Nanomedicine, Drug Delivery, Model Systems, Vessel-on-a-Chip, Bioreactors, Joint Drug Delivery, Cartilage Transport*



Details?
How?
Simple explanation?

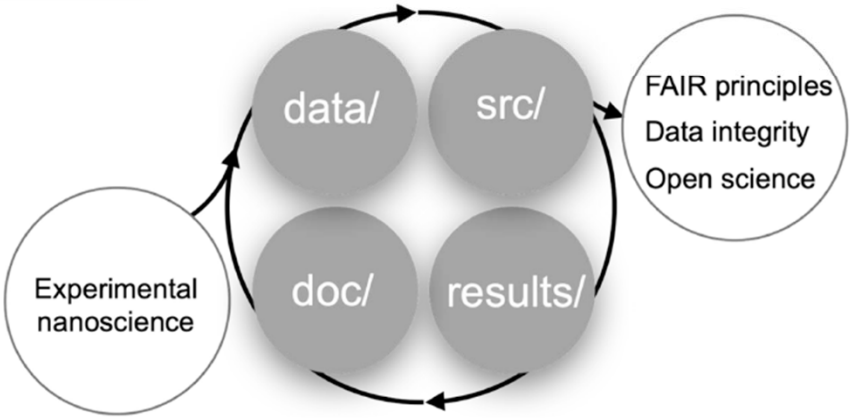
Figure 1. Models of NC delivery to target organs and cells.

Svensson 2024, Achieving precision healthcare through nanomedicine and enhanced model systems

Nanoscience Needs Standardized Protocols

ABSTRACT: Nanoscience is a relatively young research field that has been built on the shoulders of consolidated areas ranging from solid-state physics to biology. Its interdisciplinary nature imposes the flow of heterogeneous data from various domains of predefined conventions that ultimately prevents workflow standardization, raising the possibility of further fragmentation and compromising the reproducibility. This is the time to establish good practices for experimental nanoscientists. This work proposes a set of simple rules that can facilitate data management and improve their reusability. Implementing the proposed protocol can have high initial cognitive costs but can also save energy and time in the long term. By adopting these practices, researchers can ensure the reusability of their data early in a project and accelerate the writing process.

The knowledge sector, particularly within academia, needs standardized work protocols to align with FAIR principles (findability, accessibility, interoperability, and reusability) (https://www.go-fair.org/fair-principles/) imposed by funding entities. But what kind of standardized protocols can we design and implement? Notably, software developers possess valuable insights in this regard.



Grzelczak 2025, Why nanoscience needs standardized protocols - and how to get there

Self-Assembly

Life began with self-assembly.

Natural (Bottom-up) and Synthetic Systems (Top-down)

Natural Systems

Efficacy and Simplicity
at the Molecular Level
(Bottom-up)

↓

Survival

↓

Biological Needs

In nature, bottom-up approaches are achieved through self-assembly of molecules. No matter how small or large a structure is, it must have a building block. If building blocks are assembled by themselves, it can be called self-assembly. But if the building blocks have to be assembled by external forces, it cannot be called self-assembly.

Synthetic Systems

Efficiency and Selectivity
at the Macro Level
(**Top-down**)

↓

Miniaturization

↓

Clinical Efficacy

Bottoms-up Approach: Building brick by brick the Great Wall (>20,000 km long) or the Great Pyramid (230 m x 230 m x 147 m).

Self-Assembly

10.3 PRINCIPLES OF SELF-ASSEMBLY

Self-assembly is **the reversible and cooperative assembly of predefined parts into an ordered structure**, which assembles with no external influences after the initial trigger. Currently, self-assembly has been broken down into two categories: static and dynamic. **Static self-assembly** refers to systems at equilibrium which do not dissipate energy. The formation of the nanostructure may require energy, but the structure is stable once it has been formed. **Dynamic self-assembly** refers to the formation or patterning of structures when the system does, in fact, dissipate energy.

Self-assembly in materials relies on the fact that **the fluctuations in the orientation and position** of the molecules or particles due to random movements have energies in the order of **thermal energy**. Thermal energy has a significant impact on materials on the nanoscale as non-covalent bonds are often broken and reformed in a new manner. Due to these non-covalent interactions between molecules, structure changes can be obtained by changes in the conditions provided for the molecules. For instance, temperature and pH changes help to initiate the transition of a structure to another.

Dahman 2017, Self-assembling nanostructures, Nanotechnology and Functional Materials for Engineers, pp. 207-228.

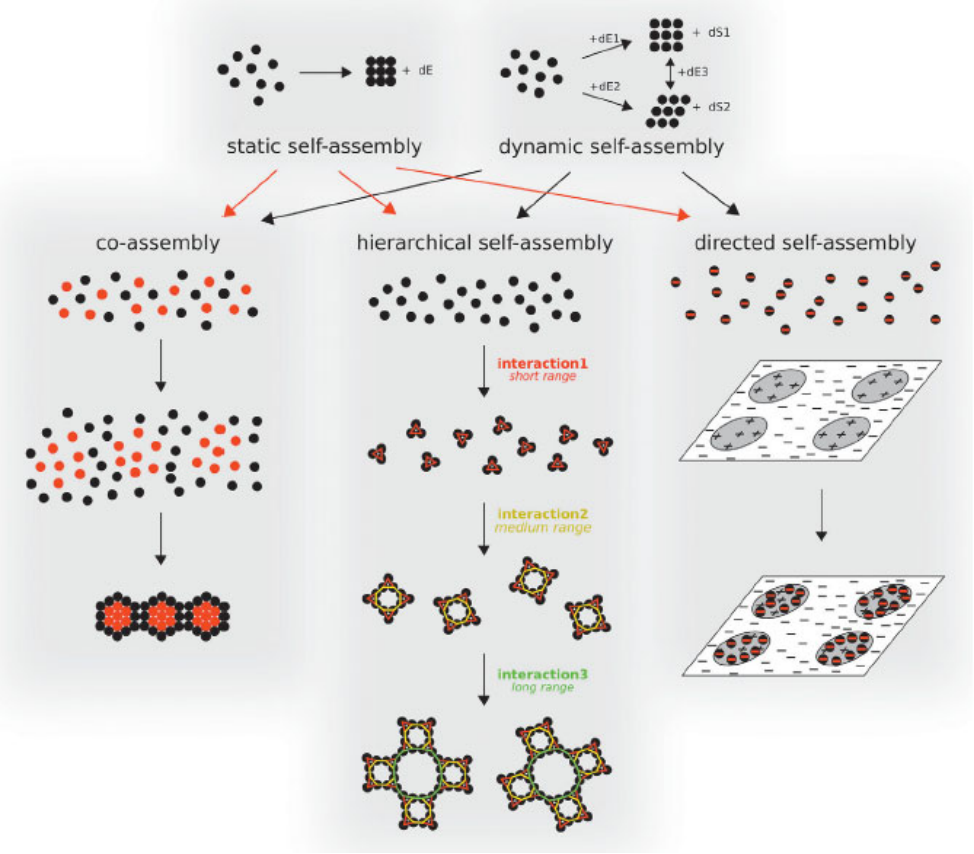


Fig. 1. Graphical rendition of static and dynamic self-assembly and how they relate to co-assembly, hierarchical assembly and directed assembly.

Ozin 2020, Nanofabrication by self-assembly, Materials Today, 12(5):12-23, 2009.

Self-Assembly

Self-assembly is the process by which individual components arrange themselves into an ordered structure. While sufficiently broad to include crystallization of atomic solids, the term is generally reserved for **building blocks** not linked together via covalent bonds but ordered through weak forces (e.g., van der Waals, hydrogen bonding) or hard-particle (e.g., excluded volume) interactions. Following this classification, examples of self-assembled structures include DNA, proteins, lipid vesicles, block copolymer melts, opals, and nanocrystal superlattices. Self-assembly can also make use of external forces such as electric/magnetic fields or fluid flows, but the term does not extend to serial manipulation of building blocks (e.g., dragging individual particles into position).

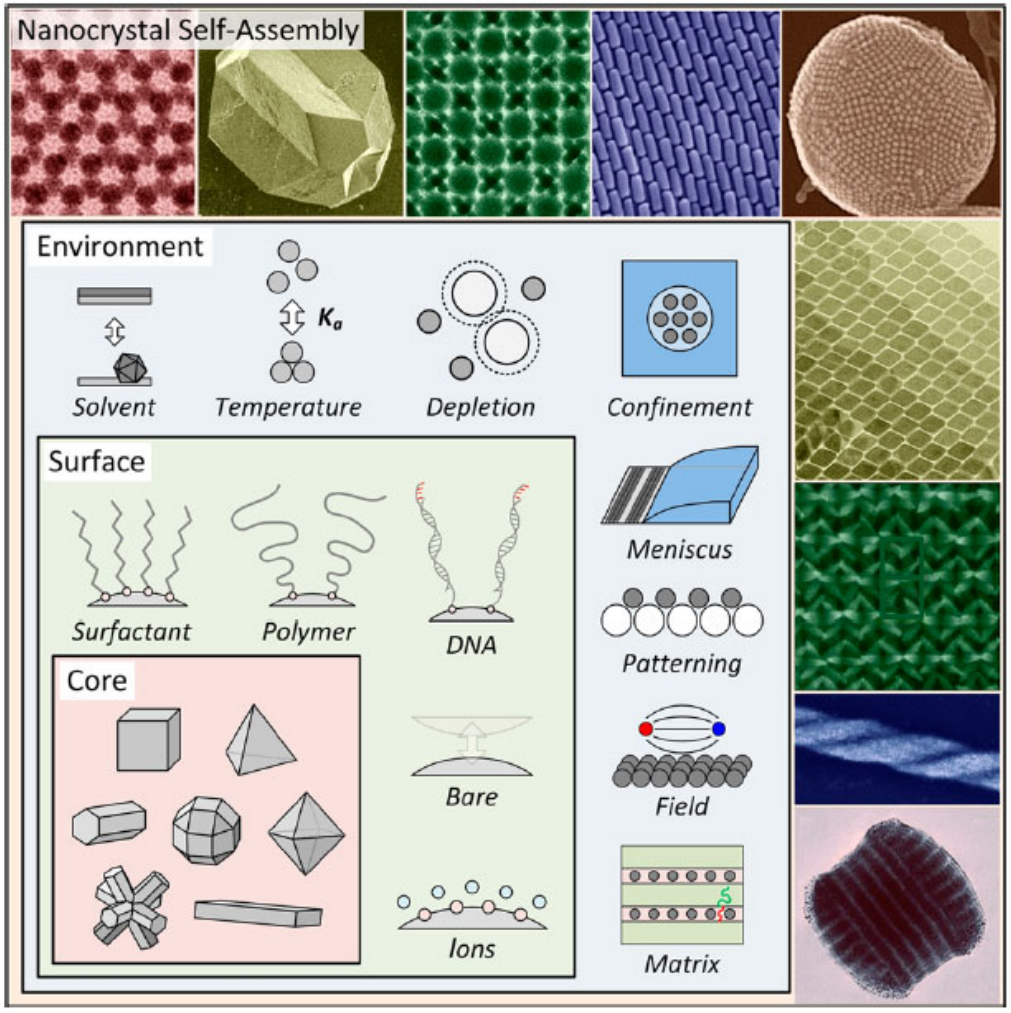


Figure 2. Nanocrystal self-assembly is a process that involves control over several length scales. The nanocrystal core (typically 1−100 nm across) is surrounded by a layer of surface ligands (with length typically between 1 nm and up to tens of nanometers). The assembly environment can be used to control interparticle interactions and impart geometric constraints with characteristic length scale exceeding nanocrystal size. The resulting superstructures are typically produced with domain size falling between 1 μm and several millimeters. Details about the nanocrystal composition, assembly conditions, and references for the systems shown in this figure are given in Table 1.

Boles 2016, Self-assembly of colloidal nanocrystals, Chem. Rev. 2016, 116, 11220−11289

Building Blocks

TABLE 1. Synthetic and Biological Building Blocks Used in Supramolecular Self-Assembly for Obtaining Diverse Complex Structures and Their Potential Biomedical Applications.

Building-Blocks			Supramolecular Assemblies	Applications
Synthetic	Polymers	Linear (e.g. block-co-polymers) AB ABA ABC	Micelles Vesicles Tubes	Nanoreactors; artificial organelles; nanocarriers drug delivery[21, 22]
		Branched (e.g. dendrimers) Dendrons	Nanoparticles Nanofibers	Nanocarriers for drug and gene delivery[23–25]
	Surfactants	Anionic Cationic Neutral	Micelles Vesicles	Drug and gene delivery systems; antimicrobial and antifungal activity[26, 27]
	Others	Graphene Porphyrin Rotaxane	Nanotubes Toroids Carbon nanotubes	Nanomedicine; drug delivery; hydrogels[8, 28, 29]
Biological	Viruses	CPMV λ phage hHPBV	Aligned phage film Fibrils Particles	Biomaterials; cell culture substrates[30–33]
	Nucleic acids	RNA DNA	DNA origami	Therapeutics (vehicles for drug delivery); diagnostics (biosensing)[11, 34, 35]
	Lipids	Fatty acid Phospholipid Cholesterol	Lipid bilayer Vesicles Films	Nanoreactors; artificial organelles; controled drug delivery[19, 36–37]
	Saccharides Amylose (helical)	Cyclodextrin (cyclic)	Double helix Nanotube Spherical micelle	Drug delivery; biosensors[38,39]
	Peptides	VSYK EACQ	Random coil β-sheet α-helix Helix protein	Hydrogel biomaterials; drug delivery; tissue engineering; 3D cell culture[40–48]

Mendes 2013, Self-assembly in nature,

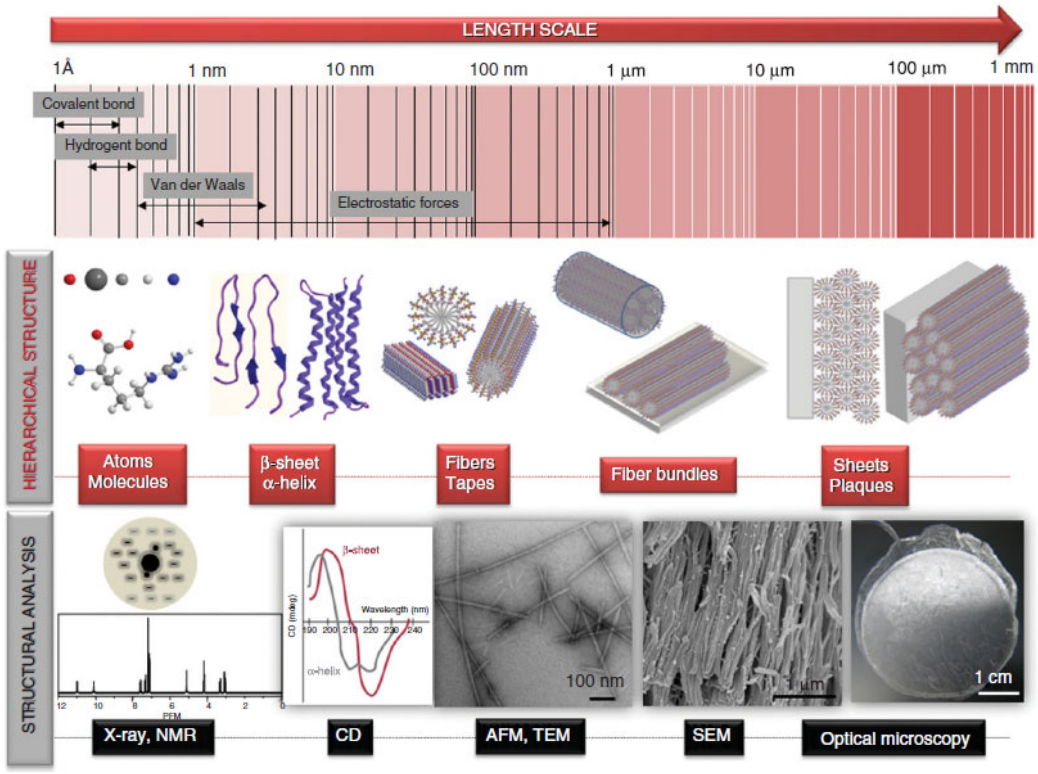


FIGURE 4. Length scales of the forces involved in self-assembly (first panel) and the hierarchical complex structures generated by peptide self-assembly (second panel). Spectroscopy and microscopy techniques used for structural characterization of peptide molecules and assemblies from the nanometer to centimeter length scales (third panel). NMR, nuclear magnetic resonance; X-ray, X-ray diffraction; CD, circular dichroism; AFM, atomic force microscopy; TEM, transmission electron microscopy; SEM, scanning electron microscopy.

Self-Assembly

10.3.1 NON-COVALENT INTERACTIONS

In order for self-assembly to occur, the non-covalent forces between the molecules need to be broken and reformed. In doing so, the molecules are not changed chemically, but are structured in a different orientation. The weak intermolecular interactions that govern molecular ordering in materials include hydrogen bonds, ionic interactions, dipolar interactions, van der Waals forces, and hydrophobic interactions.

Hydrogen bonding is especially important in biological systems. Protein structures in water are held together by hydrogen bonds (Kelsall et al., 2005). Hydrogen bonds are weaker than covalent bonds (about 20 kJ/mol compared to about 500 kJ/mol for hydrogen bonds and covalent bonds, respectively) (Kelsall et al., 2005). As a result, structures can self-assemble without chemical reactions needing to occur, and the bonds are strong enough to hold the structures together once they have been formed.

Dipolar interactions follow the same principles as hydrogen bonding, except they are not limited to just hydrogen atoms. Dipolar interactions refer to the direct interactions between two magnetic dipoles. The dipoles are a result of the difference in electronegativity within molecules creating partial positive and negative charges within the molecule.

The van der Waals forces are the sum of the attractive or repulsive forces between molecules—other than those due to covalent bonds. The forces include those between a permanent dipole and a corresponding dipole, as well as the London dispersion forces.

The hydrophobic effect arises when a nonpolar solute is inserted into water. The hydrophobic effect is attributed to the ordering of water molecules around a hydrophobic molecule. The ordering leads to a reduction in entropy (Kelsall et al., 2005). The entropy loss can be offset when association of hydrophobic molecules into micelles occurs, as this results in an increase in entropy.

Dahman 2017, Self-assembling nanostructures, Nanotechnology and Functional Materials for Engineers, pp. 207-228.

Self-Assembly

10.3.2 INTERMOLECULAR PACKING

At higher concentrations, the packing of block copolymer or amphiphilic molecules in solution leads to the formation of lyotropic liquid crystal phases (Kelsall et al., 2005). These crystal phases include cubic-packed spherical micelles, hexagonal-packed cylindrical micelles, lamellae, and bicontinuous cubic phases. The phase that forms is dependent on the curvature of the surfactant–water interface. To understand the lyotropic phase behavior, there exist two approaches. The first approach computes the free energy associated with curved interfaces; the curvature is analyzed using differential geometry, while not incorporating details of the organization of the molecules. The second approach uses a molecular packing parameter to describe the interfacial curvature.

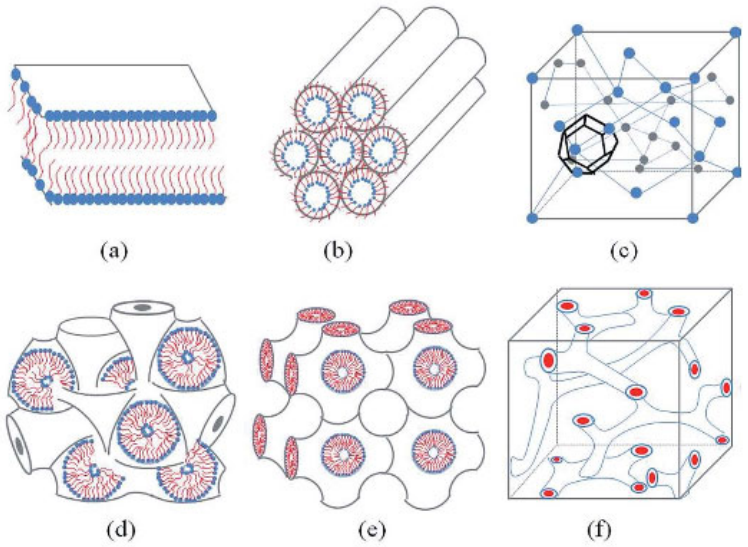


Fig. 1. Schematic representation of the lyotropic liquid crystalline phases commonly found in neutral lipid/water systems. (a) Lamellar phase (b) reverse hexagonal phase (c) reversed micellar cubic of Fd3m (d) reversed bicontinuous cubic (Im3m) (e) reversed bicontinuous cubic (Pn3m) (f)reversed bicontinuous cubic (Ia3).

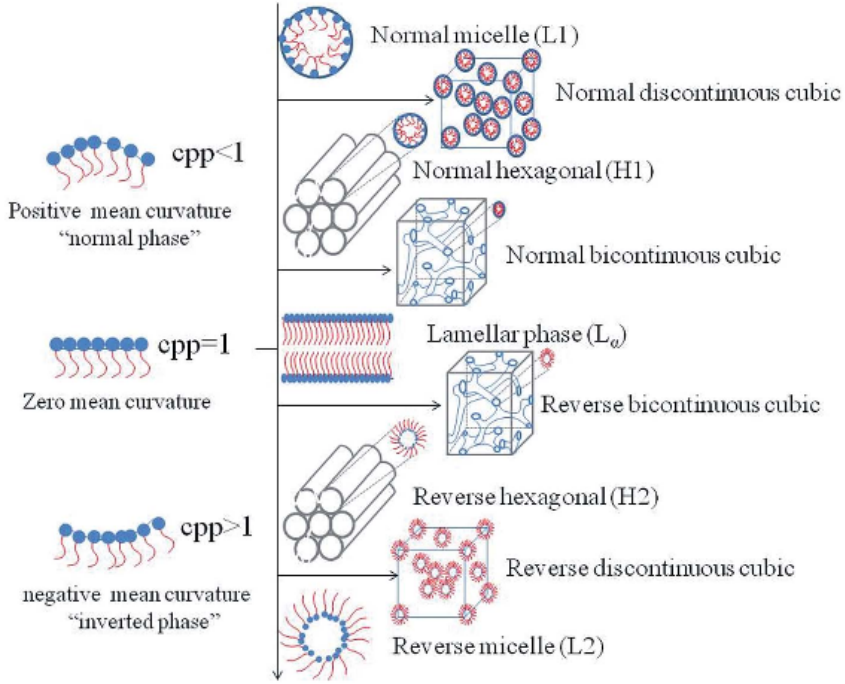


Fig. 2. Schematic representations of common structures and their corresponding CPP.bicontinuous cubic (Ia3).

Dahman 2017, Self-assembling nanostructures, Nanotechnology and Functional Materials for Engineers, pp. 207-228.

Huang 2018, Factors affecting the structure of lyotropic liquidcrystals and the correlation between structure and drug diffusion, RSC Adv.,2018,8, 6978-6987.

Self-Assembly to Generate Complex Structure

Only some selected classes of chemical compounds are capable to lead to useful self-assembled structures. Amphiphiles, simultaneously possessing polar and apolar moieties within their molecular architecture, can give a wide scenario of possible intermolecular interactions: polar–polar, polar–apolar, apolar–apolar interactions, eventual directional H-bonds, steric hindrance and so on. This peculiarity efficiently triggers the possibility of originating complex behavior, i.e., the formation of interacting structures at hierarchical length-scales characterized by emerging and specific properties and functions. However, if one places in a becher the molecules constituting a living cell, he does not observe the formation of a living cell even after vigorous and prolonged stirring and/or heating. This consideration suggests that the building up of complex structures is not only an affair of molecular structure, system composition and self-assembling processes but additional subtle features can contribute to the overall process.

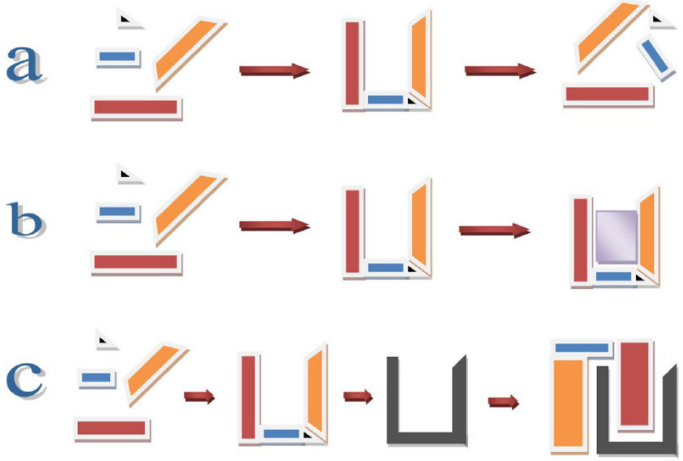


Fig. 3. Different mechanisms for complexity generation. (a) the building blocks are assembled through soft interactions. The structure formation is reversible and usually temperature-dependent. The assemblies show emerging properties with respect to those possessed by their constituents. (b) the building blocks are assembled in such away to template or to drive the formation of successive structures. See for example nanoparticle synthesis through the use of microemulsions. (c) the building blocks are assembled through strong interactions. Such structures are less sensitive to temperature changes and may be needed for the preparation of building blocks for the formation of complex structures of successive level of complexity.

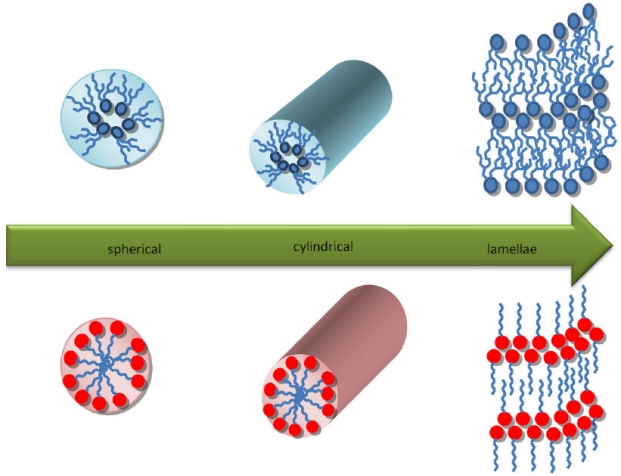
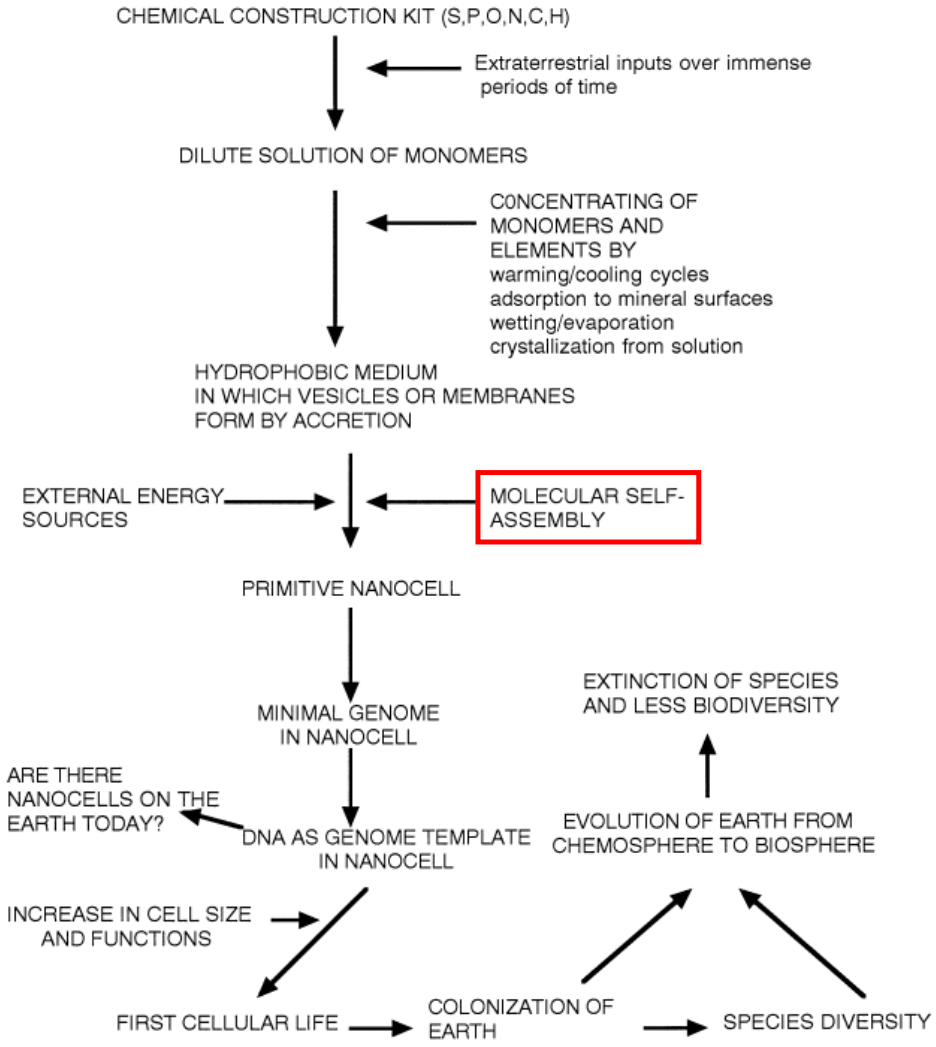


Fig. 4. The aggregation of amphiphiles can give supra-structures with various dimensonalities: 0D (micelles) 1D (cylinders or cylindrical micelles), 2D (lamelles). The sestructures can be reversed (upper panel) or direct (lower panel) depending on the polarity of the solvent. In apolar solvent reversed structures are formed, in polar solvent direct structures are the stable ones.

Calandra 2015, How self-assembly of amphiphilic molecules can generate complexity in the nanoscale.

Colloids and Surfaces A: Physicochemical and Engineering Aspects, Volume 484, 5 November 2015, Pages 164-183.

Self-assembly of Life



Trevors 2001, From self-assembly of life to present-day bacteria, FEMS Microbiology Reviews 25 (2001) 573-582.

The self-assembly events that led to the first minimal cell and genome capable of growth and division are highly debated. Fig. 1 is a proposed sequence of major events that may have occurred initially at a molecular level and then progressed to a nanocell level and finally to the bacterial cell dimensions (μm) that we know today. In this review we will examine the major self-assembly events for cells as outlined in Fig. 1. We will also discuss the possibility that nanobacteria, which are small spherical and ovoid structures discovered in rocks and minerals, may be the fossil evidence of the earliest life forms on Earth and outer space. Fig. 1 also indicates a role for extraterrestrial inputs which may have included living spores.

Fig. 1. Proposed sequence of major events in the origin of a cell capable of growth, division and diversification.

Self-assembly of Life

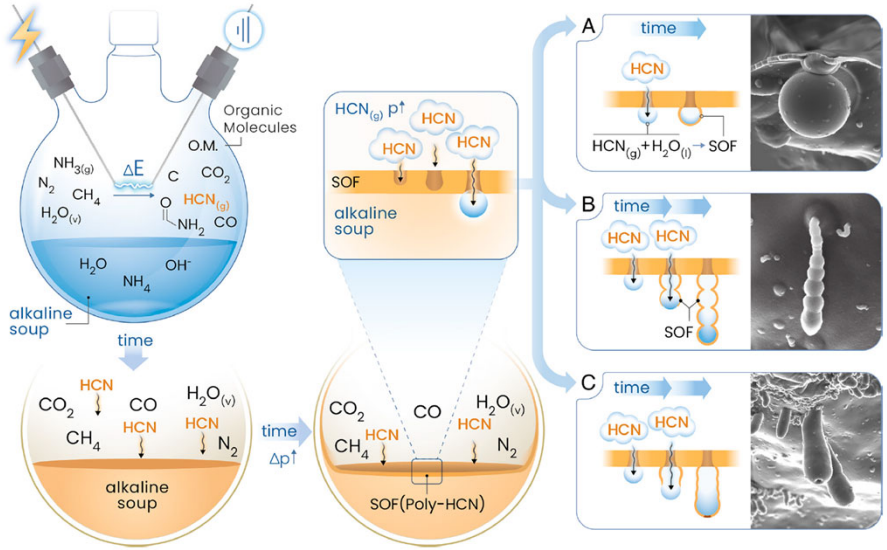


Fig. 4. Mechanistic sketch of the morphogenesis of organic biomorphs. HCN forming inside the Miller reactor reacts with water to form a SOF made of HCN-polymers that cover reactor walls and the water–gas interface of the alkaline soup. The continuous formation of HCN and other HCN derivatives increases the partial pressures and concentration of poly-HCN precursors. Gaseous byproducts of the reaction of these molecules in the porous parts of the SOF lead to the formation of bubbles below the film. (*A*) In contact with the alkaline soup, the HCN polymerizes at the bubble interface forming a thin SOF surrounding the bubble, ultimately resulting in spherical protocells. (*B*) Under specific local conditions, when bubble encapsulation is slow, a continuous flow of precursor molecules results in the formation of a new bubble on the former one. The repetition of this pupping phenomenon is the origin of caterpillar-like biomorphs. (*C*) A slow precipitation of HCN-polymer combined with a steady growth of the bubble allows for elongation, ultimately resulting in polyp-like biomorphs.

Morphogenesis of Organic Biomorphs. The proposed mechanism of morphogenesis of poly-HCN biomorphs is illustrated in Fig. 4. The formation of hydrogen cyanide (HCN) driven by electrical discharge and UV radiation is well known to convert into formamide ($HCONH_2$) or directly polymerize into poly-HCN in the presence of water (30–33). In our experiments, atmospheric water vapor promotes the formation of electrically charged nanometer-sized HCN-rich nanodroplets. These droplets deposit on the borosilicate or water interfaces of the reactor, where they fuse and polymerize into a continuous solid organic film (SOF), occasionally encapsulating other organic molecules or liquid droplets. The continuous generation of HCN, with its high vapor pressure and low melting point (25.6 °C) as well as the formation of other, gaseous molecules driven by the electrical discharge, slowly increases the pressure inside the reactor by up to 62% from an initial pressure of 793 mbar to 1,283 mbar. After the formation of an initial layer of HCN-polymer, the interaction of HCN and other molecules with water appears to predominantly occur within the porous structures of the SOF. Gaseous byproducts of these reactions, as well as unpolymerized HCN derivates, are concentrated in the SOF, likely leading to the formation of bubbles when they escape into the alkaline soup (Figs. 1*C* and 4*A*). On the newly formed bubble–water interface, the HCN-rich precursors in contact with water will result in the precipitation of poly-HCN, encapsulating the bubble and creating the hollow structures that we observed (Fig. 4 *A*–*C*). The precipitation rate of this process depends on several factors, like the precursor production rate, the partial pressure of HCN, and the pH of the soup. Therefore, the inhomogeneous local conditions will determine the different morphologies of the observed biomorphs. The formation of a single gas bubble beneath the film (Fig. 4*A*) results in spherical particles that either remain attached to the film or are dislodged by the induced convection and dispersed into the solution (Fig. 4). Low concentrations of HCN and/or low pH slow the precipitation of polymer at the bubble interface. Thus, before full-encapsulation, the intruding precursor molecules may trigger the formation of a secondary bubble (Fig. 2*C*) or, by iteration of this mechanism, the caterpillar-like structures shown in Figs. 2*A* and *B* and 4*B*. A continuous and steady intrusion of precursor molecules without a full encapsulation will result in the elongated, polyp-like structures (Figs. 2*D* and 4*C*). Whether the poly-HCN skin is permeable, and the protocells are later filled with soup is yet to be confirmed. Nevertheless, the clear silanol signature in the Raman spectra of washed biomorphs (Fig. 3*B*), and their relatively high densities obtained from analytical ultracentrifugation (AUC) suggest that they are filled with liquids rather than gas. In both cases, these protocells potentially work as microreactors of relevance for prebiotic chemistry because HCN is considered the source of RNA and protein precursors (34).

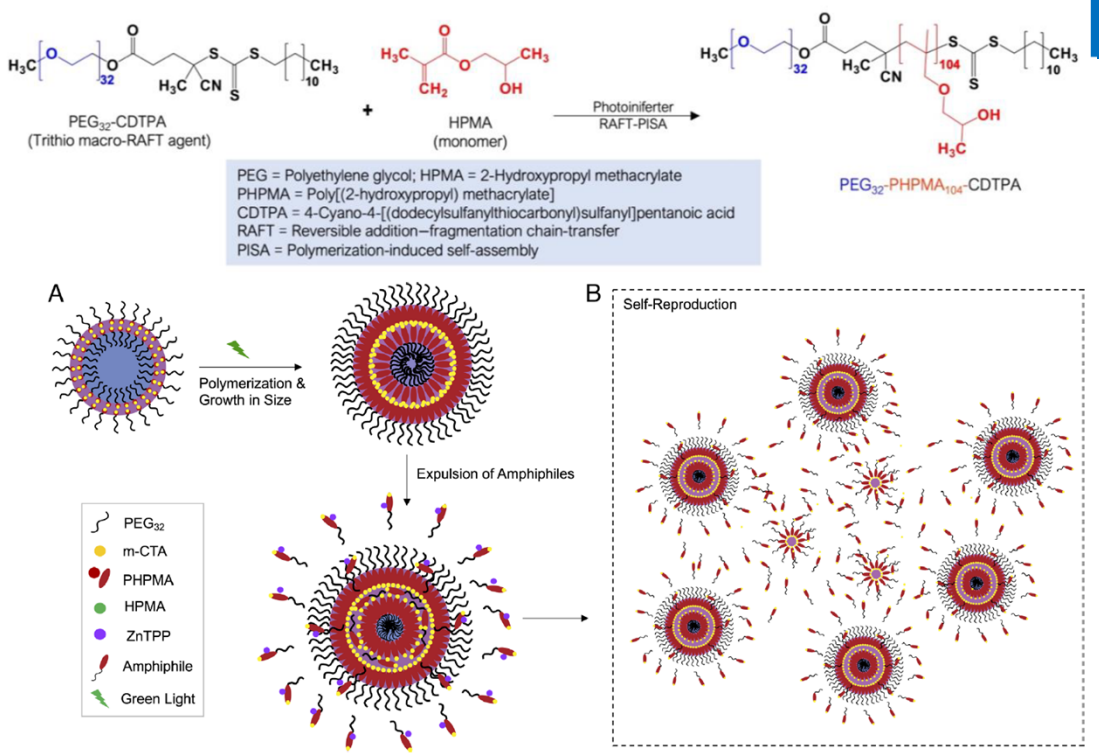


Fig. 1. (*A*) Illustration showing the different stages of polymer vesicle growth leading to the action of expulsion of amphiphiles. (*B*) Illustration showing the formation of new vesicles from the reorganization through self-reproduction of amphiphiles expelled into the bulk.

Self-reproduction is one of the most fundamental features of natural life. This study introduces a biochemistry-free method for creating self-reproducing polymeric vesicles. In this process, nonamphiphilic molecules are mixed and illuminated with green light, initiating polymerization into amphiphiles that self-assemble into vesicles. These vesicles evolve through feedback between polymerization, degradation, and chemiosmotic gradients, resulting in self-reproduction. As vesicles grow, they polymerize their contents, leading to their partial release and their reproduction into new vesicles, exhibiting a loose form of heritable variation. This process mimics key aspects of living systems, offering a path for developing a broad class of abiotic, life-like systems.

Jenewein 2025, Concomitant formation of protocells and prebiotic compounds under a plausible early Earth atmosphere
Katla 2025, Self- reproduction as an autonomous process of growth and reorganization in fully abiotic, artificial and synthetic cells

Assembly Index (AI) & Assembly Threshold (AT)

Assembly Theory

The more complex a given object, the less likely an identical copy can exist without selection of some information-driven mechanism that generates that object. An object that exists in multiple copies allows the signatures describing the set of constraints that built it to be measured experimentally.

Complex molecules that occur in multiple copies suggest they are assembled by a biological process.

Assembly Index (AI)

For each object, the most important feature is the assembly index *ai*, which corresponds to **the shortest number of steps required to generate the object from basic building blocks**. This can be quantified as the length of the shortest assembly pathway that can generate the object (Fig. 1).

Assembly Threshold (AT)

In AT, the information required at each step to construct the object is 'stored' within the object (Fig. 2). Each time two objects are combined from an assembly pool, the specificity of the combination process constitutes selection. **Randomly combining objects** within the assembly pool at each step does not constitute selection because **no combinations exist in memory to be used again** for building the same object. **If, instead, certain combinations are preferentially used, it implies that a mechanism exists that selects the specific operations and, by extension, specific target objects to be generated**.

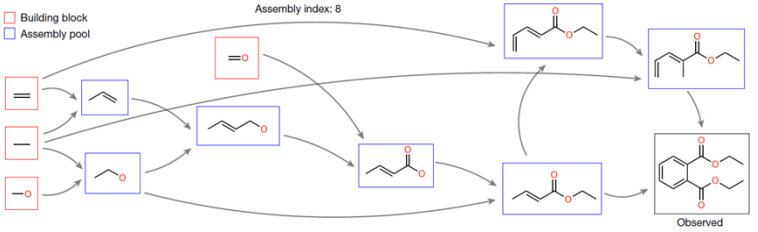


Fig. 1. Assembly index and shortest path, AT is generalizable to different classes of objects.

Assembly pathway to construct diethyl phthalate molecule considering molecular bonds as the building blocks. The figure shows the pathway starting with the irreducible constructs to create the molecule with assembly index 8.

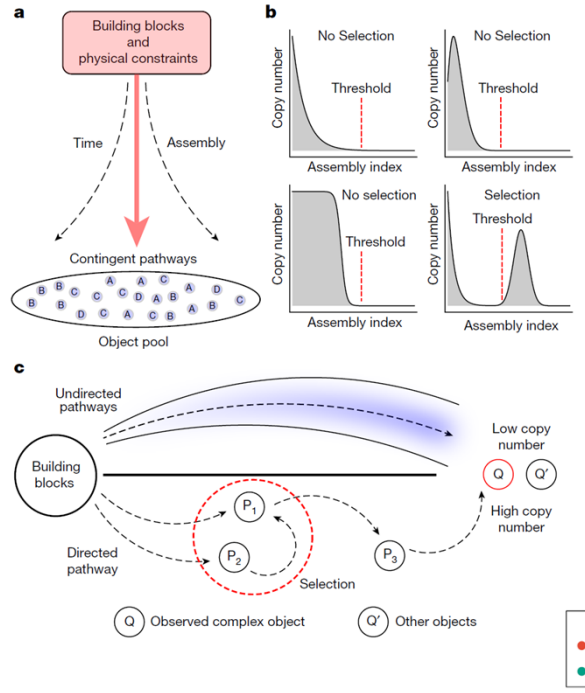


Fig. 2. Selection in assembly space.

a, Pictorial representation of the assembly space representing the formation of combinatorial object space from building blocks and physical constraints.

b, Observed copy number distributions of objects at different assembly indices as an outcome of selection or no selection.

c, Representation of physical pathways to construct objects with undirected and directed pathways (selected) leading to the low and high copy numbers of the observed object.

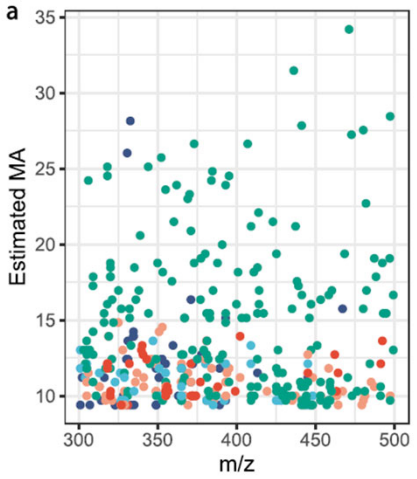


Fig. 4. Estimated molecular AI (MI) of laboratory and environmental samples.
Only living samples produced molecular AI (MI) measurement above ~15.

Marshall 2021, Identifying molecules as biosignatures with assembly theory and mass spectrometry
Sharma 2023, Assembly theory explains and quantifies selection and evolution
https://www.tiktok.com/@tilscience/video/7572245586552818999?_r=1&_t=ZT-93jFbQcdJjq

Self-assembly of Life

LUCA: Last Universal Common Ancestor, emerged 4 Billion Years ago.
What happened during the first 0.5 billion years?

Proteins cannot reproduce. Prions (misfolded proteins) can self-assemble.
RNA can replicate itself. RNA is unstable in water, especially at high temperatures.
Cooperation of proteins and RNAs?

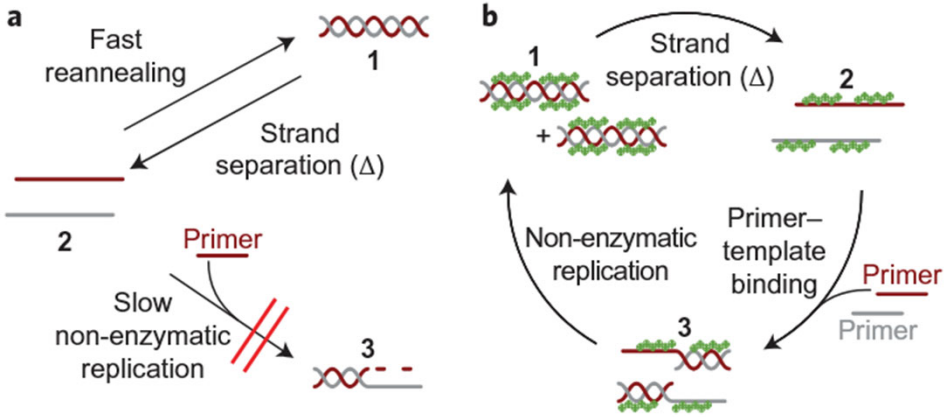


Figure 1. The reannealing problem and a proposed solution.
a, Complete template-directed primer extension results in a full-length duplex 1 (newly synthesized strand in maroon, original template in grey). After strand separation by heating (Δ) to give 2, subsequent cooling results in rapid reannealing of the newly synthesized complementary strand to the template strand 1, which prevents primer–template binding, outcompeting the slow process of non-enzymatic RNA polymerization that gives 3 and thereby prevents further rounds of RNA replication.
b, RNA-binding oligoarginine peptides (green) inhibit strand annealing and promote further rounds of non-enzymatic replication. After an RNA duplex is formed, 1, the strands are separated by heating (Δ) to give 2. Subsequent cooling allows the peptide to bind to the separated complementary strands, but not to the shorter RNA primers. This selectivity prevents reannealing of the full-length replicated strands, which allows each strand to act as a template to which shorter primers can then bind 3. The non-enzymatic polymerization reaction is free to proceed, which results in a complete replication cycle that would not be possible without the peptide.

Zia 2016, Oligoarginine peptides slow strand annealing and assist non-enzymatic RNA replication.

https://www.tiktok.com/@tilscience/video/7603855452941618445?_r=1&_t=ZT-93jCswppO7a

Self-Assembly of Virus

Viruses infect cells in all kingdoms of life and, from a physicochemical perspective, can be regarded as molecular machines that have successfully evolved to spread between related organisms. They hijack their host cell's machineries in a highly efficient and minimalistic manner, in order to ensure their propagation. The molecular mechanisms behind the viral life cycle are not only complex, these processes also require a remarkably low number of essential viral components to be successful.

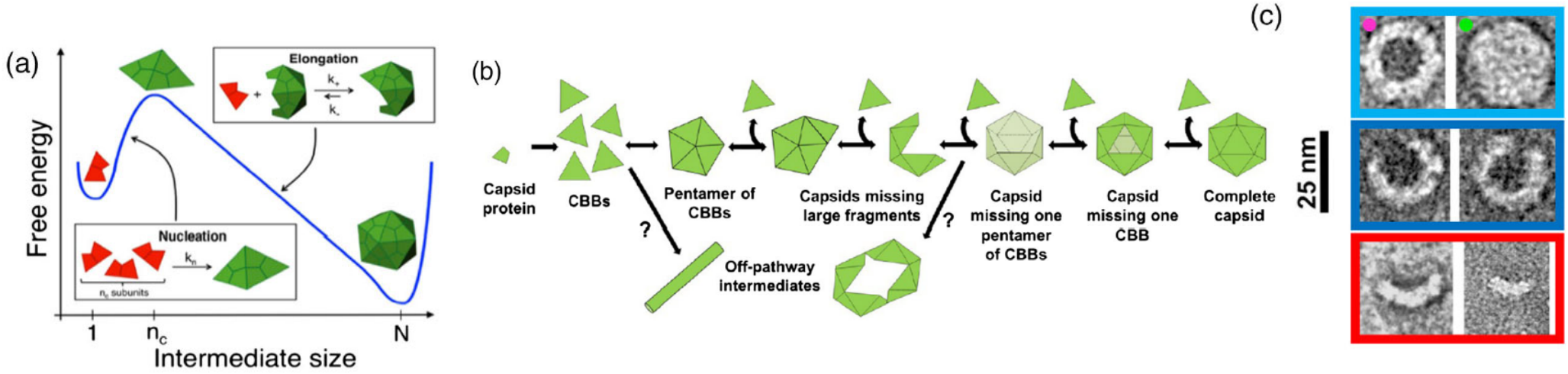
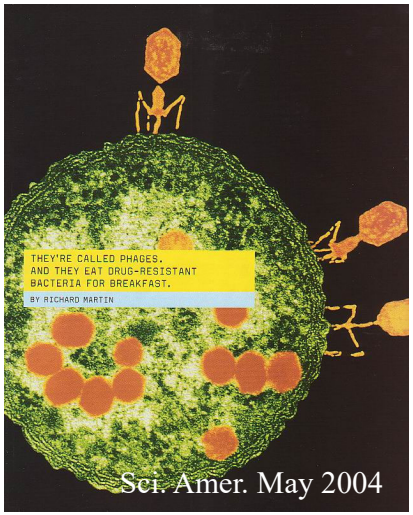


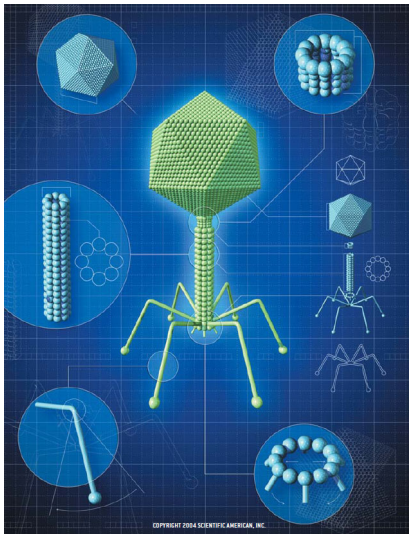
FIGURE 1 Assembly of empty particles through the nucleation, growth, and completion pathway. (a) Schematic representation of the free energy profile of the nucleation-and-growth/elongation pathway: first, nuclei are formed; then, the reaction proceeds downhill until the complete closure of the capsid. (Reprinted with permission from Michaels, Bellaiche, Hagan, and Knowles (2017)). (b) Self-assembly model proposed for MVM empty capsids based on the sequential addition of trimeric subunits, or CBBs (capsid building blocks). (Reprinted with permission from Medrano et al. (2016)). (c) MVM particles imaged by TEM (left): light blue, Types I + II particles (complete capsids); green, Type I (complete capsids in basal state); magenta, Type II (complete rearranged capsids); blue, Type IIIA (large incomplete capsids); red, Type IIIB (smaller incomplete capsids). Progression of the total number of particles during disassembly (left graph) and assembly (right graph) over time. (Reprinted with permission from Medrano et al. (2016)).

Buzon 2019, Physical virology, WIREs Nanomed Nanobiotechnol. 2020;e1613

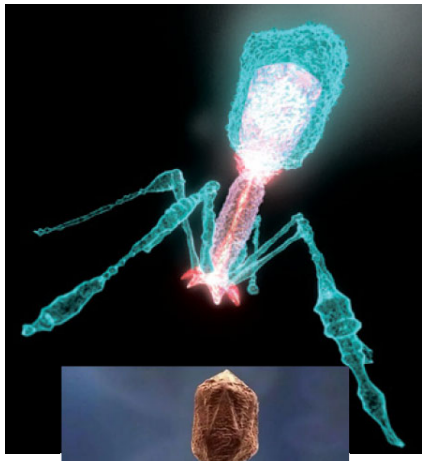
The Ultimate Nanofabrication: Synthetic Bacteriophage



Sci. Amer. May 2004

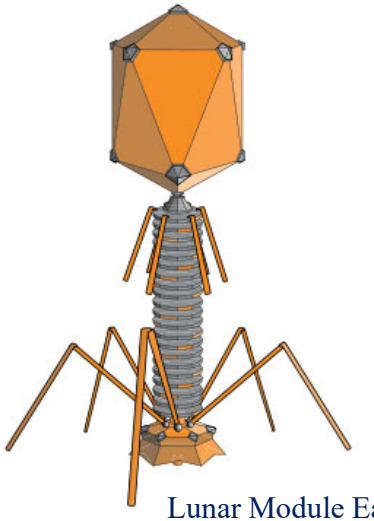


The ultimate nanofabrication will be the technology that can fabricate synthetic bacteriophage-type machines that can deliver a high drug load into only the targeted cells and, if necessary, reproduce itself in the cell to continuously supply the drug, e.g., insulin. The nanofabrication that scientists are talking about now is basically Lego assembly by babies. Probably 100 years from now, scientists can engineer such an artificial machine, and you will be at the forefront of these efforts. Dream Big!



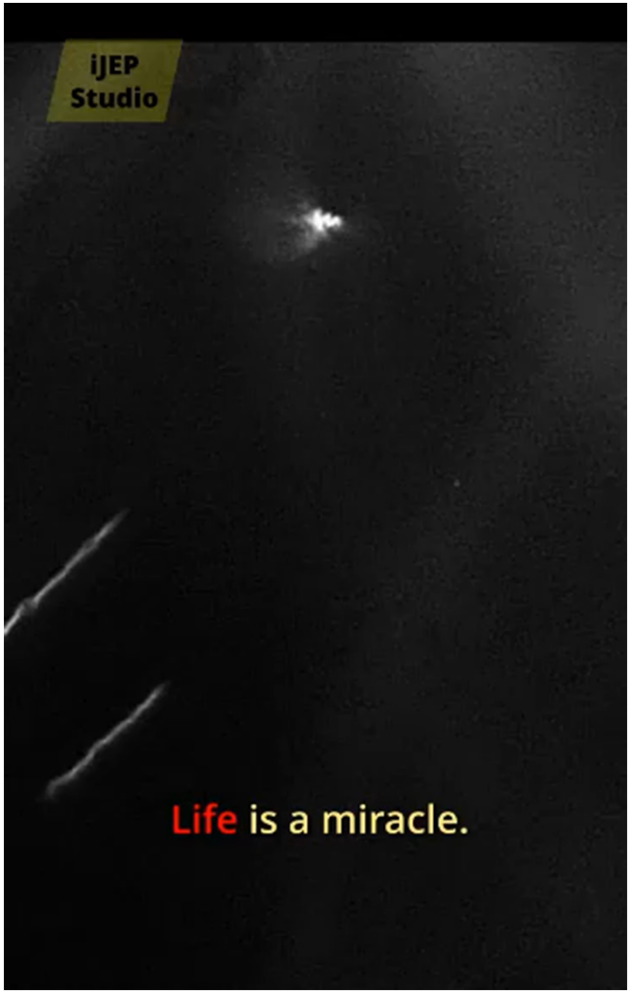
https://tigerscroll.com/rare-pictures-that-will-show-you-the-unseen-side-of-things-long/22/

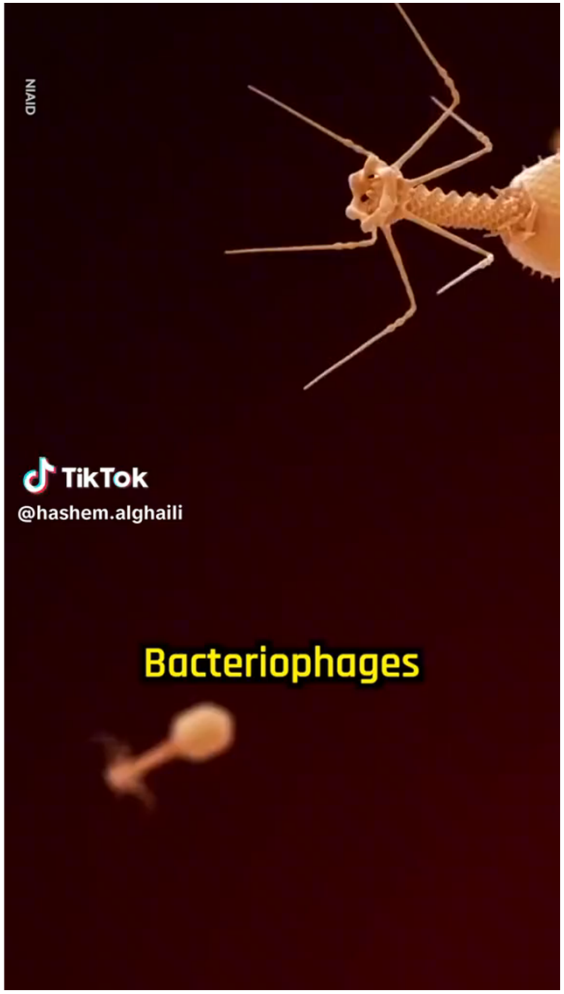
See the similarity in the structures? Engineers can copy what the nature provides, as the nature has learned the good-enough form through millions of years of evolution.



Lunar Module Eagle

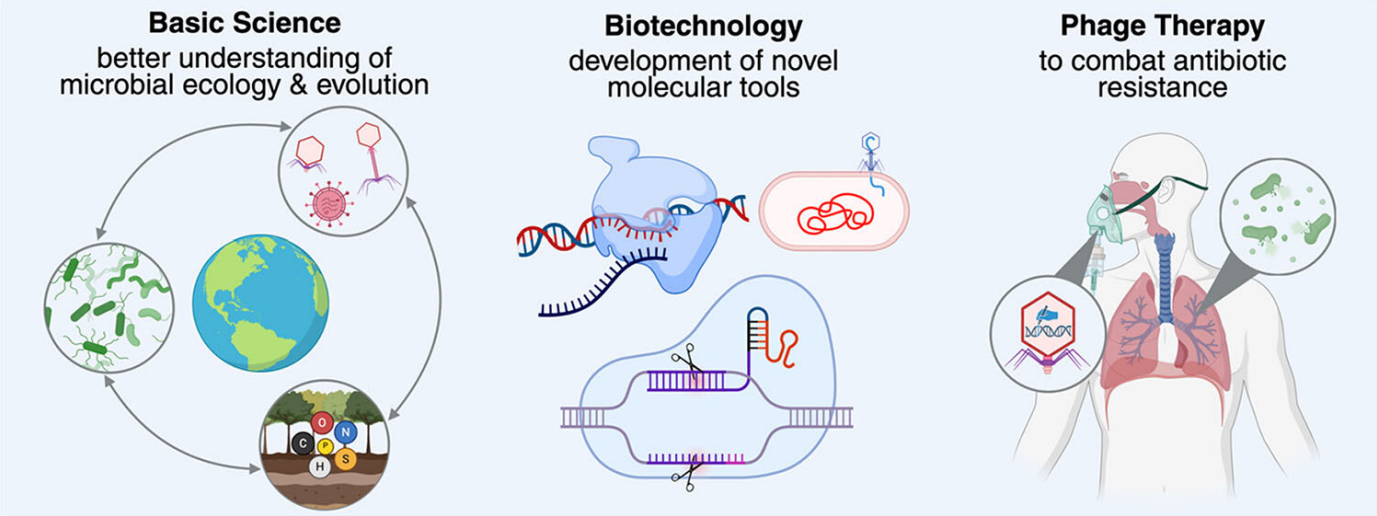
Bacteria & Bacteriophages





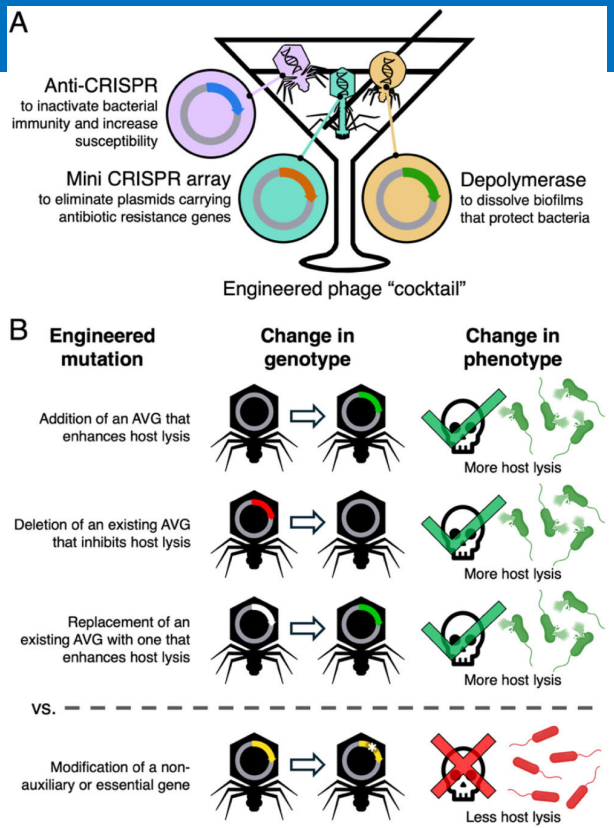
Viral Dark Matter

Owing to viral genomic diversity and rapid evolution, our ability to assign functions to viral proteins by sequence similarity is severely limited. Environmental surveys consistently show that a large fraction of viral genes lack functional annotation. In environmental studies, 40−90% of viral DNA sequences (mostly encoded by double-stranded DNA (dsDNA) phages and sometimes dsDNA eukaryotic viruses) cannot be assigned to known functions or even align to previously described viral sequences, a phenomenon often termed "viral dark matter." Notably, recent advances in sequencing ssDNA and RNA viruses reveal that these groups also harbor extensive dark matter, potentially exceeding that of dsDNA viruses, highlighting that the challenge extends across all viral genome types.



Applications for the study of viral dark matter. Uncovering and characterizing virus-encoded proteins, particularly those with metabolic or previously unknown functions, holds tremendous potential to advance basic science, enable the development of novel molecular tools, and support phage-based therapies to combat antibiotic-resistant infections.

Kosmopoulos 2025, Viral dark matter- Illuminating protein function, ecology, and biotechnological promises



Auxiliary viral genes as targets for engineering phage therapies. (A) A hypothetical "cocktail" of engineered phages designed to improve phage therapy outcomes. Examples of auxiliary viral genes (AVGs) shown here include an anti-CRISPR protein to disable host immunity, a miniature CRISPR array that targets plasmids carrying antibiotic resistance genes, and a depolymerase that degrades biofilms and thereby exposes bacteria to more phages and antibiotics. (B) The benefits of targeting AVGs over nonauxiliary or essential phage genes. The top three rows illustrate that the addition, deletion, or replacement of AVGs can increase host lysis or susceptibility without disrupting core phage functions. In contrast, the bottom row shows that modifying nonauxiliary or essential genes can impair lysis or phage fitness and reduce therapeutic efficacy.

Nanofabrication & Microfabrication

Nanofabrication deals with smaller structural sizes than microfabrication, but the borderline size is not well-defined and unnecessary.

Except for the manufacturing of evermore powerful computer chips, nanofabrication and microfabrication in most applications, especially in biomedical applications, are intimately tied together.

Thus, the two terms are frequently used together and/or used interchangeably.

Nanofabrication

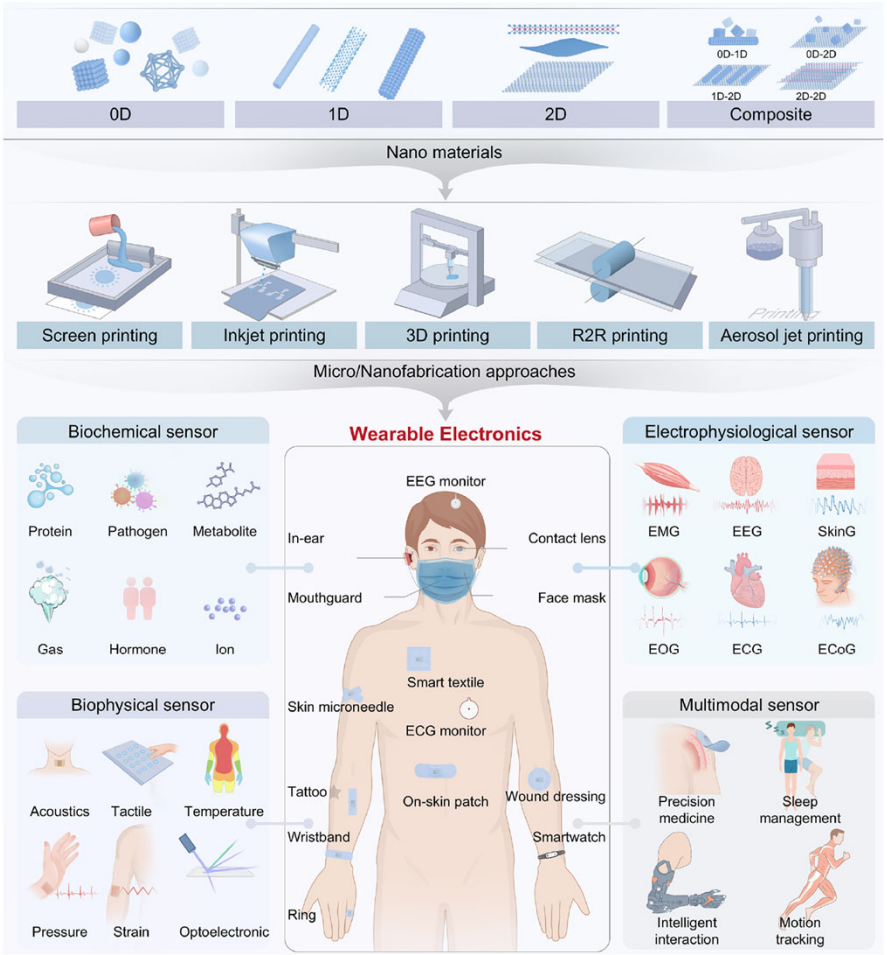
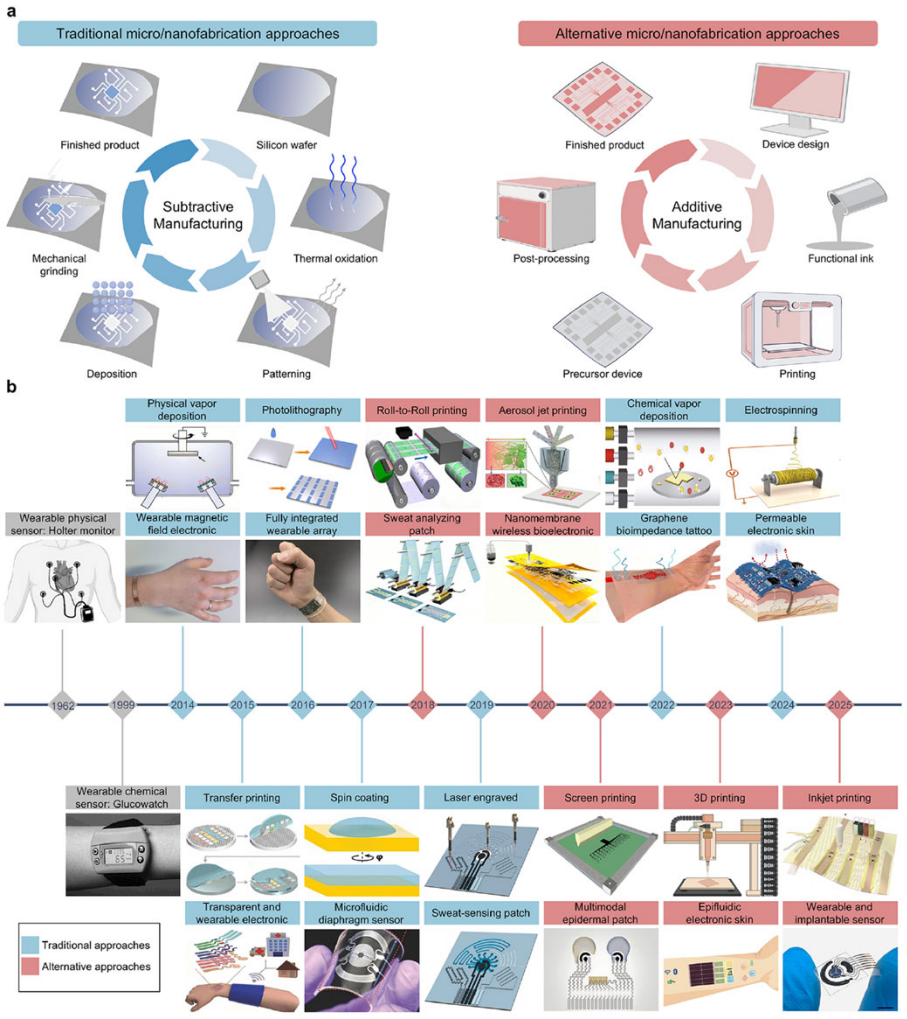


Figure 1. Overview of alternative micro/nanofabrication approaches for wearable electronics. Abbreviations: 0D, zero-dimensional; 1D, onedimensional; 2D, two-dimensional; 3D, three-dimensional; R2R, roll-to-roll; EMG, electromyography; EEG, electroencephalography; SkinG, skin conductance; EOG, electrooculography; ECG, electrocardiography; ECoG, electrocorticography.



Zhang 2026, Alternative micro-nanofabrication approaches for wearable electronics

Nanofabrication

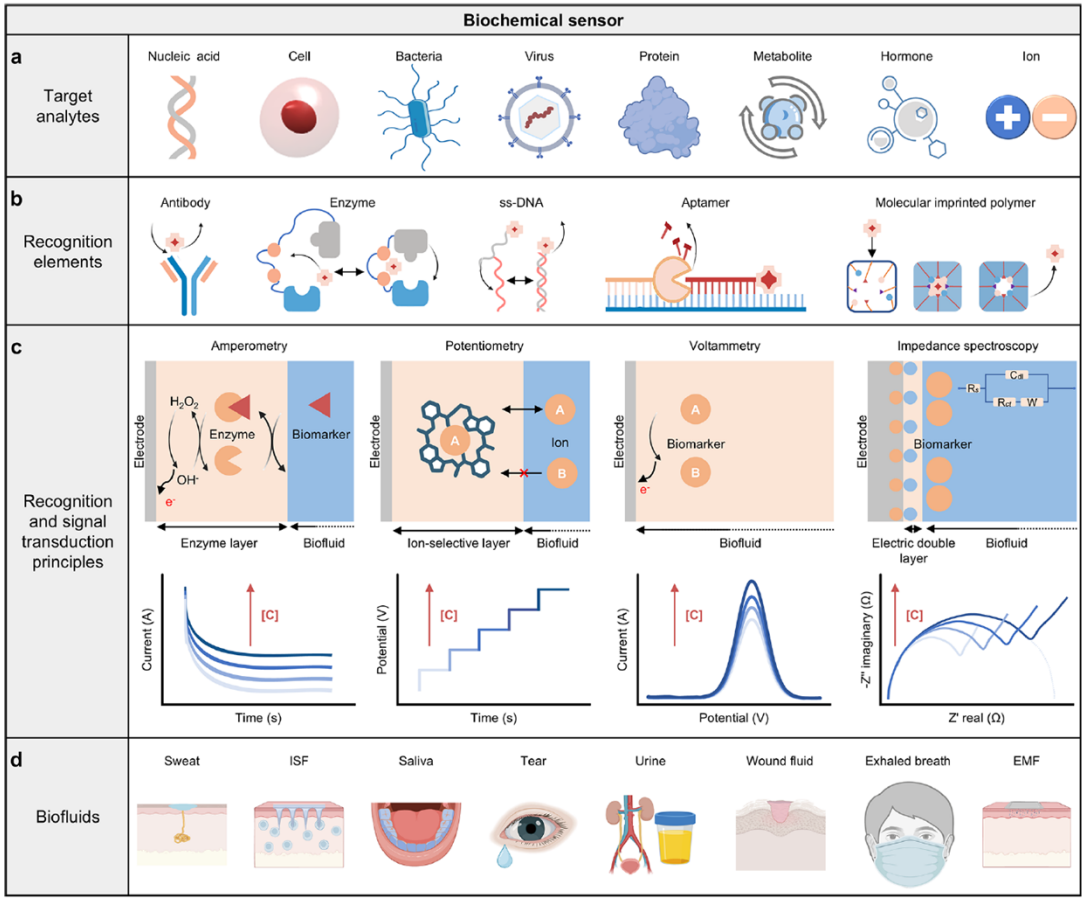


Figure 5. The primary biorecognition and signal transduction strategies in wearable biochemical sensors. (a) Schematic representation of various biochemical analytes. (b) Target recognition mechanisms involving bioaffinity receptors and biochemical sensing molecular switches. (c) Recognition and signal transduction principles for wearable electrochemical biosensors. (d) Wearable biochemical sensors for sweat, ISF, saliva, tear, urine, wound fluid, exhaled breath, and EMF analysis. Abbreviations: Rct, charge transfer resistance; W, Warburg impedance; Cdl, double-layer capacitance; Rs, solution resistance; C, concentration; ISF, interstitial fluid; EMF, epidermal molecular flux.

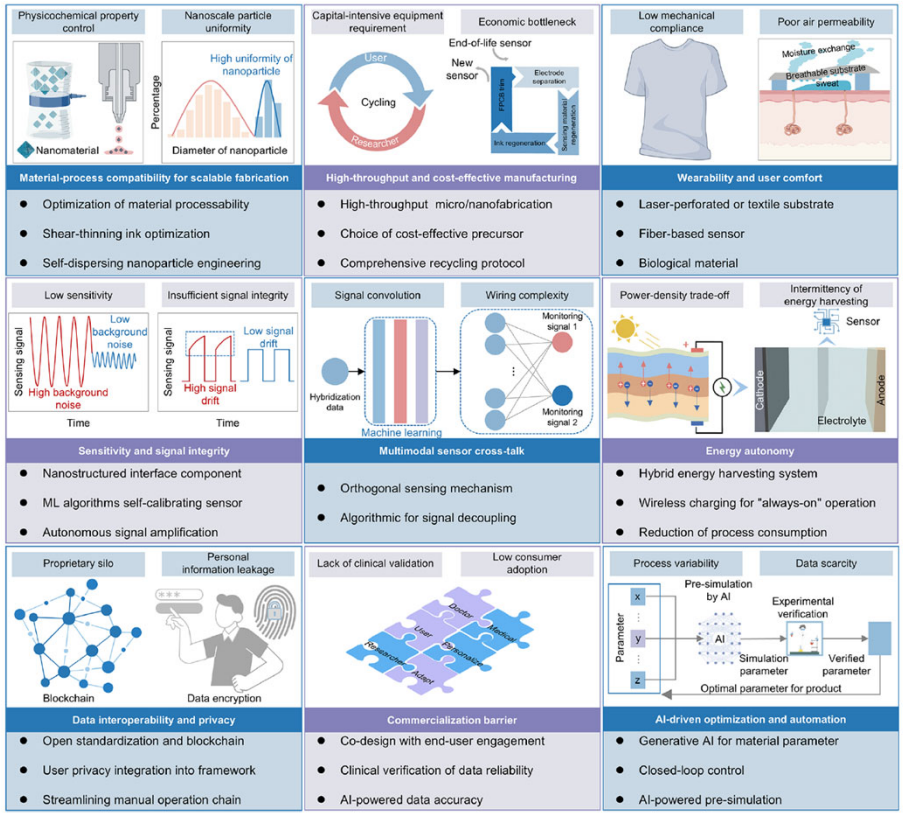
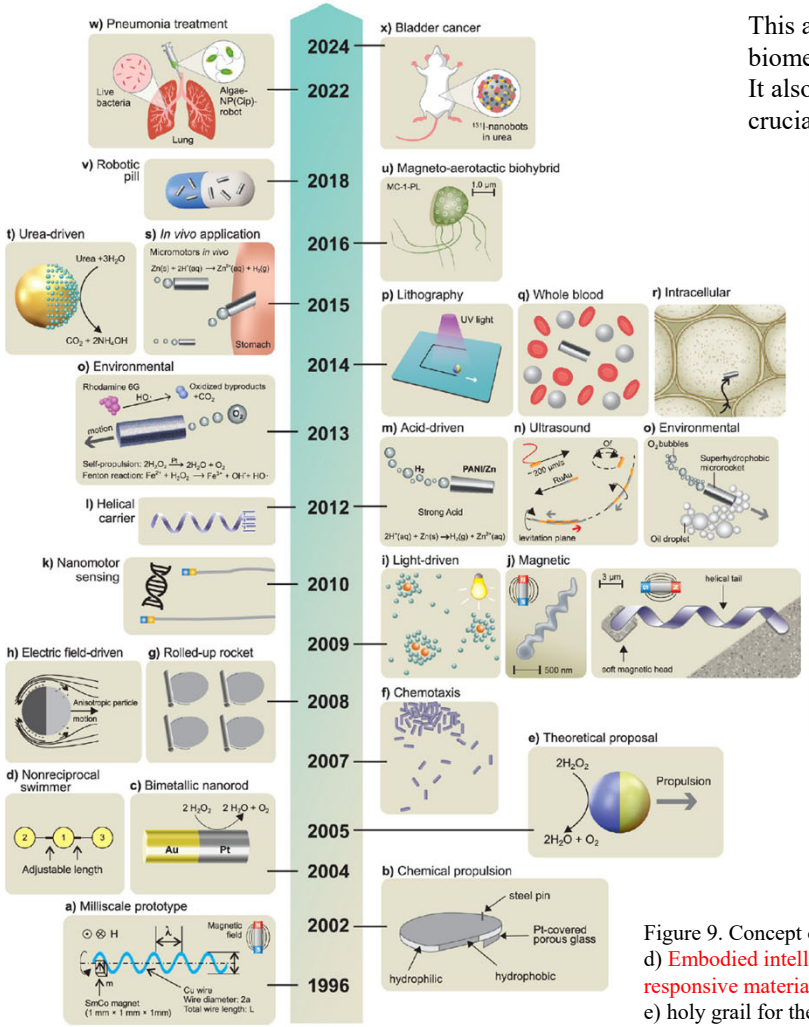


Figure 21. Conclusion and Perspective of wearable electronics. Abbreviations: AI, artificial intelligence; FPCB, flexible printed circuit board; F, force; M, metal; WIFI, wireless fidelity; 5G, fifth-generation mobile communication technology.

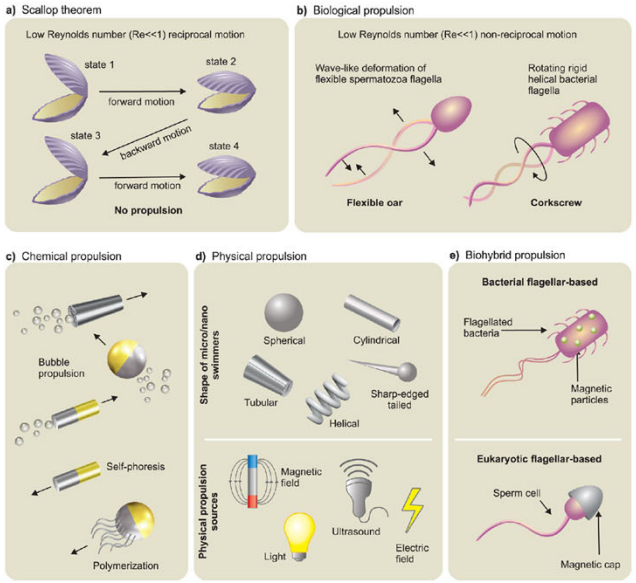
Zhang 2026, Alternative micro-nanofabrication approaches for wearable electronics

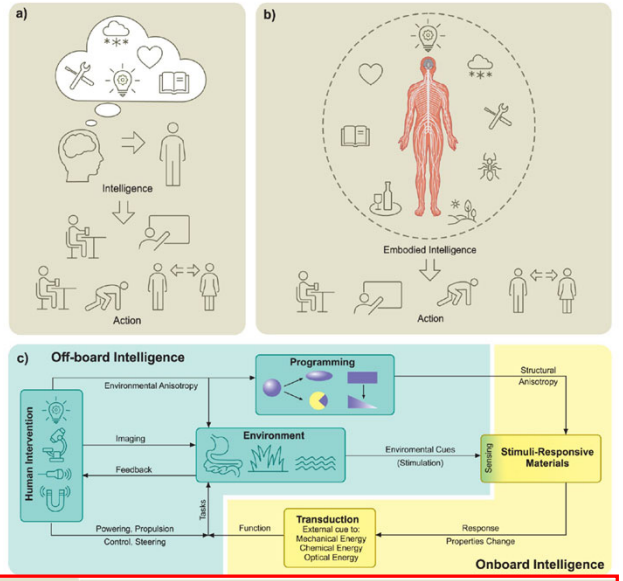
Micro/Nanorobots



Ju 2025, Technology Roadmap of Micro/Nanorobots

This article explores the current state of micro/nanorobot technology, with an emphasis on applications in biomedicine, environmental remediation, analytical sensing, and other industrial technological aspects. It also analyzes issues related to scaling up production, commercialization, and regulatory frameworks that are crucial for transitioning from research to practical applications.





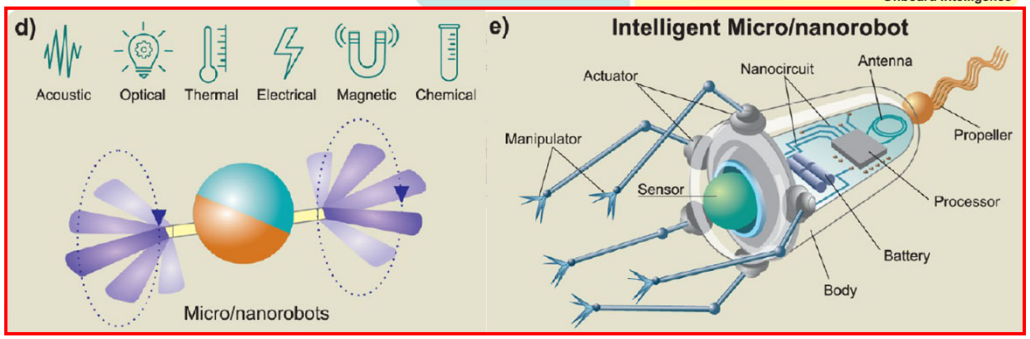
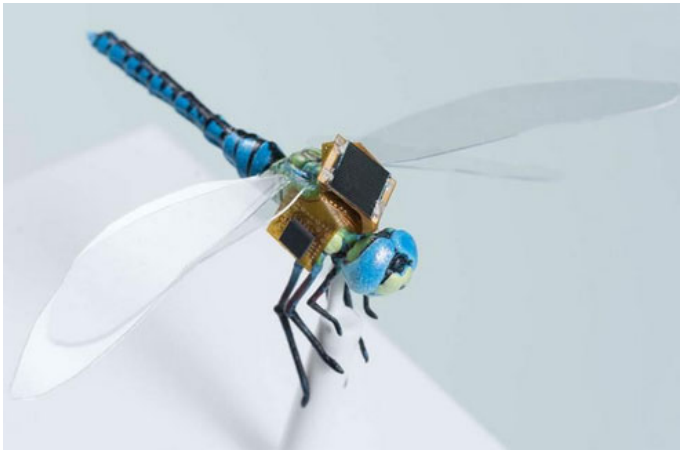
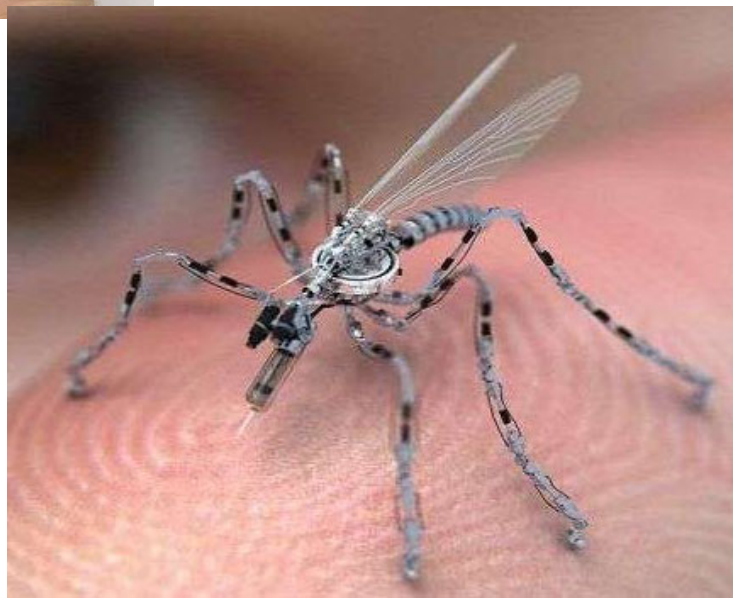


Figure 9. Concept of intelligence.
d) Embodied intelligence in stimuli-responsive materials for micro/nanorobots.
e) holy grail for the field of micro/nanorobotics.

Miniaturization



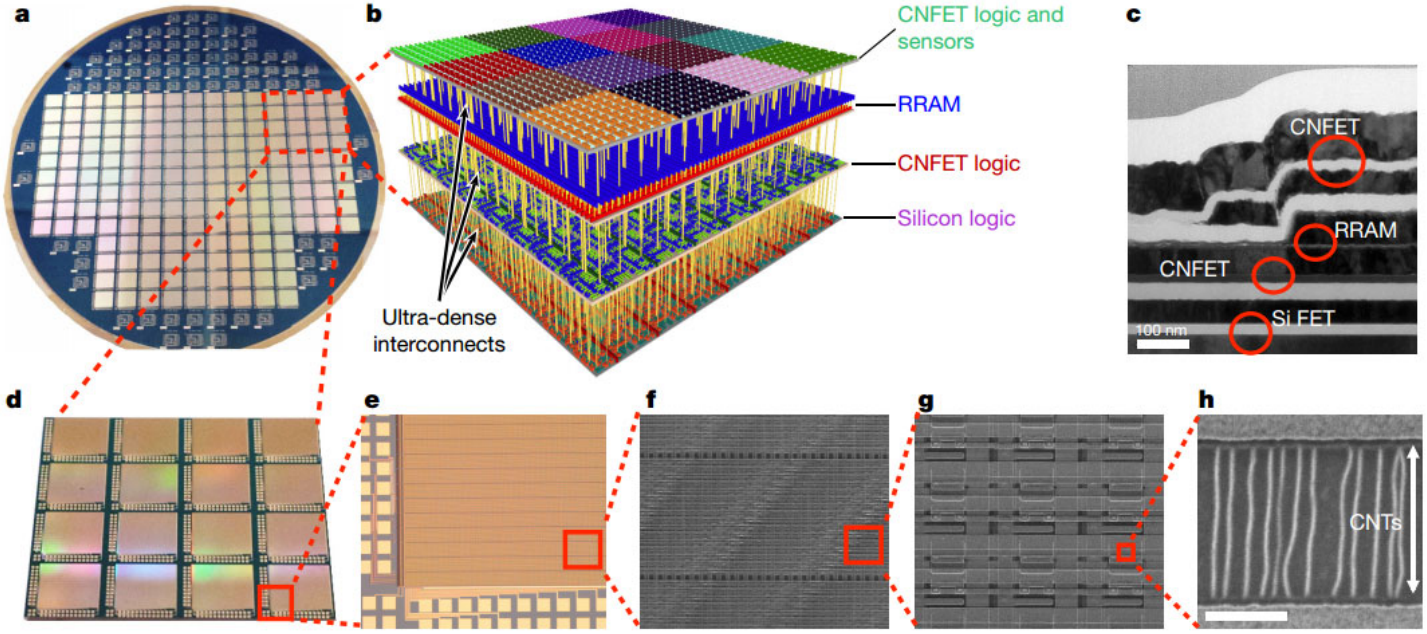


https://defense-update.com/20101231_miniature_weapons.html
https://news.mit.edu/2017/miniaturizing-brain-smart-drones-0712
https://www.islamtimes.org/en/news/183106/us-military-developing-insect-surveillance-drones
https://www.defenceiq.com/defence-technology/articles/nano-drone-tech-is-advancing

Nanofabrication: Three-Dimensional Chip

Nanofabrication

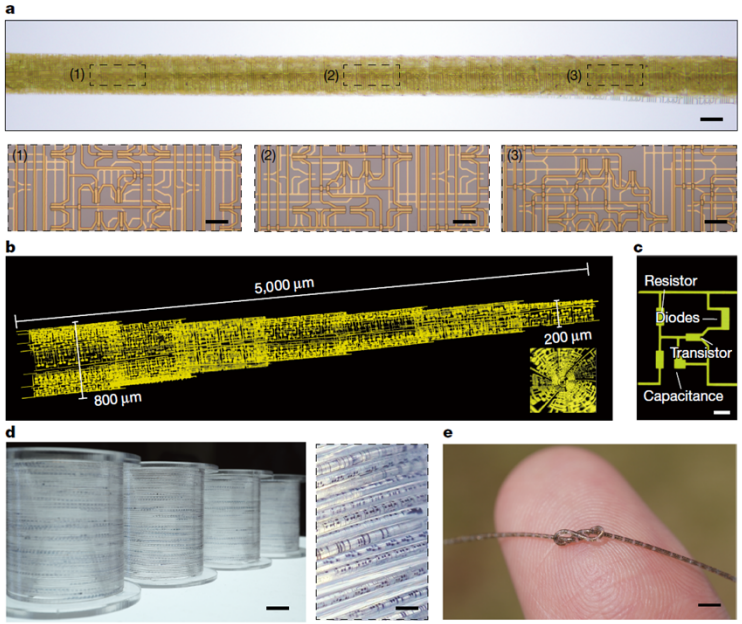
Computers today comprise different chips cobbled together. There is a chip for computing and a separate chip for data storage, and the connections between the two are limited. As applications analyze increasingly massive volumes of data, the limited rate at which data can be moved between different chips is creating a critical communication "bottleneck." And with limited real estate on the chip, there is not enough room to place them side-by-side, even as they have been miniaturized (a phenomenon known as Moore's Law).



The new prototype chip is a radical change from today's chips. It uses multiple nanotechnologies, together with a new computer architecture, to reverse both of these trends. Instead of relying on silicon-based devices, the chip uses carbon nanotubes, which are sheets of 2-D graphene formed into nanocylinders, and resistive random-access memory (RRAM) cells, a type of nonvolatile memory that operates by changing the resistance of a solid dielectric material. The researchers integrated over 1 million RRAM cells and 2 million carbon nanotube field-effect transistors, making the most complex nanoelectronic system ever made with emerging nanotechnologies. The RRAM and carbon nanotubes are built vertically over one another, making a new, dense 3-D computer architecture with interleaving layers of logic and memory. By inserting ultradense wires between these layers, this 3-D architecture promises to address the communication bottleneck.

https://phys.org/news/2017-07-three-dimensional-chip-combines-storage.html

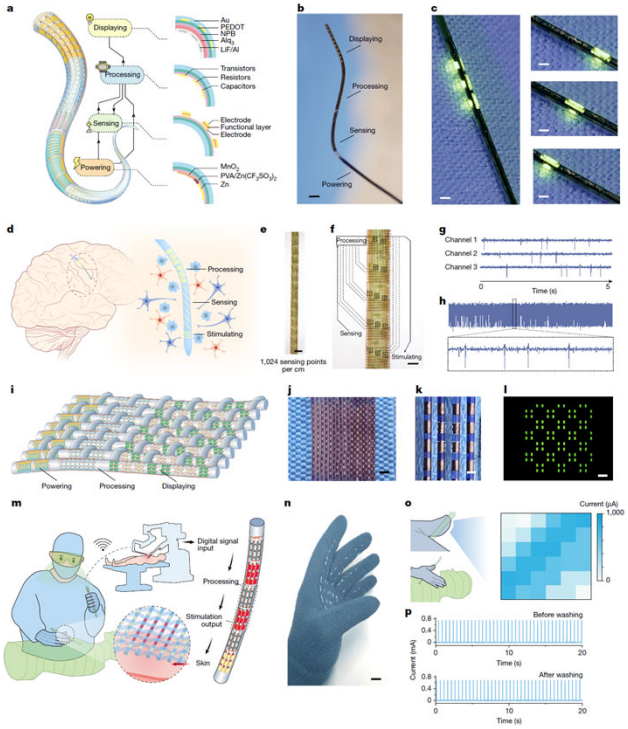
Fiber Integrated Circuits (FIC)

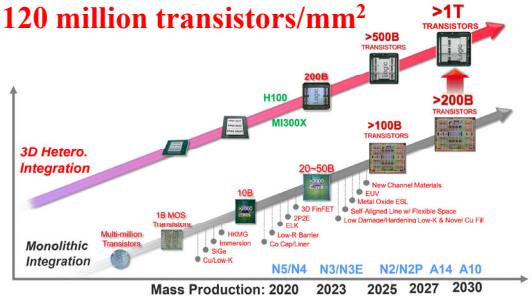


TFig. 1. Photographs showing the structure of FICs. a, Photograph of a FIC with XOR circuits on the fibre surface (scale bar, 200 μm) and enlarged views (scale bars, 40 μm). (1), (2) and (3) show the uniformity of the circuits in the FIC. **b**, Reconstructed three-dimensional fluorescence photomicrograph showing the connectivity of the microdevices in a FIC. The circuit can be distributed 360° around the fibre circumference. **c**, Fluorescence photomicrograph showing an active driving circuit unit inside a FIC, suggesting that a wide variety of devices can be integrated into the fibre. Scale bar, 40 μm. **d**, Photograph of FICs being produced at a large scale. The enlarged photograph shows the continuity of circuits in the FICs. Scale bars, 1 cm (left); 1 mm (right). **e**, Photograph of a FIC being knotted and placed on a thumb, exhibiting the flexibility and structural integrity of the FIC. Scale bar, 2 mm.

Wang 2026, Fibre integrated circuits by a multilayered spiral architecture

The integration density reaches 100,000 transistors/cm, which effectively satisfies the requirements for interactive fibre systems. The FICs can not only process digital and analogue signals similar to typical commercial arithmetic chips but also achieve high-recognition-accuracy neural computing similar to that of the state-of-the-art in-memory image processors. The FICs are stable under harsh service conditions that bulky and planar counterparts have difficulty withstanding, such as repeated bending and abrasion for 10,000 cycles, stretching to 30%, twisting at an angle of 180°/cm and even crushing by a container truck weighing 15.6 tons.





https://www.tomshardware.com/tech-industry/manufacturing/tsmc-charts-a-course-to-trillion-transistor-chips-eyes-monolithic-chips-with-200-billion-transistors-built-on-1nm-node

Fig. 4. Integration and application of intelligent fibre systems. a, Schematic showing the structural design of a closed-loop intelligent fibre system in which several functional modules are seamlessly integrated. The powering module included both energy-harvesting and energy-storage units. NPB, *N*,*N*′-bis(naphthalen-1-yl)-*N*,*N*′-bis(phenyl)-benzidine; PEDOT, poly(3,4-ethylenedioxythiophene). b, Photograph showing the intelligent fibre system with different functional modules integrated in segments. Scale bar, 800 μm. c, Photograph showing that the display pixels could be individually controlled through circuits integrated in the intelligent fibre system. Scale bars, 300 μm. d, Schematic showing that the intelligent fibre system allows integration of high-density sensing arrays with in situ signal-processing circuits and stimulation electrodes. e, Photograph showing a 50-μm-diameter FIC integrated with a 1,024-channel-per-cm sensing electrode array. Scale bar, 50 μm. f, Zoomed-in photograph showing the sensing/stimulating electrode around the intelligent fibre system. Scale bar, 25 μm. g, Neural signal obtained from three randomly selected channels. h, Zoomed-in diagram of the neural signal collected from in situ signal-amplification circuits. i, Schematic showing that an intelligent fibre system could be easily woven into integrated electronic textiles. j, Photograph showing the pixel display textile woven from activematrix- driving-circuit-integrated fibre systems. Scale bar, 1 mm. k, Zoomed-in photograph showing the pixel pitch of the pixel display textiles. Scale bar, 500 μm. l, Photograph showing the ability of pixel-display textiles to display complex images. Scale bar, 500 μm. m, Schematic showing intelligent-fibre system-woven smart textiles as flexible haptic interfaces enabling fine touch and free movement in virtual-reality scenarios (for example, remote surgery). n, Photograph showing haptic gloves woven from an intelligent fibre system. Scale bar, 8 mm. o, Heatmap showing the designable distribution of the electrical stimulation intensity on the surface of the haptic glove. p, Statistical diagram of the stimulus output from the haptic gloves before and after washing.

Microfabrication of Microfluidics

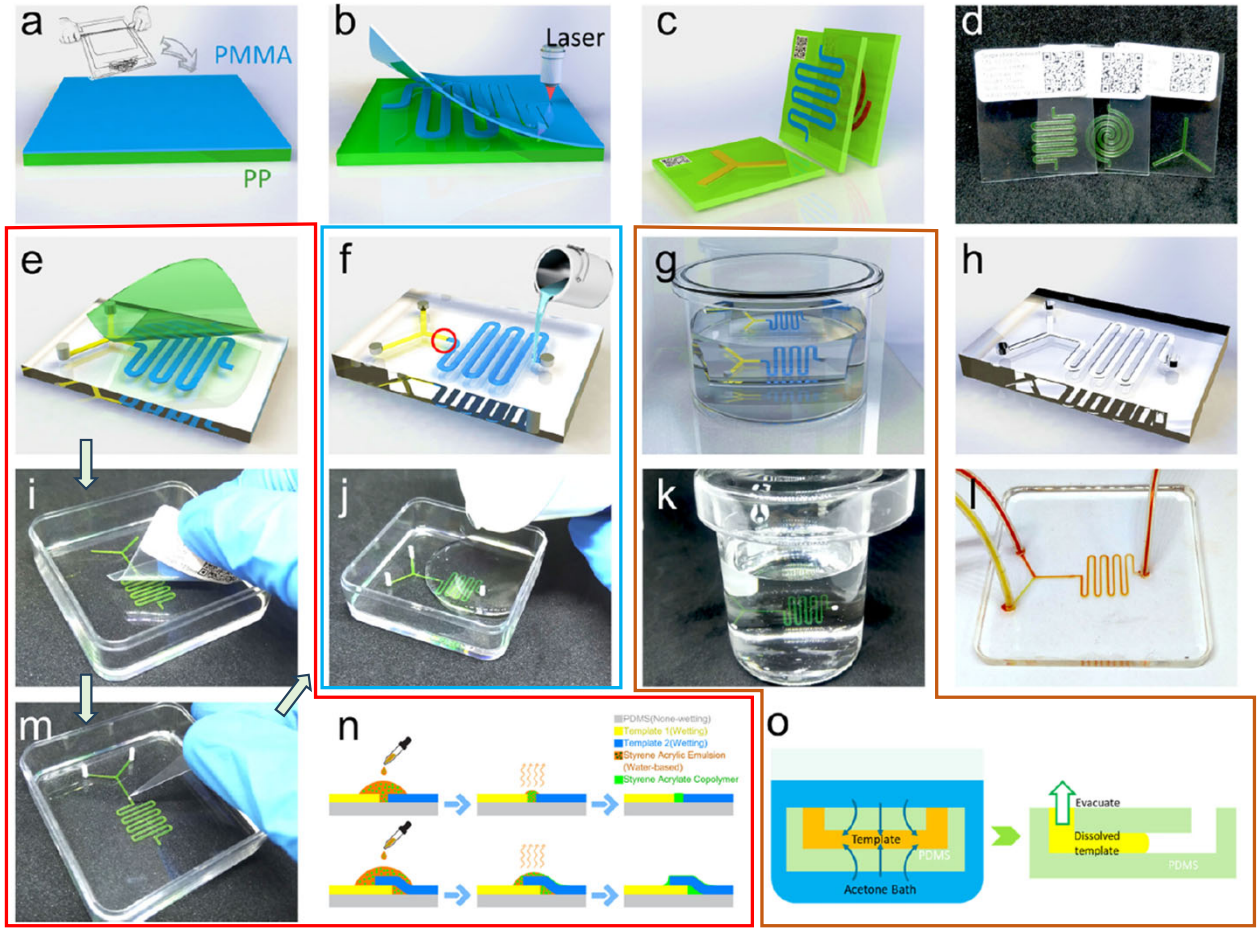


Figure 2. Fabrication process of creating microfluidic devices.
(a–c) Schematic illustrations of preparing PMMA stickers on PP backing using laser cutting.
(a) Coating the PMMA film on the PP sheet.
(b) Laser cutting of PMMA patterns and removal of the unnecessary PMMA film.
(c) Stickers of different microfluidic structures.
(d) Laser-cut microfluidic stickers.
(e–h) Schematic illustrations of creating microfluidics using the stickers.
(e) Arranging and sticking the stickers on PDMS substrate.
(f) Casting liquid PDMS and curing.
(g) Acetone bathing (to dissolve PMMA and polystyrene-acrylate copolymer).
(h) Completed microfluidic chip.
(i–l) Photograph of the process shown in (e)–(g).
(m) Photograph of linking separate stickers with styrene acrylate copolymer emulsion.
(n) Schematic illustration of wettability-guided emulsion linking of the stickers shown in (f) when two stickers are not in contact (top) and stickers overlap (bottom).
(o) Schematic illustration of dissolving the template and evacuating the chip. Left: dissolving the template sticker in an acetone bath. Right: evacuation of the chip.

Lai 2019, Sticker Microfluidics- A Method for Fabrication of Customized Monolithic Microfluidics

Microinjection Moulding

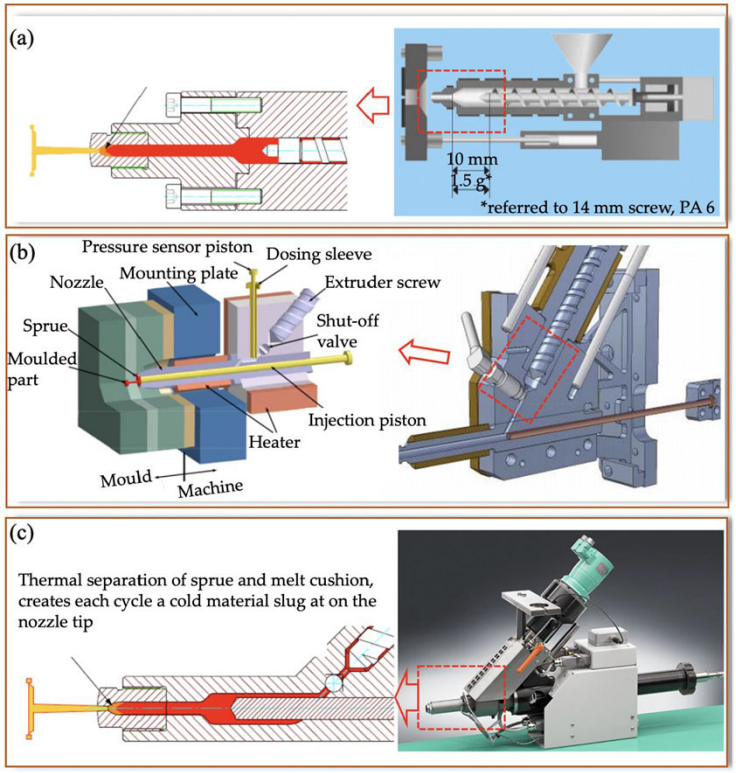


Figure 5. Microinjection moulding system: (a) one-step system, (b) two-step system (Arburg new microinjection module), and (c) three-step system (Microsystem50).

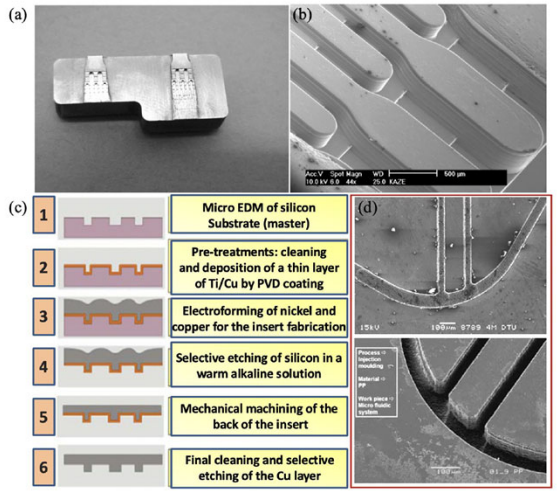


Figure 20. (**a**) Details of microchannel network of electroplated nickel mould insert and (**b**) microinjection moulded part for agglutination assays [93], (**c**) process chain, and (**d**) nickel mould insert and microchannels on microinjection moulded part [95].

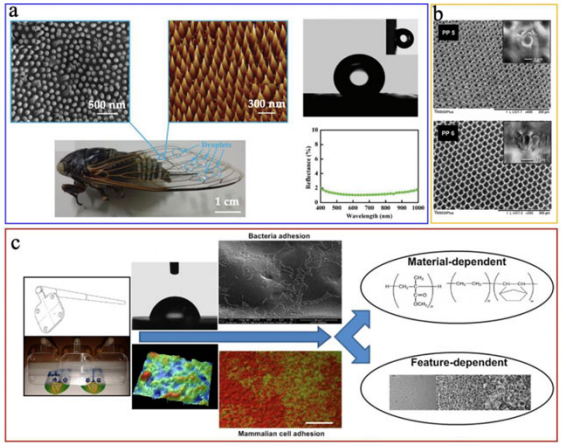


Figure 29. Applications of microinjection moulded functional micro/nano structured surfaces: (**a**) antireflective surfaces [127], (**b**) hydrophobic surfaces [128], (**c**) cell-adhesion surface [131].

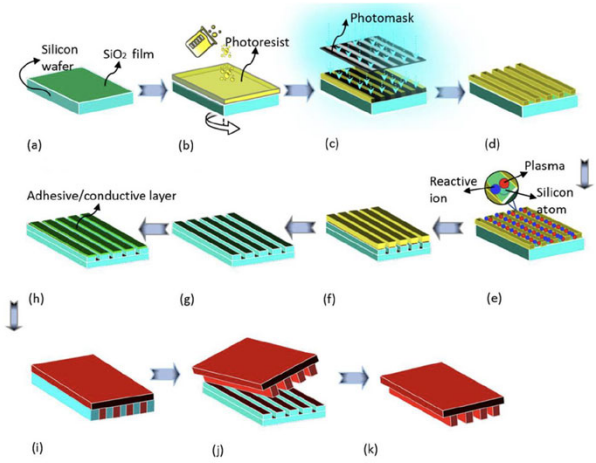


Figure 21. Processing steps required for preparing nickel mould insert: (**a**) silicon wafer preparation, (**b**) spin coating of photoresist, (**c**) exposure, (**d**) development, (**e**) silicon etching, (**f**) etched silicon with the photoresist, (**g**) patterned silicon, (**h**) metallization, (**i**) electroforming, (**j**) demoulding, and (**k**) electroformed nickel mould [96].

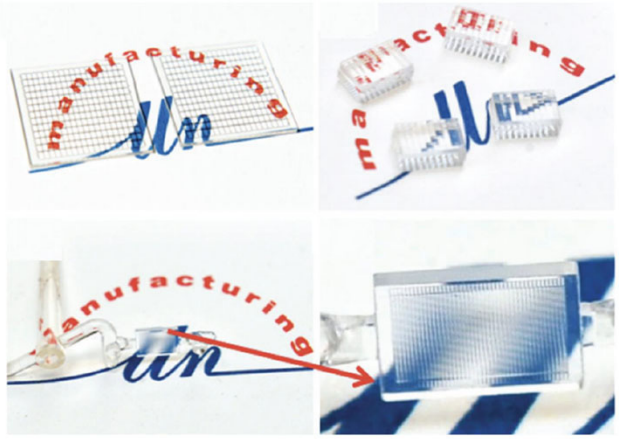


Figure 30. Microinjection moulded micro lenes array [133].

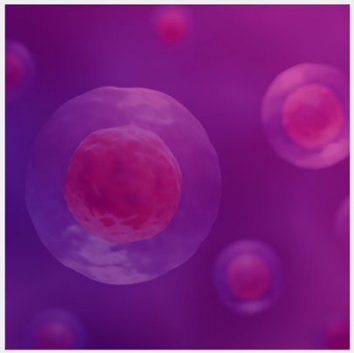
Zhang 2022, A review of microinjection moulding of polymeric micro devices

Nanozyme

Nanozyme

SPECIAL ISSUE

Nanozymes: Design, Mechanisms and Applications



Nanozymes—nanomaterials with intrinsic enzyme-like catalytic activity—have emerged as powerful platforms bridging materials chemistry, catalysis, and biomedicine. This joint special issue by *ACS Applied Materials & Interfaces* and *ACS Applied Nano Materials* presents a comprehensive collection of more than 50 cutting-edge papers by authors from 8 countries, spanning rational design, mechanistic insights, and emerging applications of nanozymes.

Nanozymes - nanomaterials with intrinsic enzyme-like catalytic activity - have emerged as powerful platforms bridging materials chemistry, catalysis, and biomedicine. Since their taking off in the field in 2007, they have evolved from serendipitous catalytic materials to intelligent catalytic systems capable of precise regulation of biological reactions and environmental adaptation. Recent advances in single-atom anozymes (SAzymes), oxygen-vacancy engineering, and biointerface adaptation have greatly accelerated the understanding and applications of nanozyme catalysis.

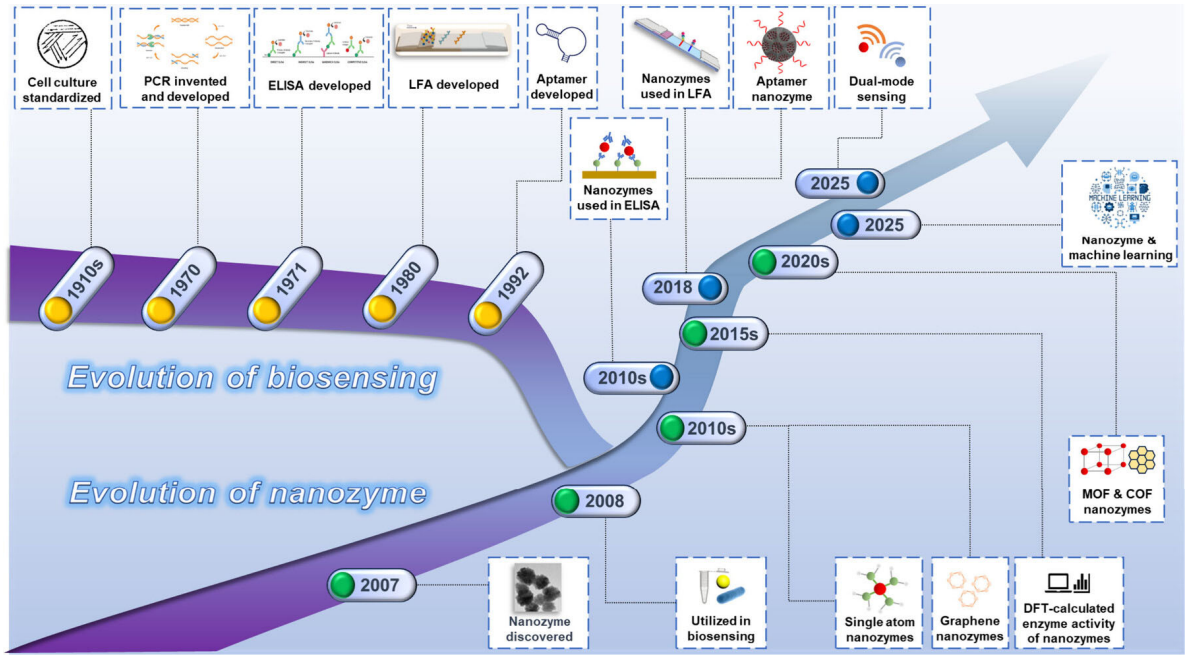


Figure 1. Development of biosensing (from cell culture to nanozymes as biosensors)

Fan 2026, A new era of nanozyme research- Rational design, mechanistic insights, and emerging applications

https://pubs.acs.org/page/vi/nanozymes?

Cheng 2025, Biomimetic design of tunable nanozymes for microbial detection- A review

Nanozyme

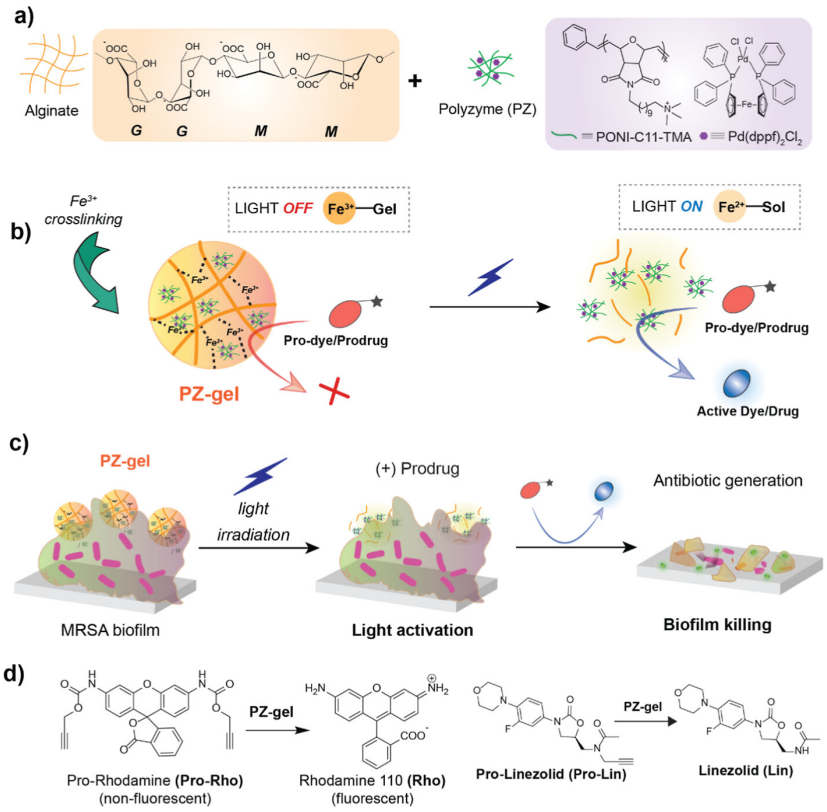
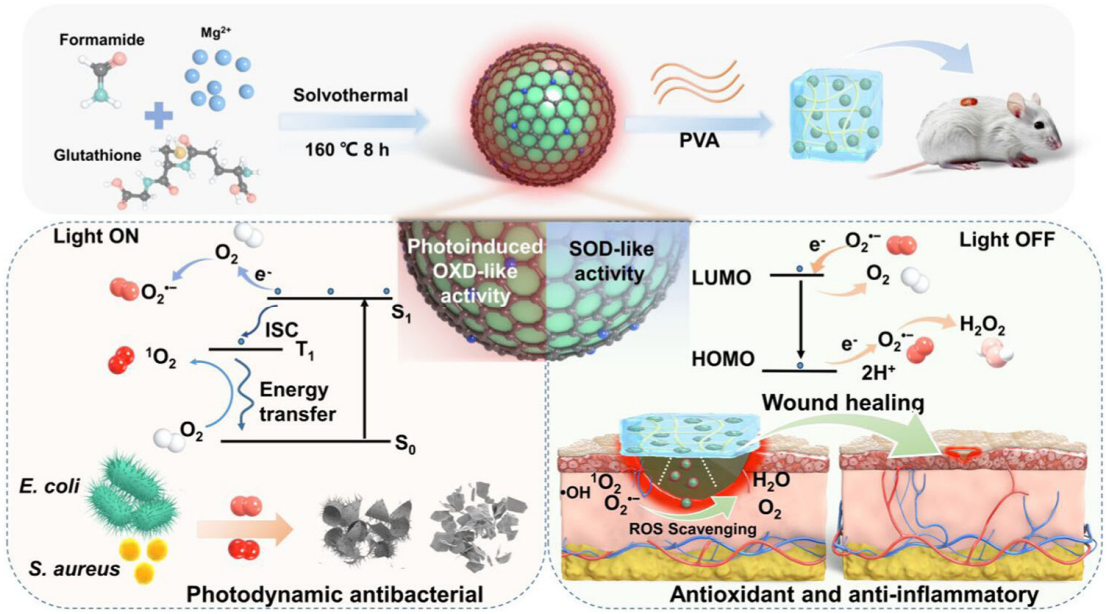


Figure 1. (a) Structures of alginate, Pd catalyst, and polymer. (b) Schematic representation of light-triggered "turn-on" PZ-gel dissolution and bioorthogonal activation. (c) Schematic representation of bioorthogonal activation of a pro-antibiotic with PZ-gel in light for biofilm reduction. (d) Pro-dye/dye (Pro-Rho/Rho) and pro-antibiotic/antibiotic (Pro-Lin/Lin) used in studies.

Gupta 2025, Light-triggered bioorthogonal nanozyme hydrogels for prodrug activation and treatment of bacterial biofilms



Scheme 1. Synthesis of Mg-CDs and their antibacterial and anti-inflammatory applications.

Shi 2025, Photoswitchable antioxidant and prooxidant activities of Mg-doped carbon dot nanozymes as antibacterial and anti- inflammatory agents

Nanozyme

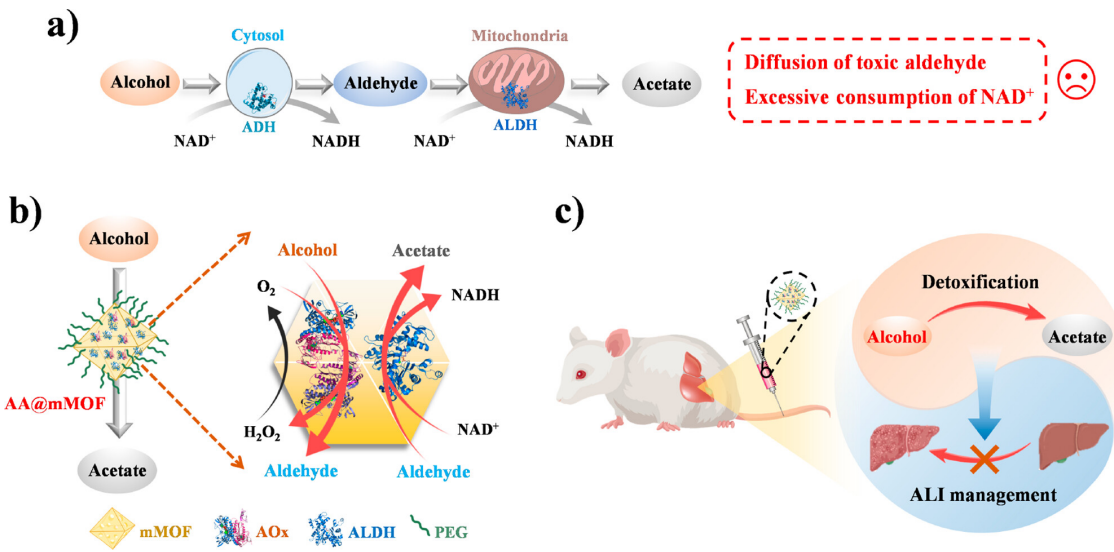
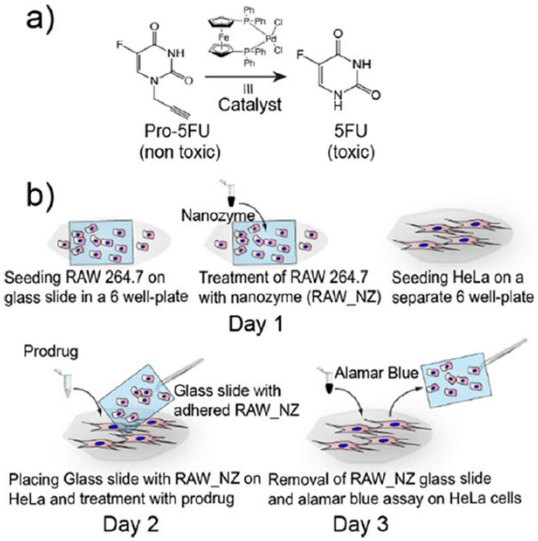
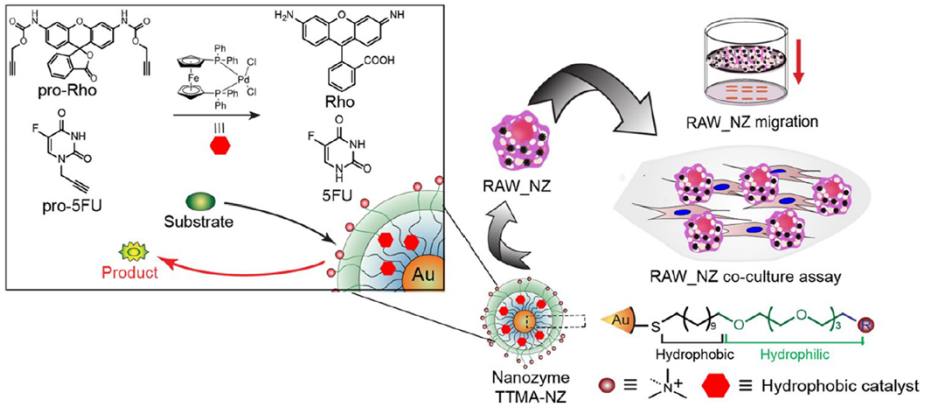


Figure 1. Schematic illustration of the design of confined cascade metabolic reprogramming nanoreactor for targeted alcohol detoxification and ALI management. (a) Alcohol metabolism pathway in hepatocytes. (b) Reprogramming of alcohol metabolism in AA@mMOF nanoreactor via confined cascade AOx/CAT/ALDH reaction. (c) AA@mMOF nanoreactor for *in vivo* alcohol detoxification and ALI management.

Geng 2023, Confined cascade metabolic reprogramming nanoreactor for targeted alcohol detoxification and alcoholic liver injury management





Das 2022, Macrophage-encapsulated bioorthogonal nanozymes for targeting cancer cells

Drink Twice More!

Aids for drinkers

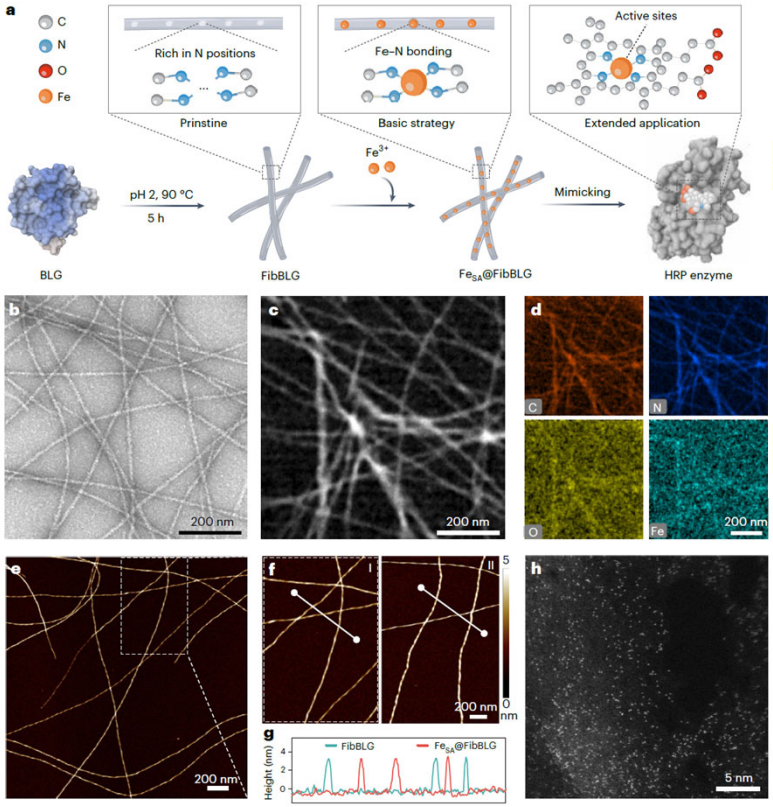
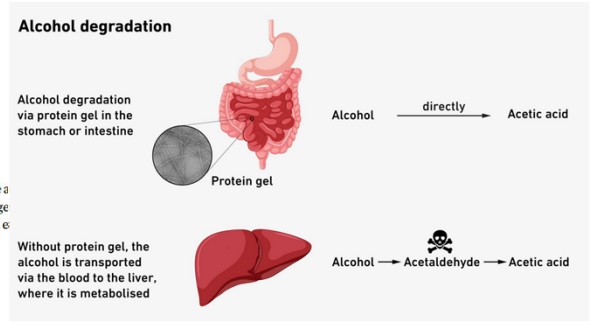
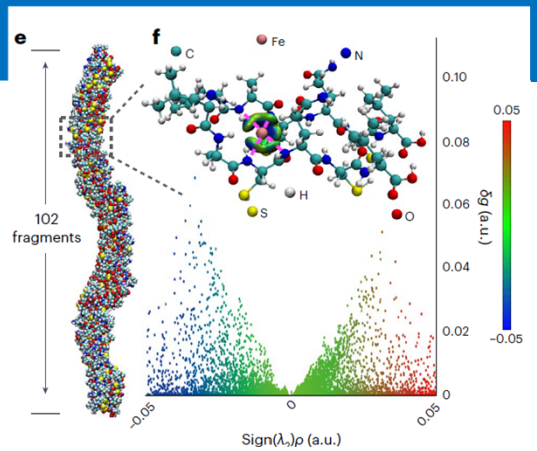


Fig. 1 | Synthesis and morphology characterization of Fe_{SA}@FibBLG. **a**, Illustration of the synthesis process of Fe_{SA}@FibBLG. **b**–**d**, TEM image (**b**), HAADF-STEM image (**c**) and the corresponding EDS mapping images (**d**) of Fe_{SA}@FibBLG. **e**–**g**, AFM images of Fe_{SA}@FibBLG (**e**, **f** (**I**)) and FibBLG (**f** (**II**)) on the mica surface and (**g**) the corresponding height profiles of the white a lines. **h**, Representative HAADF-STEM image of Fe_{SA}@FibBLG. The image presented in **b**–**f**,**h** are representative of six technical replicates ($n = 6$), e yielding similar results.

Constructing effective antidotes to reduce global health impacts induced by alcohol prevalence is a challenging topic. Despite the positive effects observed with intravenous applications of natural enzyme complexes, their insufficient activities and complicated usage often result in the accumulation of toxic acetaldehyde, which raises important clinical concerns, highlighting the pressing need for stable oral strategies. Here we present an effective solution for alcohol detoxification by employing a biomimetic-nanozyme amyloid hydrogel as an orally administered catalytic platform. We exploit amyloid fibrils derived from β-lactoglobulin, a readily accessible milk protein that is rich in coordinable nitrogen atoms, as a nanocarrier to stabilize atomically dispersed iron (ferrous-dominated). By emulating the coordination structure of the horseradish peroxidase enzyme, the single-site iron nanozyme demonstrates the capability to selectively catalyse alcohol oxidation into acetic acid, as opposed to the more toxic acetaldehyde. Administering the gelatinous nanozyme to mice suffering from alcohol intoxication significantly reduced their blood-alcohol levels (decreased by 55.8% 300 min post-alcohol intake) without causing additional acetaldehyde build-up. Our hydrogel further demonstrates a protective effect on the liver, while simultaneously mitigating intestinal damage and dysbiosis associated with chronic alcohol consumption, introducing a promising strategy in effective alcohol detoxification.





Hydrogel formation

Gelation of Fe_{SA}@FibBLG dispersion containing AuNPs (Fe_{SA}@AH) was achieved following our previously reported procedure with some modifications[40]. For the synthesis of AuNPs, all glassware was cleaned with freshly prepared aqua regia (HCl:HNO_3 = 3:1 vol/vol) and then thoroughly rinsed with water. A 2 ml solution of BLG fibrils (2.0 wt%, pH 2.0) was mixed with a 40 mM $HAuCl_4$ solution to reach a final protein:gold mass ratio of 14.7:1. The mixture underwent a chemical reduction through the dropwise addition of a $NaBH_4$ solution (0.8 ml) under a nitrogen atmosphere. The resulting solution was then dialysed to remove any remaining $NaBH_4$ and concentrated to 2 ml with a dialysis membrane (Spectra/Por, molecular weight cut-off, 6–8 kDa, Spectrum Laboratories) against a 6 wt% PEG solution ($M_r \approx 35{,}000$, Sigma-Aldrich) at pH 2.0. TEM imaging of AuNPs stabilized by BLG fibrils revealed three-dimensional particles with an average size of 1.32 nm (Supplementary Fig. 21a), determined by analysing six TEM images using ImageJ software v.1.8.0. For the preparation of Fe_{SA}@AH, 2 g of Fe_{SA}@FibBLG powder was dissolved in the resulting AuNP-attached BLG fibril solution (2 ml). The mixture was then transferred into a plastic syringe, the top part of which had been previously cut. The plastic syringe was covered with a section of a dialysis tube (Spectra/Por, molecular weight cut-off, 6–8 kDa), and the head of the syringe was positioned in direct contact with an excess of 300 mM NaCl solution at pH 7.4 for at least 16 h in a 4 °C cold room to facilitate gelation. The resulting hydrogel sample was kept under 4 °C. The working hydrogel was freshly prepared by mixing the aforementioned hydrogel with 0.1 ml of a glucose solution (8.0 M) immediately before further characterization or detoxification use. A BLG fibril hydrogel was obtained using the same procedure, except that the Fe_{SA}@FibBLG was replaced with an equal amount of BLG fibril dispersion.

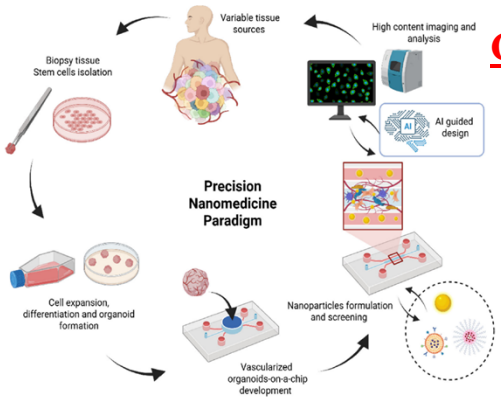
Su 2024, Single-site iron-anchored amyloid hydrogels as catalytic platforms for alcohol detoxificationw

Amandolare 2024, New gel makes alcohol 50% less toxic, curbs organ damage

https://ethz.ch/en/news-and-events/eth-news/news/2024/05/press-release-new-gel-breaks-down-alcohol-in-the-body.html

Nanomedicine

Precision Nanomedicine



Cell culture in 3D

Figure 1. Schematic depicting the emerging paradigm of nanoparticle development for precision nanomedicine.

Table 1. Comparison of preclinical models for anoparticle development

Model	Advantages	Disadvantages
2D Cell Culture *Fast, cheap, but oversimplified*	◆ High-throughput Nanoparticles screening ◆ Simple and cost-effective ◆ Easy to analyze uptake and toxicity ◆ Standardized protocols across labs	▼ No tissue-like barriers or ECM ▼ Overestimates Nanoparticles uptake ▼ No gradients (oxygen, nutrients) ▼ Poor predictor of in vivo behaviour
3D Spheroids *Tumor-like, scalable, semi-physiological*	◆ Nanoparticles penetration and retention modelling ◆ Tumour resistance and hypoxia mimicking ◆ Spatial toxicity distribution ◆ Compatible with imaging and HTP platforms	▼ Limited cell diversity ▼ Lacks vasculature and immune components ▼ Difficult to control spheroid uniformity ▼ Still lacks systemic response modelling
Organoids *Patient-relevant, architecturally complex*	◆ Personalized Nanoparticles efficacy testing ◆ Genetic background and disease state modelling ◆ Organ-specific Nanoparticles transport mimicking ◆ Long-term tracking of Nanoparticles fate	▼ Batch-to-batch variability ▼ Time- and resource-intensive ▼ Lower throughput than 2D/3D ▼ Limited vasculature and immune crosstalk
Microphysiological Systems *Dynamic, systemic, human-relevant*	◆ Real-time monitoring of Nanoparticles biodistribution ◆ Flow, shear stress, and organ–organ interactions simulation ◆ Immune and vascular Nanoparticles interaction studies ◆ Reduced reliance on animal models	▼ Technically complex ▼ High cost and specialized equipment ▼ Not yet standardized ▼ Low throughput, limited scalability

Usability ↓ Relevance

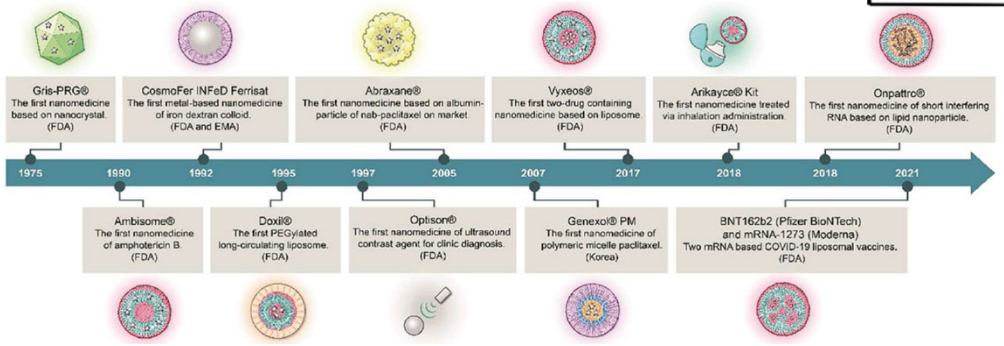


Figure 3. Historical timeline of major nanomedicine development. (Liu, Q.; Zou, J.; Chen, Z.; He, W.; Wu, W. Current research trends of nanomedicines. Acta Pharmaceutica Sinica B 2023, 13 (11), 4391−4416.)

Silvani 2025, Precision nanomedicine A necessary convergence of nanodrug development, organotypic models and microphysiological systems

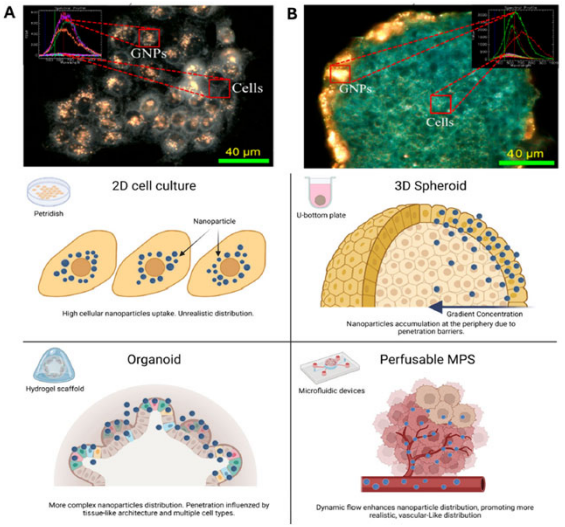


Figure 4. Preclinical models for testing efficacy of nanoparticles. (A) Gold nanoparticles uptake in 2D monolayer of HeLa in a 96-well microplate. (B) Gold nanoparticle uptake in 3D spheroid of HeLa in a U-bottom 96-well microplate. (Bromma, K.; Alhussan, A.; Perez, M. M.; Howard, P.; Beckham, W.; Chithrani, D. B. **Three-dimensional tumor spheroids** as a tool for reliable investigation of combined gold)

Current Hurdles of Nanomedicines

The field of nanomedicine has significantly influenced research areas such as drug delivery, diagnostics, theranostics, and regenerative medicine; however, the further development of this field will face significant challenges at the regulatory level if related guidance remains unclear and unconsolidated.

The major challenges associated with nanomedicine regulation.
- Lack of a unified definition or classification of nanomedicines/nanomaterials.
- Lack of agreed regulations.
- Analytical methods differ for each nanomaterial.
- PK profiles diverge from standardized constituent materials.
- Stability issues after scale-up for manufacturing.

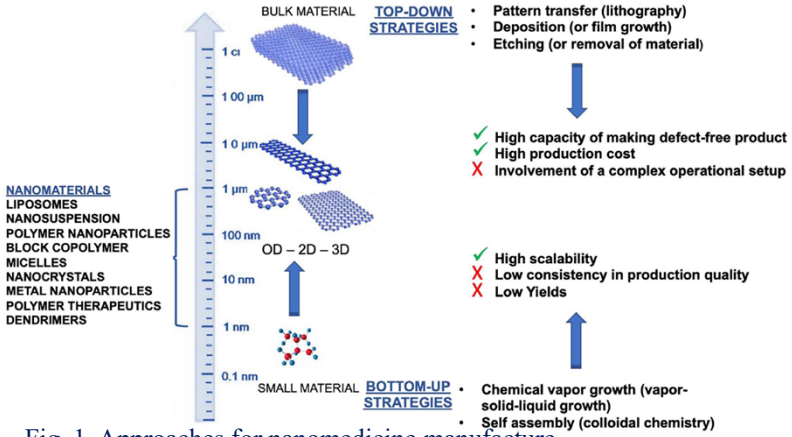


Fig. 1. Approaches for nanomedicine manufacture.

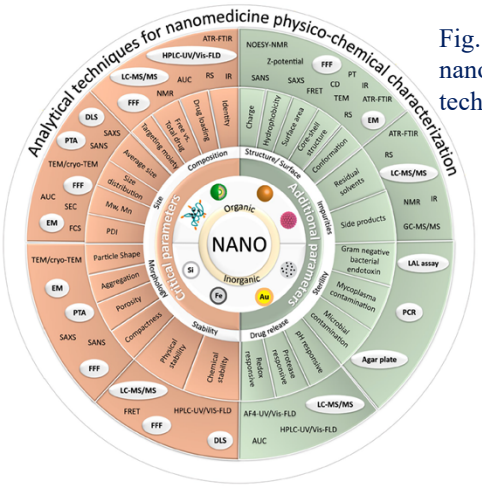


Fig. 3. Critical and additional parameters of nanomedicines and corresponding analytical techniques for their characterization.

Quality by Design (QbD)

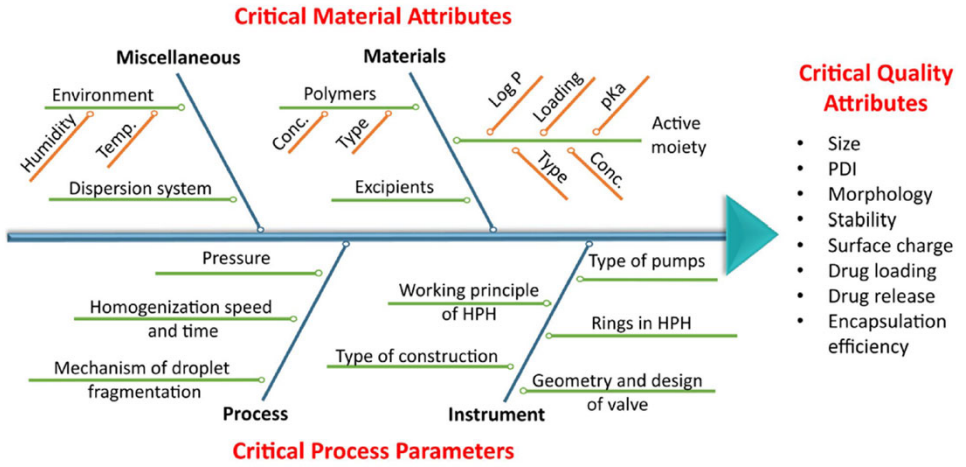


Fig. 2. Representation of those **critical material attributes (CMAs)** and **critical process parameters (CPPs)** that cause discrepancy and variability of **critical quality attributes (CQAs)** during the rational design and production of nanomedicines.

Despite the promising advances made in preclinical animal models, the clinical translation of nanomedicines remains a slow, biased, and often failed affair. There exists a general lack of specific protocols, and the characterization of materials and biological mechanisms and the statistical analyses often employed remain inadequate. Moreover, **the vast and significant heterogeneity of models adopted**, a reluctance to share results, and **the inaccuracy of study design** have hampered the translation of nanomedicines into late clinical trial stages.

Đorđević 2022, Current hurdles to the translation of nanomedicines from bench to the clinic

Lipid Nanoparticles

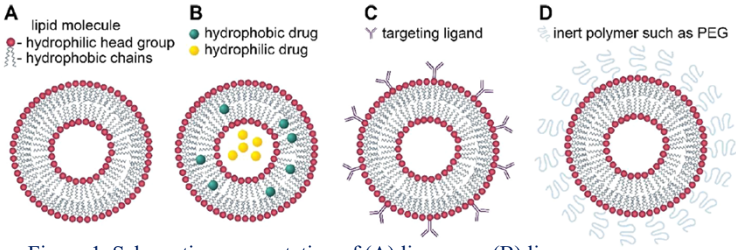


Figure 1. Schematic representation of (A) liposome, (B) liposome encapsulating hydrophobic and hydrophilic drugs, (C) immunoliposome functionalized with targeting ligands, and (D) sterically stabilized ("stealth") liposome functionalized with inert polymers such as PEG.

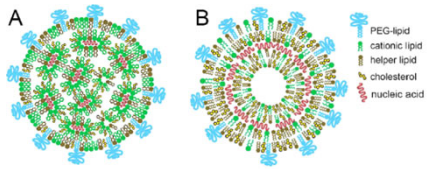


Figure 2. Suggested structures of lipid nanoparticle nucleic acid carriers: nucleic acids organized in inverse lipid micelles inside the nanoparticle (A); nucleic acids intercalated between the lipid bilayers (B).

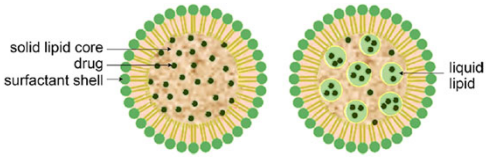


Figure 3. Schematic presentation of a solid lipid nanoparticle (left) and a nanostructured lipid carrier (right).

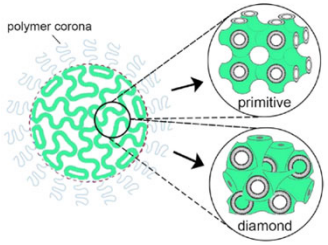


Figure 4. Cubosomes are nanoparticles comprising lipid in a bicontinuous bilayer cubic phase (either primitive or diamond type).

Liquid-crystalline lipid cubic phases consist of single lipid bilayers that form a bicontinuous periodic lattice structure with pores formed by two interwoven water channels.

Lipid nanoparticles (LNPs) play a key role in effectively protecting and transporting mRNA to cells. LNPs exhibit more complex architectures and enhanced physical stabilities than liposomes (an early version of LNPs)

Note: Liposome ≠ LNP

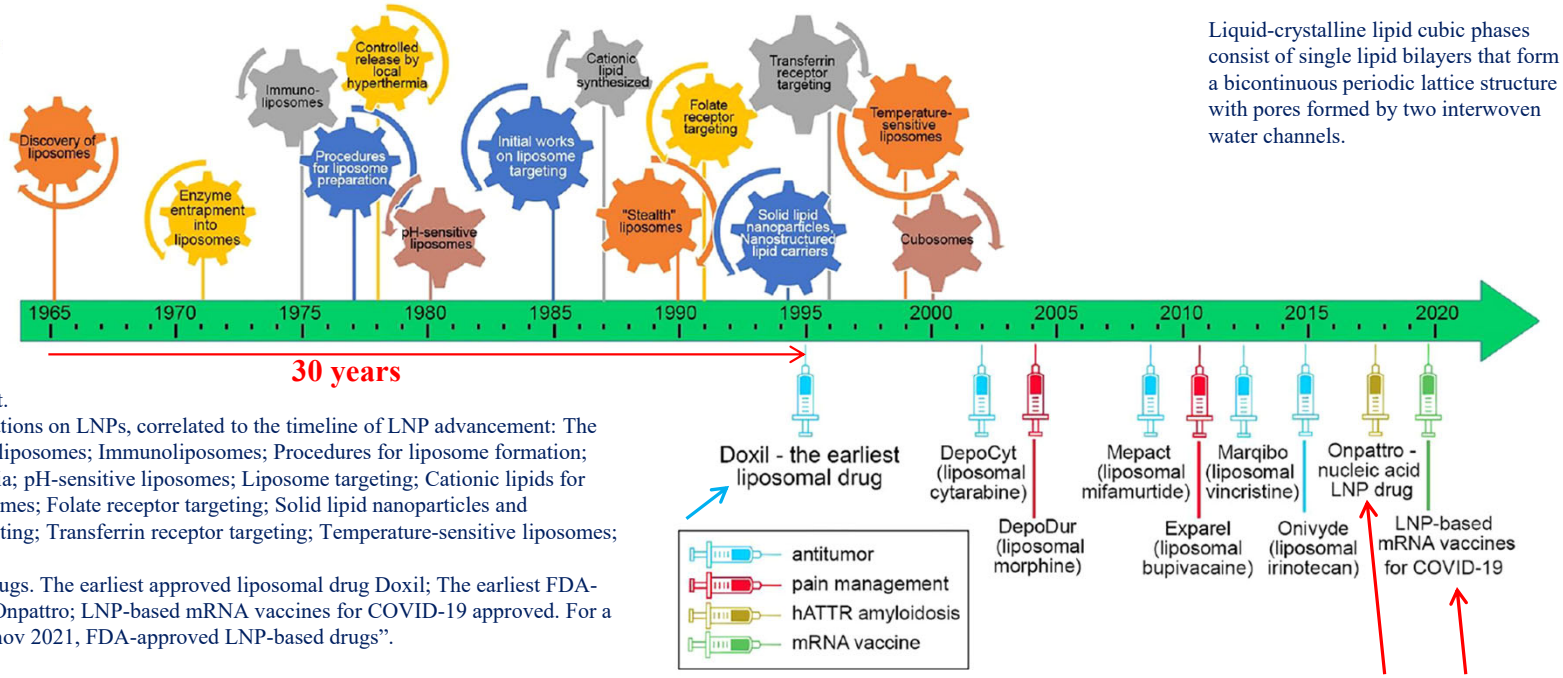


Figure 5. Timeline of liposome/LNP advancement.
(Upper part) Technological advancement. Publications on LNPs, correlated to the timeline of LNP advancement: The discovery of liposomes; Enzyme entrapment into liposomes; Immunoliposomes; Procedures for liposome formation; Thermoresponsive liposomes to local hyperthermia; pH-sensitive liposomes; Liposome targeting; Cationic lipids for gene delivery; Long-circulating ("Stealth") liposomes; Folate receptor targeting; Solid lipid nanoparticles and nanostructures lipid carriers; HER2 receptor targeting; Transferrin receptor targeting; Temperature-sensitive liposomes; Stimuli-responsive liposomes; Cubosomes.
(Lower part) Examples of FDA-approved LNP drugs. The earliest approved liposomal drug Doxil; The earliest FDA-approved LNP-based nucleic acid (siRNA) drug Onpattro; LNP-based mRNA vaccines for COVID-19 approved. For a full list of approved LNP-based drugs, see "Tenchov 2021, FDA-approved LNP-based drugs".

Tenchov 2021, Lipid Nanoparticles - From liposomes to mRNA vaccine delivery, a landscape of research diversity and advancement

mRNA Lipid Nanoparticle Vaccines for COVID-19

Ethanol (1 vol)

Buffer (3 vol)

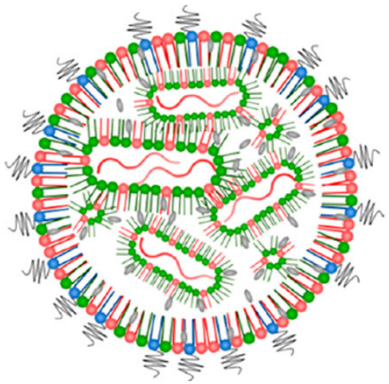
Cholesterol (47.5)

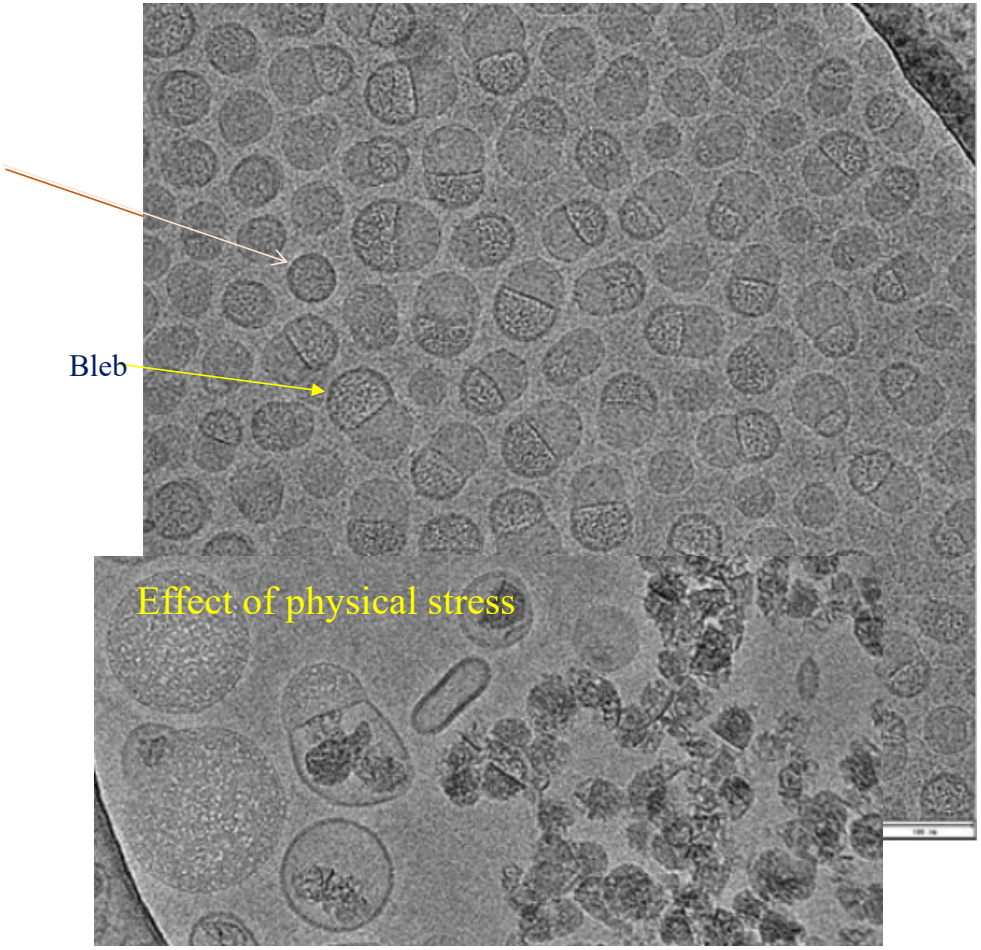
Ionizable lipid (40)

DSPC (10.5)

PEG-DMG (2)

Polyanionic mRNA (4% w/w to lipid)





Pfizer-BioNTech, BNT162b2

- Cholesterol
- ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate)
- 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC)
- 2-[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide
- Nucleoside modified RNA

Moderna, mRNA-1273

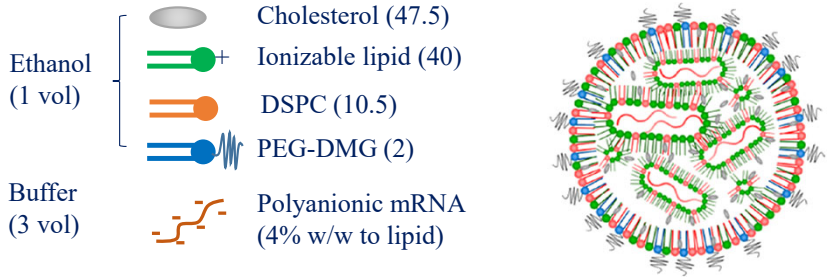
- Cholesterol
- Sphingomyelin-102(SM-102)
- 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC)
- Polyethylene glycol [PEG]2000 dimyristoyl glycerol [DMG]
- mRNA encoding S protein

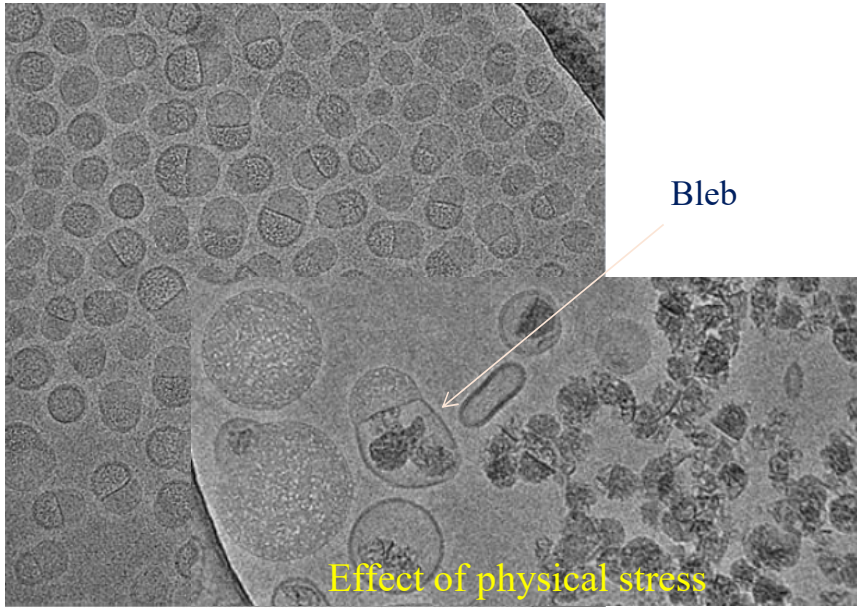
Elia 2021, Design of SARS-CoV-2 hFc-conjugated receptor-binding domain mRNA vaccine delivered via lipid nanoparticles, ACS Nano

Khurana 2021, Role of nanotechnology behind the success of mRNA vaccines for COVID-19. Nano Today 38: 101142
Park 2021, Non-viral COVID-19 vaccine delivery systems, Adv. Drug Del. Rev. 169: 137-151
Schoenmaker 2021, mRNA-lipid nanoparticle COVID-19 vaccines. Int. J. Pharm. 601: 120586

Brader 2021, Encapsulation state of messenger RNA inside lipid nanoparticles. Biophys. J. 120: 1-5.

Beyond Lipid Nanoparticle Delivery Systems





Elia 2021, Design of SARS-CoV-2 hFc-conjugated receptor-binding domain mRNA vaccine delivered via lipid nanoparticles, ACS Nano

Khurana 2021, Role of nanotechnology behind the success of mRNA vaccines for COVID-19. Nano Today 38: 101142

Park 2021, Non-viral COVID-19 vaccine delivery systems, Adv. Drug Del. Rev. 169: 137-151

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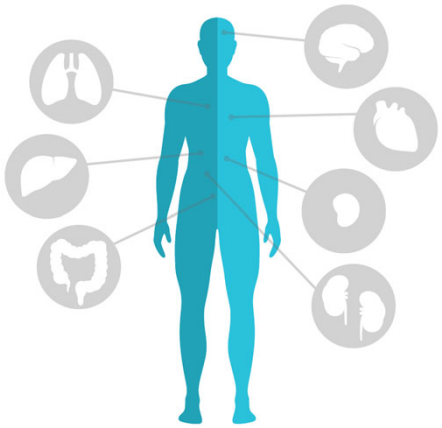
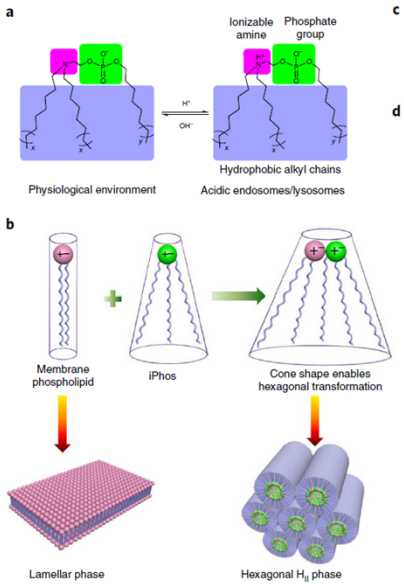
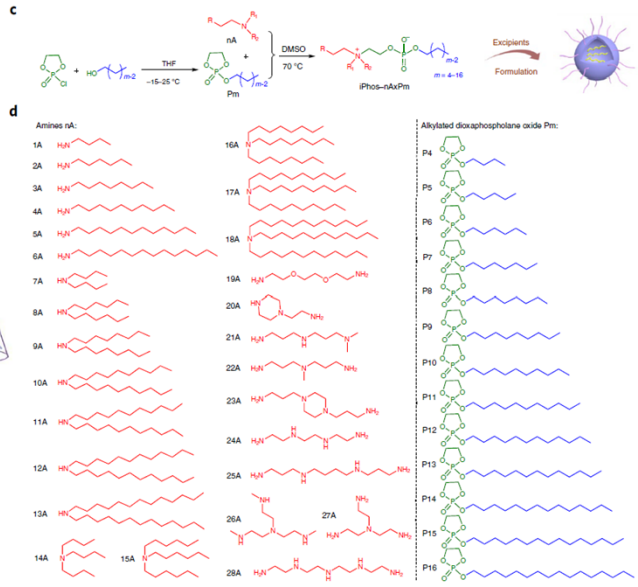


Biodistribution is fundamental to identifying target organs and anticipating safety and efficacy

Precision Nanosystems 2023, Lipid nanoparticles (LNPs) gold standard delivery technology for small molecules and nucleic acids

Organ-selective mRNA delivery?





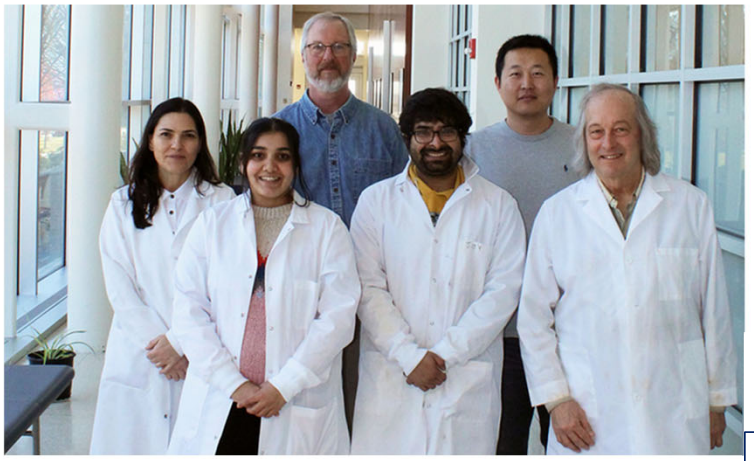
Liu 2021, Membrane-destabilizing ionizable phospholipids for organ-selective mRNA delivery and CRISPR–Cas gene editing, Nature Materials 20: 701-710, 2021.

Optimized mRNA Delivery

Purdue mRNA therapy delivery system proves to be shelf-stable, storable

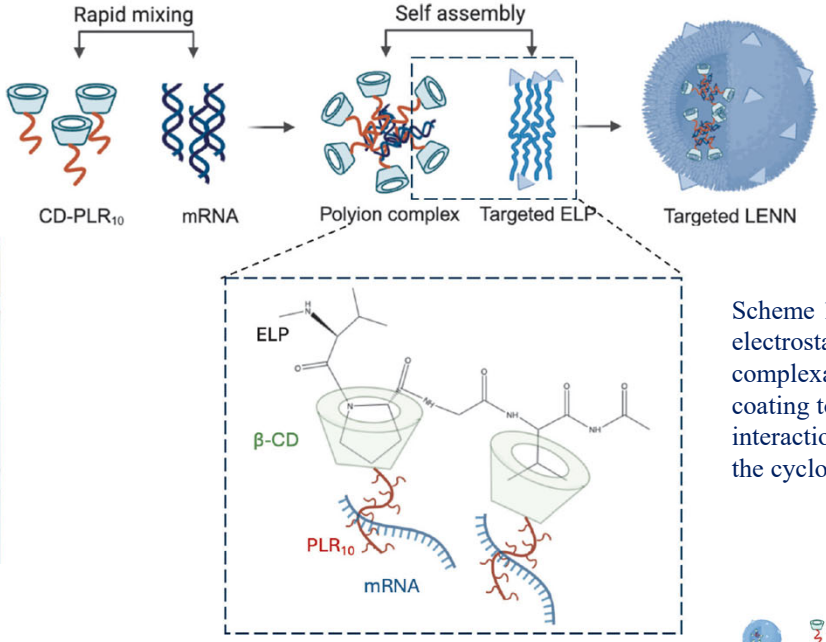
System targets upregulated receptors on bladder cancer cells, leading to new protein expression within them

January 16, 2026



(From left, Christina Ferreira, Saloni Darji, Bennett Elzey, Joydeep Rakshit, Feng Qu, and David Thompson)

https://www.purdue.edu/newsroom/2026/Q1/purdue-mrna-therapy-delivery-system-proves-to-be-shelf-stable-storable/



Scheme 1. Conceptual diagram of the initial electrostatic condensation step for mRNA complexation with CD-PLR10 followed by ELP coating to form LENN via hydrophobic host:guest interactions between the ELP prosthetic groups and the cyclodextrin cavities.

LENN: layer-by-layer elastin-like polypeptide nucleic acid nanoparticle (LENN), a delivery vehicle formed via self-assembly of elastin-like polypeptides (ELP) and cyclodextrin-polyarginine (CD-PLR10) components that are biorenewable and versatile for nucleic acid delivery. LENN formulations maintain their stability, encapsulation efficiency, excellent in vitro and in vivo performance, while retaining their activity after lyophilization and rehydration.

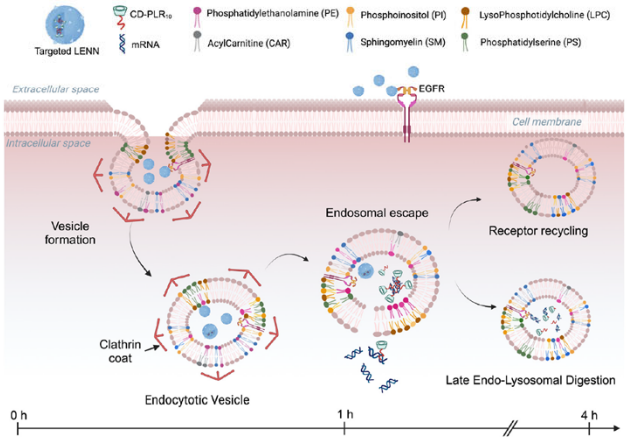
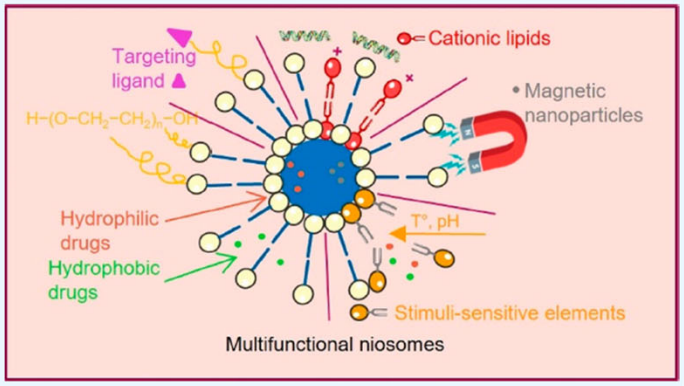


Fig. 7. Conceptual diagram of the endocytosis mechanism and endosomal escape of V24-EGF LENN mRNA cargo in T24 bladder cancer cells.

Darji 2025, Optimizing mRNA delivery with targeted elastin-like polypeptide-based LENN formulations Insights into the endocytosis mechanism

Niosomes

ABSTRACT: Niosomes are a type of vesicular nanocarrier exploited for enhancing the therapeutic efficacy of various drugs in clinical practice. Niosomes comprise a bilayer hydrophobic membrane enclosing a central cavity filled with an aqueous phase, and therefore, they can encapsulate and deliver both hydrophobic and hydrophilic substances. Niosomal nanocarriers are preferred over other bilayer structures such as liposomes due to their chemical stability, biodegradability, biocompatibility, low production cost, low toxicity, and easy storage and handling. In addition, the niosomal membrane can be easy modified by the inclusion of ligands or stimulus-sensitive segments for achieving targeted delivery and triggered release of the encapsulated cargo. This mini-review outlines the current advances in designing functional niosomes and their use as platforms for developing advanced drug and gene delivery systems.



Liposomes and niosomes are both lamellar vesicular systems.
Liposomes are composed of phospholipids (natural/synthetic lipids), while niosomes are formed from non-ionic surfactants.

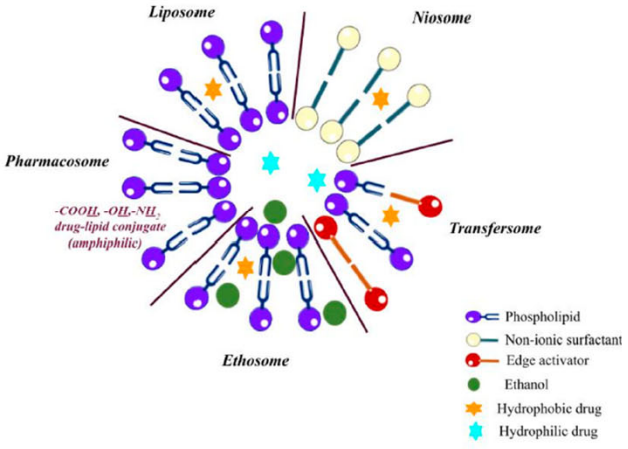


Figure 1. Sketch of different types of vesicular nanocarriers.

Niosomes are vesicular systems formed by nonionic surfactants via self-assembly in aqueous solution assisted by physical agitation or elevated temperature.[2] The use of nonionic surfactants as membrane forming constituents instead of phospholipids overcomes many of the disadvantages associated with liposomes, such as insufficient chemical stability, predisposition of phospholipids to oxidation, high production cost, necessity of special handling, and storage conditions.[3] Their specific structure—an inner aqueous compartment surrounded by a hydrophobic membrane—allows incorporation (and codelivery, respectively) of hydrophobic and hydrophilic drug molecules.[1] Furthermore, niosomes are osmotically active, nontoxic, non-immunogenic, biocompatible, and biodegradable. Initially reported in the 1970s as a feasible approach in the cosmetic industry, niosomes were patented by L'Oreal in the 1980s as a cosmetic product.[2] Their favorable characteristics determine the increased research interest, as well the wide exploitation beyond the scope of cosmetic industry. Over the years, niosomes have been investigated as a promising drug delivery platform for various routes of administration—oral, parenteral, dermal/transdermal, ocular, and pulmonary (Figure 2).[1,3]

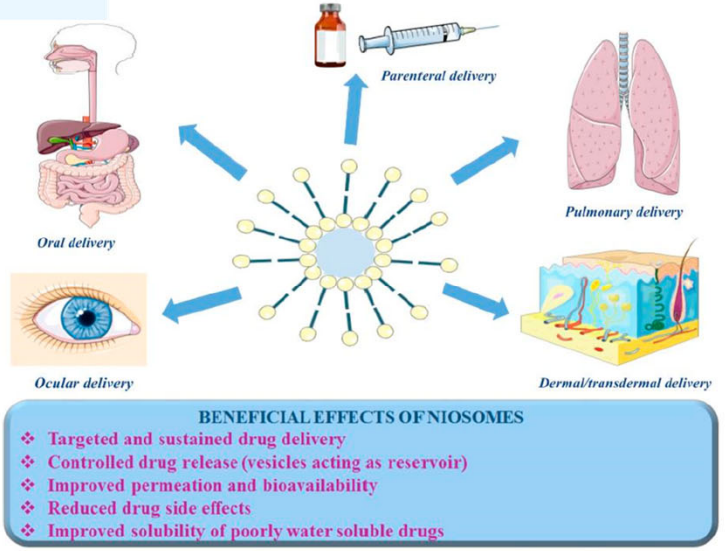


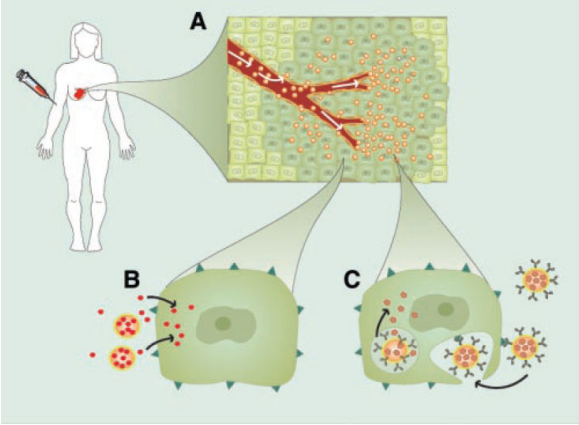
Figure 2. Beneficial effects of niosomes in accordance with the most commonly used delivery routes.

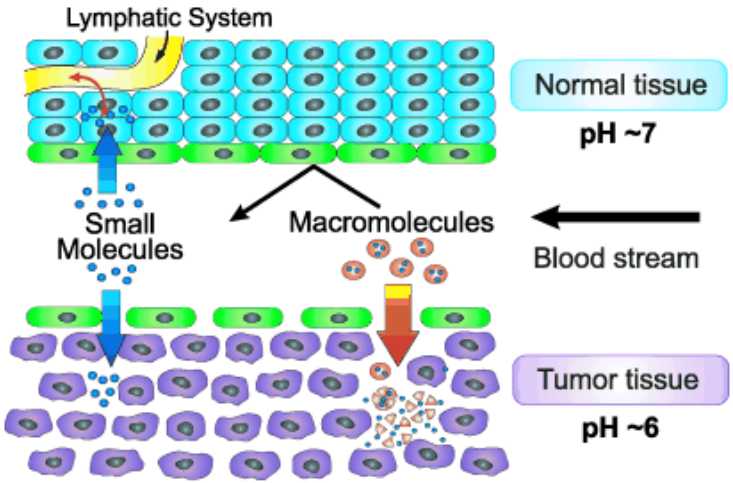
Momekova 2023, Nanoarchitectonics of multifunctional niosomes for advanced drug delivery

Misunderstanding of Nanomedicine

Current Understanding on Drug Targeting of I.V. Administered Systems

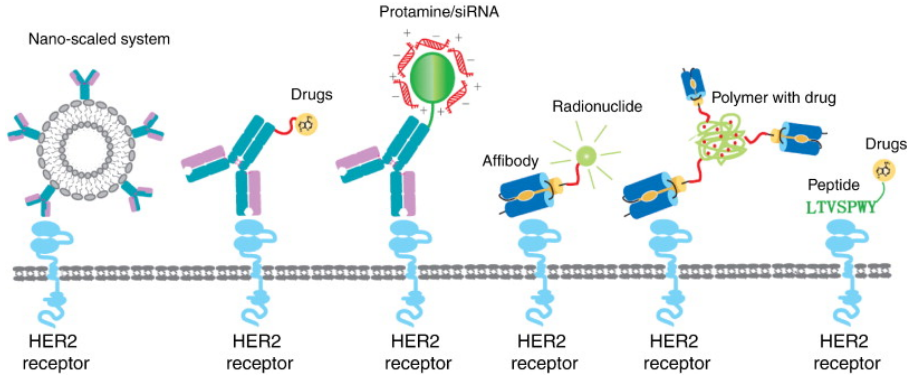
Passive Targeting:
Delivery of plain nanoparticles by blood circulation





Active Targeting:
Delivery of ligand-coated nanoparticles by blood circulation

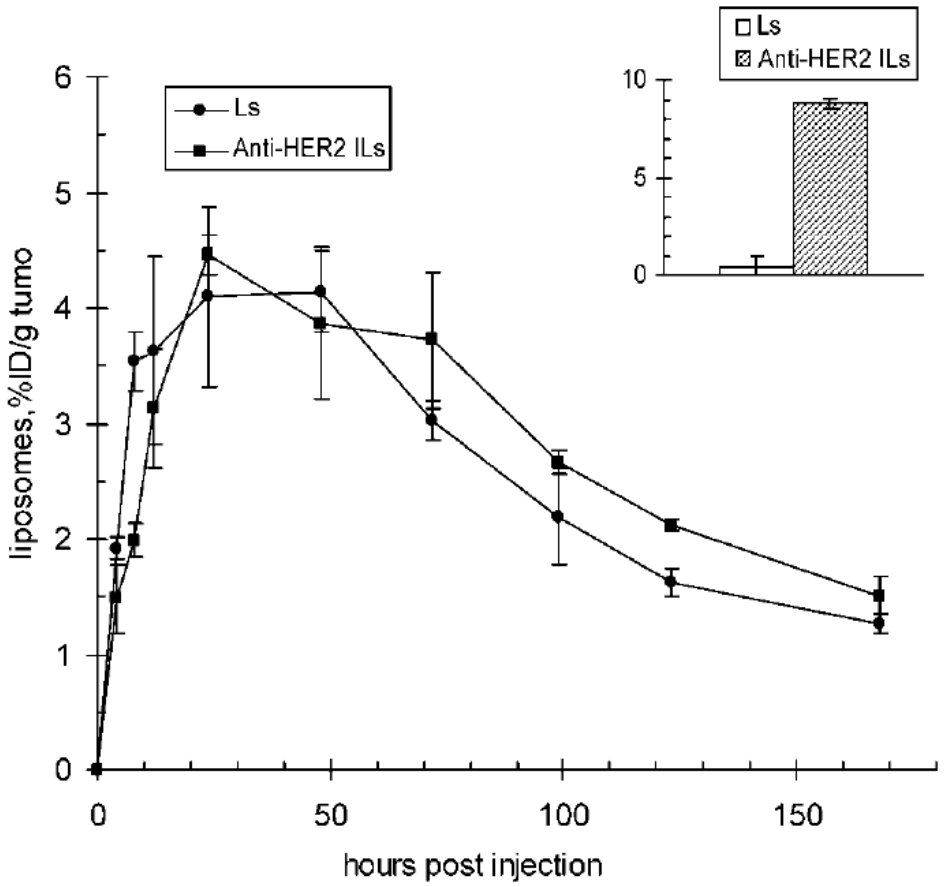
Ligand binds to target cell surface only if nanoparticle formulations reach the target!



The role of HER2 in cancer therapy and targeted drug delivery.
W. Tai, R. Mahato, . Cheng: J. Control. Release146 (3) 264-275, 2010

EPR Effect: Enhanced permeability and retention effect

No Active Targeting by Antibody-Coated Nanoparticles



Dmitri B. Kirpotin, Daryl C. Drummond, Yi Shao, M. Refaat Shalaby, Keelung Hong, Ulrik B. Nielsen, James D. Marks, Christopher C. Benz and John W. Park
Antibody targeting of long-circulating lipidic nanoparticles does not increase tumor localization but does increase internalization in animal models. Cancer Res. 66: 6732-6740, 2006.

Abstract

We describe evidence for a novel mechanism of monoclonal antibody (MAb)–directed nanoparticle (immunoliposome) targeting to solid tumors in vivo. Long-circulating immunoliposomes targeted to HER2 (ErbB2, Neu) were prepared by the conjugation of anti-HER2 MAb fragments (Fab′ or single chain Fv) to liposome-grafted polyethylene glycol chains. MAb fragment conjugation did not affect the biodistribution or long-circulating properties of i.v.-administered liposomes. However, antibody-directed targeting also did not increase the tumor localization of immunoliposomes, as both targeted and nontargeted liposomes achieved similarly high levels (7-8% injected dose/g tumor tissue) of tumor tissue accumulation in HER2-overexpressing breast cancer xenografts (BT-474). Studies using colloidal gold-labeled liposomes showed the accumulation of anti-HER2 immunoliposomes within cancer cells, whereas matched nontargeted liposomes were located predominantly in extracellular stroma or within macrophages. A similar pattern of stromal accumulation without cancer cell internalization was observed for anti-HER2 immunoliposomes in non–HER2-overexpressing breast cancer xenografts (MCF-7). Flow cytometry of disaggregated tumors posttreatment with either liposomes or immunoliposomes showed up to 6-fold greater intracellular uptake in cancer cells due to targeting. Thus, in contrast to nontargeted liposomes, anti-HER2 immunoliposomes achieved intracellular drug delivery via MAb-mediated endocytosis, and this, rather than increased uptake in tumor tissue, was correlated with superior antitumor activity. Immunoliposomes capable of selective internalization in cancer cells in vivo may provide new opportunities for drug delivery. (Cancer Res 2006; 66(13): 6732-40)

ACS Nano Medicine

Welcome to *ACS Nano Medicine*: From Nanoscale Innovation to Clinical Impact

Cite This: *ACS Nano Med.* 2026, 1, 1–2

Paul Ehrlich's early 20th century "magic bullet" (Zauberkugel) concept articulated a transformative vision for medicine, i.e., therapies that precisely target disease while minimizing collateral damage. A century later, nanomedicine has emerged as a powerful realization of this idea, harnessing nanoscale carriers to deliver potent drugs and/or contrast probes selectively to pathological cells. The field has matured from a largely exploratory discipline into a translational engine that is reshaping how we diagnose, monitor, and treat disease. What began as an effort to exploit size-dependent physicochemical phenomena has evolved into a sophisticated convergence of materials science, chemistry, biology, engineering, and clinical medicine. As we enter the next phase of growth, the field faces both unprecedented opportunity and necessary recalibration.

ACS Nano Medicine, the newly launched journal from the American Chemical Society, sits at this technological inflection point charged with capturing foundational advances while setting a clear vision for clinical translation. The journal welcomes studies that not only advance nanoscale science but also illuminate the biological, engineering, and regulatory parameters essential for real-world impact. By embracing work

Over the past year, the field has confronted hard realities as many elegant nanomaterials have struggled to progress beyond proof-of-concept. Challenges related to reproducibility and quality control, product manufacturing and scalability, biological complexity, regulatory pathways, and integration into real-world clinical workflows and care pathways have slowed translation. Rather than signaling failure, these realities mark a long-anticipated transition from a predominantly discovery-driven enterprise to a more mature translation-focused phase. The future of nanomedicine will be defined not by novelty of nanomaterials alone, but by mechanistic clarity, robustness, and clinical relevance.

Looking forward, several themes are poised to define the next decade of nanomedicine. First, a deep mechanistic understanding of nanobio interactions must take center stage. High-impact nanomedicine research must rigorously connect nanoscale structure, morphology, dynamics, and interfacial chemistry to biological function. This includes quantitative understanding of nanobio interactions, transport phenomena, pharmacokinetics and pharmacodynamics, immune engagement, metabolic processes, and degradation pathways across tissues and cellular compartments. Studies

Correct Understanding of the Magic Bullet (& Targeted Delivery)

Paul Ehrlich's Magic Bullet **is defined as a drug specifically targeting (or going straight to) its intended target to treat disease without affecting normal host cells.**

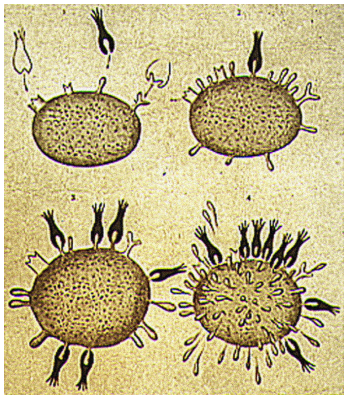
= binding to (or interacting with)

Scientific disciplines of Chemotherapy:
Binding of dyes to certain fabrics & cells.

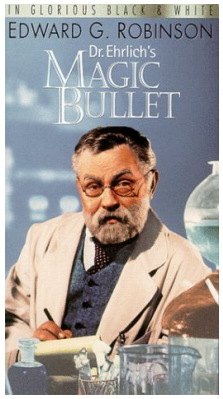
Many chemical molecules have an affinity to tissues, cells, and cellular components

- Sleeping sickness: trypan red.
- Syphilis: Sarvasan 606

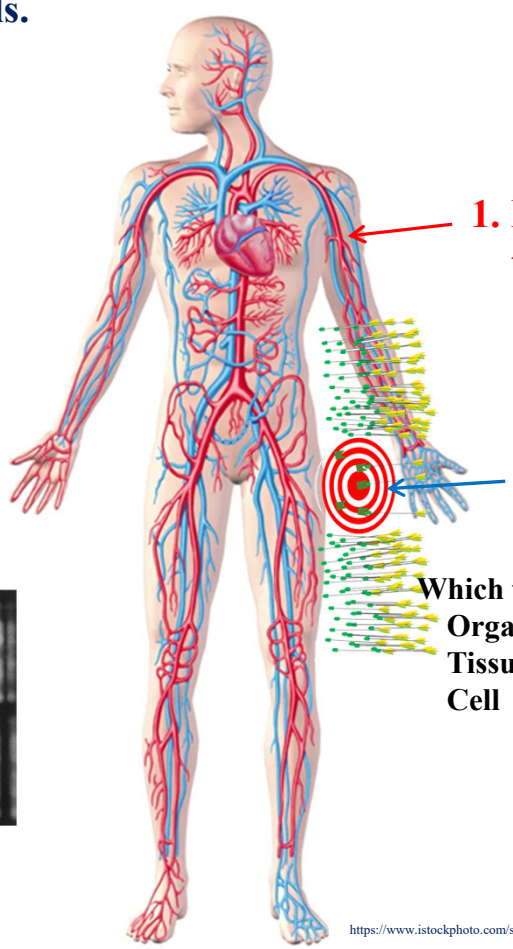
(1890s: Antitoxins = Antibodies)



Nobel Prize 1908



Paul Ehrlich (1854-1915)



1. Random distribution of drugs throughout the body!

2. Binding to a target tissue, cell, and cellular components.

Targeted Delivery

Which target?
Organ
Tissue
Cell

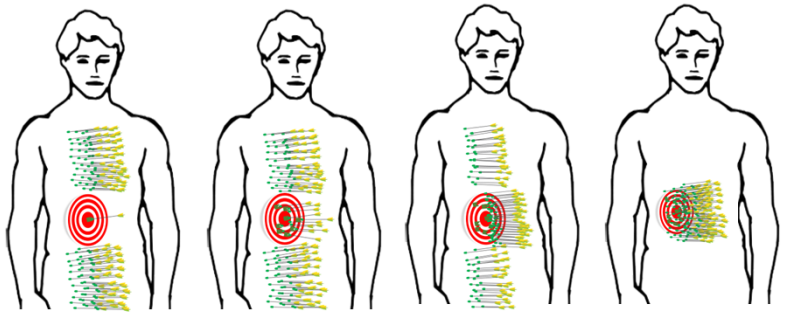
Targeted delivery =
Delivery throughout the body but no (less) harm to normal cells!

https://www.istockphoto.com/search/2/image-film?phrase=blood+circulation+system

Valent et al., Paul Ehrlich (1854–1915) and his contributions to the foundation and birth of translational medicine, J. Innate Immun. 8:111–120, 2016.

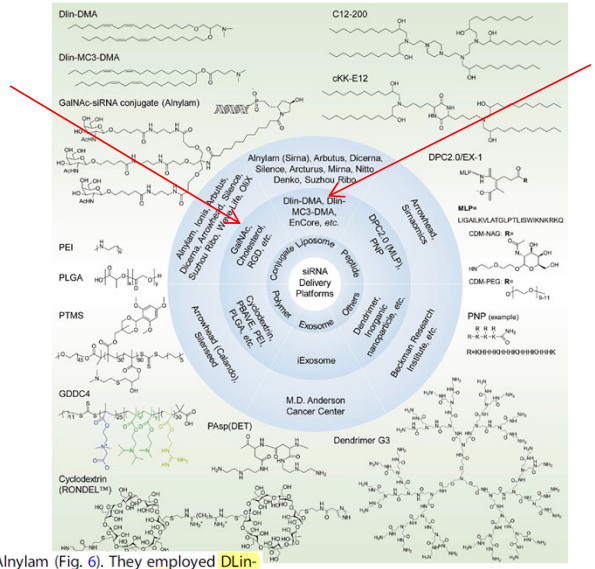
Key Question to Ask: Does It Deliver Enough Drug without Side Effect?

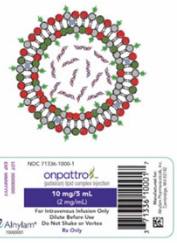
How much drug delivery is enough to be effective?



The quantity of the drug necessary to produce a given effect.

- siRNA covalently linked to a ligand (GalNac) targeting hepatocytes
- Acute hepatic porphyria
- FDA approval in 2019





- siRNA encapsulated in a lipid nanoparticle
- Hereditary transthyretin-mediated amyloidosis
- FDA approval in 2018

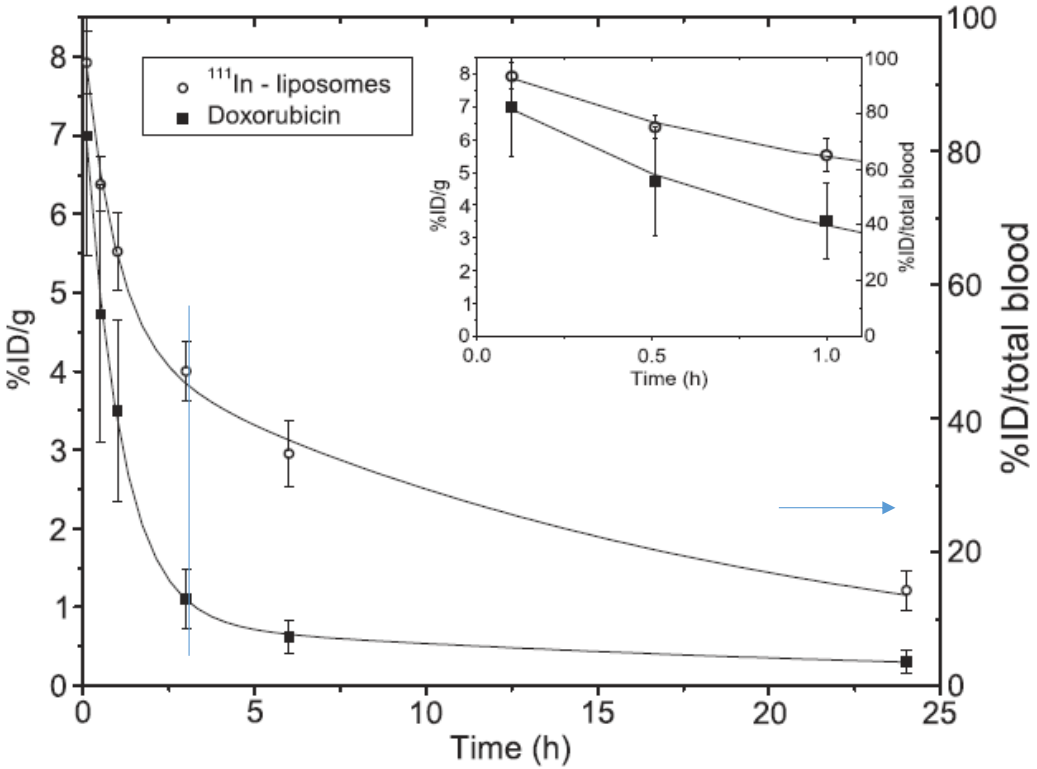
developed by Arbutus and Alnylam (Fig. 6). They employed DLin-DMA (1,2-dilinoleyloxy-3-dimethylaminopropane),[148] DLin-MC3-DMA ((6Z,9Z,28Z,31Z)-heptatriaconta-6,9,28,31-tetraen-19-yl-4-(dimethylamino) butanoate)[107] and L319 (di((Z)-non-2-en-1-yl) 9-((4-(dimethylamino) butanoyl) oxy) heptadecanedioate)[149] as the

The criteria of a new therapy is whether it is effective and safe.

effect' or 'colloid osmotic pressure effect' results in membrane destabilization[116–119] or membrane swelling,[120,121] respectively. However, the underlying mechanism of endosomal release remains to be further illuminated. Only 1–2% of internalized LNP-loaded siRNAs were released into the cytoplasm, and this only occurred within a limited time frame after internalization.[122,123] Hence, further understanding the escape mechanism and how to enhance the escape efficiency is of great importance for siRNA drug development. Recently, Wang and colleagues[124] developed novel endoplasmic reticulum (ER) membrane-modified hybrid nanoplexes (EhCv/siRNA NPs). Compared with unmodified nanoplexes, they showed much higher RNAi activity in vitro and in vivo. The functional proteins on the ER membrane have an important role in intracellular trafficking of siRNA, helping siRNA reach the cytoplasm through the endosome–Golgi–ER pathway instead of the endosome–lysosome pathway, thereby avoiding the lysosomal degradation of siRNA. In addition, electroporation enables siRNA to directly cross the cell membrane, which also constitutes an effective approach to circumvent the endosomal escape issue.[125–131]

Hu 2020, Therapeutic siRNA- State of the art

Drug vs. Drug Carrier



Blood kinetics of ^{111}In labeled TSLs containing doxorubicin. The percentage of the injected dose (%ID) is plotted per gram blood (left axis) and for the total blood (right axis). The blood clearance can be described with a biexponential time dependence.

Doxorubicin is released from liposome prematurely, and those liposomes reaching the target tumor may not even have the drug.

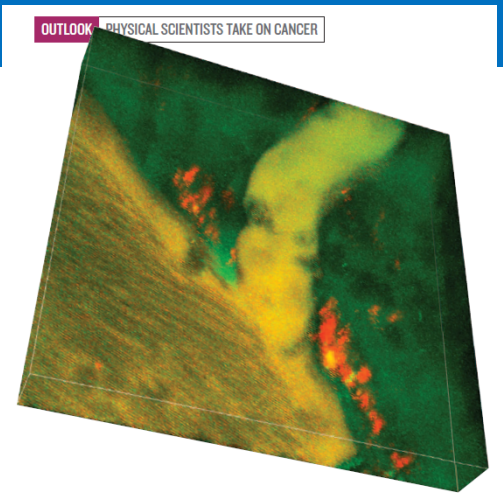
Mariska de Smet, Edwin Heijman, Sander Langereis, Nicole M. Hijnen, Holger Grüll
Magnetic resonance imaging of high intensity focused ultrasound mediated drug delivery from temperature-sensitive liposomes: An in vivo proof-of-concept study.
J. Control. Release 150: 102-110, 2011.

Failed Clinical Trials of Nanoscale Drug Carriers

NANOTECHNOLOGY

Carrying drugs

Traditional chemotherapies can be toxic but nano-sized carriers can keep them out of healthy tissue and take old drugs to new places.



A reconstructed 3D image showing the accumulation of 30-nm nanoparticles (green) in a pancreatic tumour.

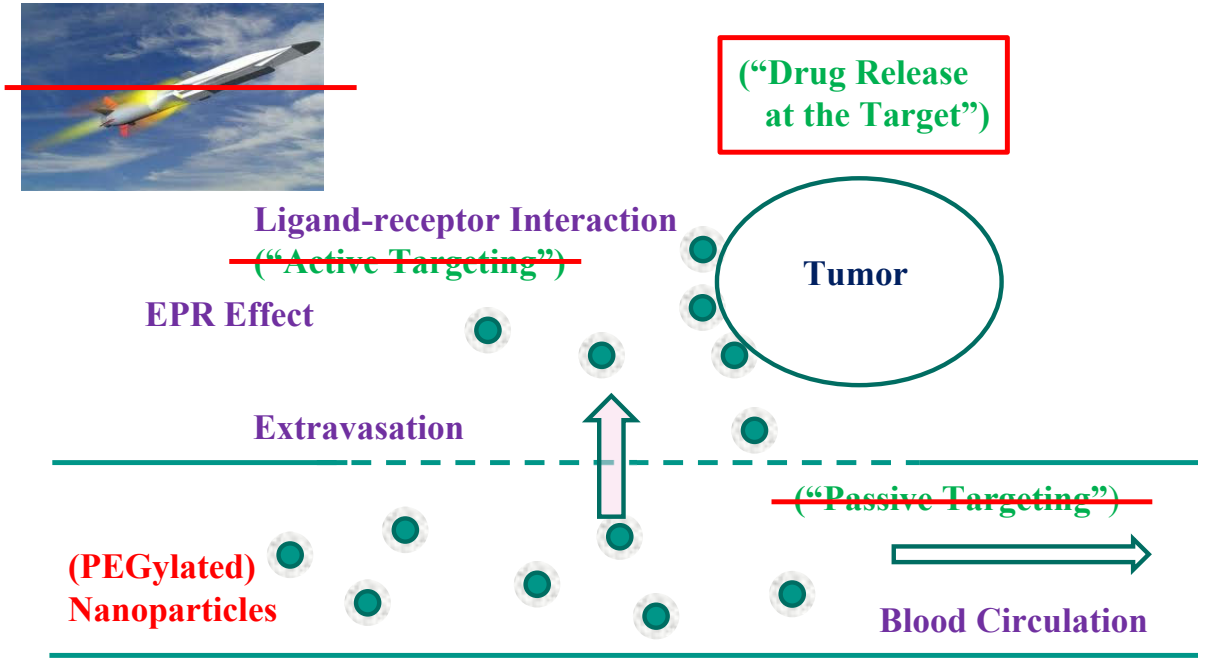
Table 1: Nanoscale drug carriers in clinical trials in 2012.

NANOMEDICINE IN CLINICAL TRIALS
Several nanoscale drug carriers are currently in clinical trials.

Company	Drug	Formulation	Status	Description	Updated Status
Calando Pharmaceuticals	CALAA-01	A polymer nanocarrier containing gene-silencing RNA	Phase I	A polymer nanocarrier holds RNA that silences a gene in solid tumours needed for DNA synthesis and replication	Terminated in 2013
BIND Biosciences	BIND-014	A polymer nanocarrier targeted to cancer cells carries docetaxel	Phase I	Targets solid or metastatic prostate cancer cells by binding to prostate-specific membrane antigen	Terminated in 2016
Nippon Kayaku	NK105	A polymer nanocarrier containing paclitaxel	Phase III	Looking for progression-free survival in patients with metastatic or recurrent breast cancer	Terminated in 2016
NanoCarrier	Nanoplatin (NC-6004)	A polymer nanocarrier containing cisplatin	Phase I/II	Evaluating Nanoplatin in combination with gemcitabine in patients with advanced or metastatic pancreatic cancer, with the aim of reducing kidney toxicity compared with cisplatin alone	Terminated in 2014
Cerulean Pharma	CRLX101	A pH-sensitive polymer nanocarrier releases camptothecin in the acidic environment of cancer cells	Phase II	Separate studies testing CRLX101 in advanced non-small cell lung cancer and in ovarian cancer	Terminated in 2016

K. Bourzac. Nanotechnology: Carrying drugs. Nature, 491 (2012) S58-S60.

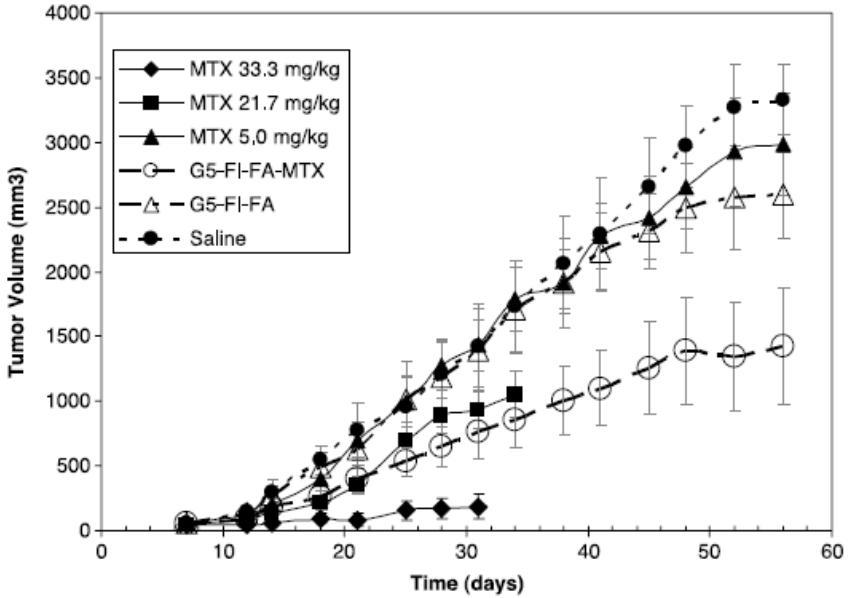
Nanomedicine: Myths and Facts



Nanoparticle Targeting of Anticancer Drug Improves Therapeutic Response in Animal Model of Human Epithelial Cancer

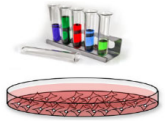
Jolanta F. Kukowska-Latallo,[1] Kimberly A. Candido,[1] Zhengyi Cao,[1] Shraddha S. Nigavekar,[2] Istvan J. Majoros,[1] Thommey P. Thomas,[1] Lajos P. Balogh,[1] Mohamed K. Khan,[2] and James R. Baker, Jr.[1]

[1]University of Michigan Center for Biologic Nanotechnology and [2]Department of Radiation Oncology, University of Michigan Health System, Ann Arbor, Michigan

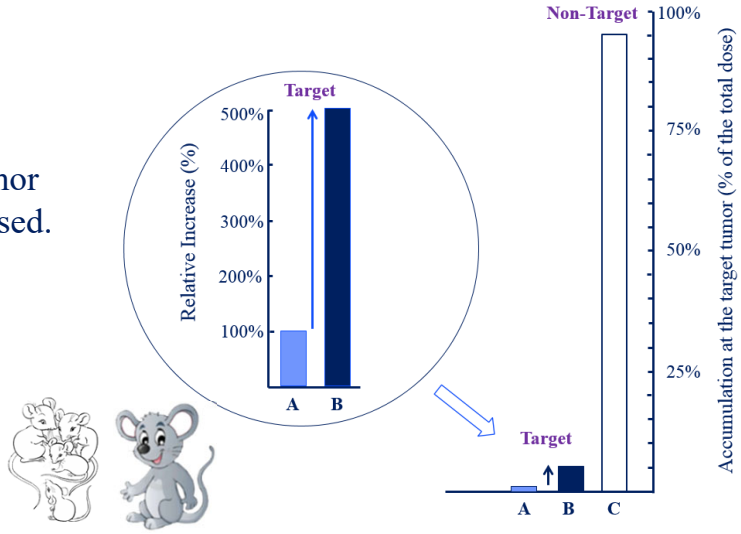


Nanomedicine: Assumptions and Facts in Targeted Drug Delivery

Assumptions used in targeted drug delivery by nanoparticles and the facts	
Assumptions	Facts
Nanoparticles deliver a drug to the target better than the solution control.	The improvement observed is small, usually from around 1% to 2% of the total administered dose.
PEGylation extends blood circulation time.	Only for a small fraction of the total nanoparticles.
Nanoparticles reach tumor by passive targeting.	Only 1~2% of the total dose.
Nanoparticles reach tumor by the EPR effect	But the EPR effect is not proven in humans.
Nanoparticles release a drug at the target tumor.	But only 1~2% of the total dose.



The target tumor cells are exposed.



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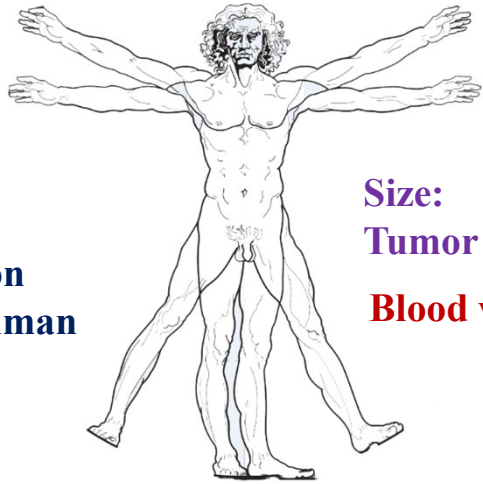
Lack of Translation from Mouse to Human



Size:
Tumor vs. Body

Blood volume

The Mechanisms of Nanoparticle Delivery to Solid Tumours

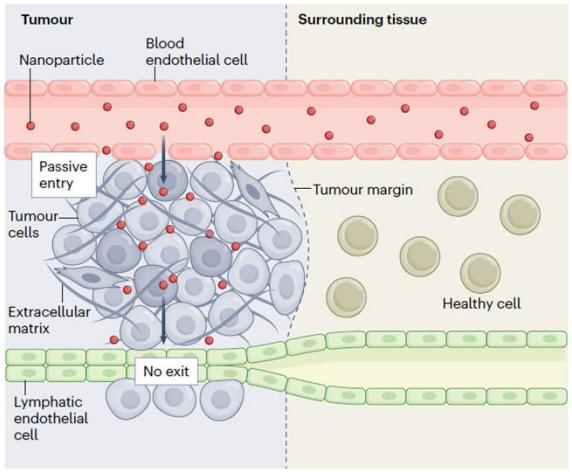


Fig. 2 | EPR mechanism of nanoparticle delivery. The enhanced permeability and retention (EPR) mechanism postulates that nanoparticles enter the tumour through gaps in the tumour blood vessel wall. Once nanoparticles are inside the tumour, the EPR effect suggests that nanoparticles are unable to exit owing to the collapse of the tumour lymphatics. The combination of nanoparticle entry and the absence of exit results in nanoparticle retention inside the tumour.

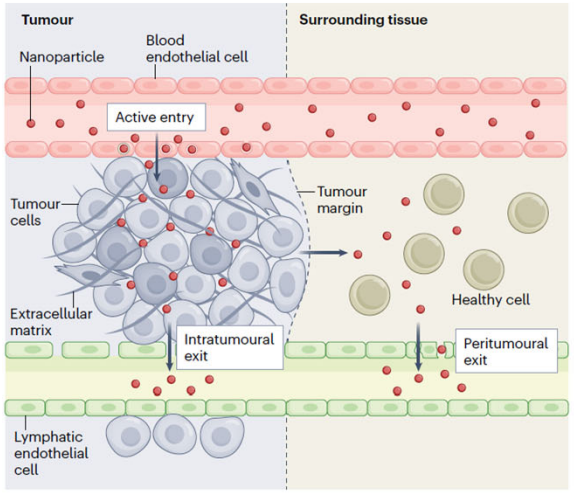


Fig. 3 | ATR mechanism of nanoparticle delivery. The active transport and retention (ATR) mechanism of nanoparticle delivery states that nanoparticles enter the tumour through both active and passive transport mechanisms. Active transport mechanisms include transcytosis mediated by nanoparticle transport endothelial cells, vesicle-vacuolar organelles and migrating cells. These active transport mechanisms are dominant over passive transport, which includes gaps and fenestrations. After entering the tumour, nanoparticles are retained owing to interactions with tumour cellular and acellular components. These tumour components sequester nanoparticles, thus slowing their transport from the entry site to the exit site. Nanoparticles exit the tumour via intratumoural or peritumoural lymphatics. Nanoparticles reach the peritumoural lymphatics by transporting out of the tumour at the tumour margin and accumulating in the tissues surrounding the tumour.

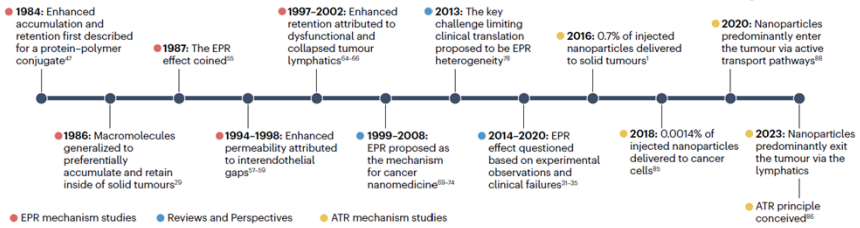


Fig. 1 | Timeline of the mechanisms of nanoparticle delivery to solid tumours. The timeline highlights key studies or a sequence of studies that led to the formulation of the enhanced permeability and retention (EPR) effect[29,47,55,57–59,64–66] (red points) and the active transport and retention (ATR) principle (yellow points)[1,85,86,88] for nanoparticle delivery to solid tumours. Key Review articles and Perspectives are included (blue points)[31–35,69–74,78].

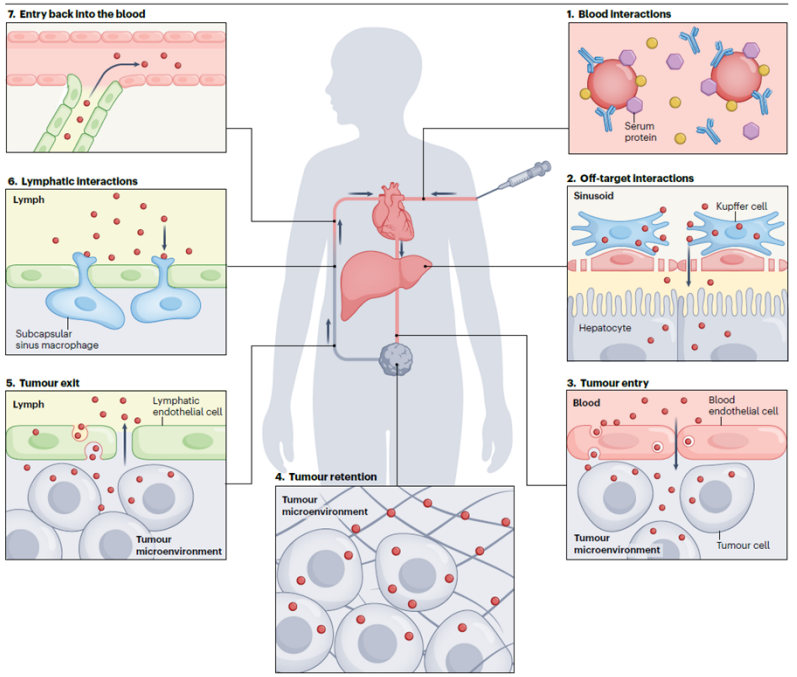
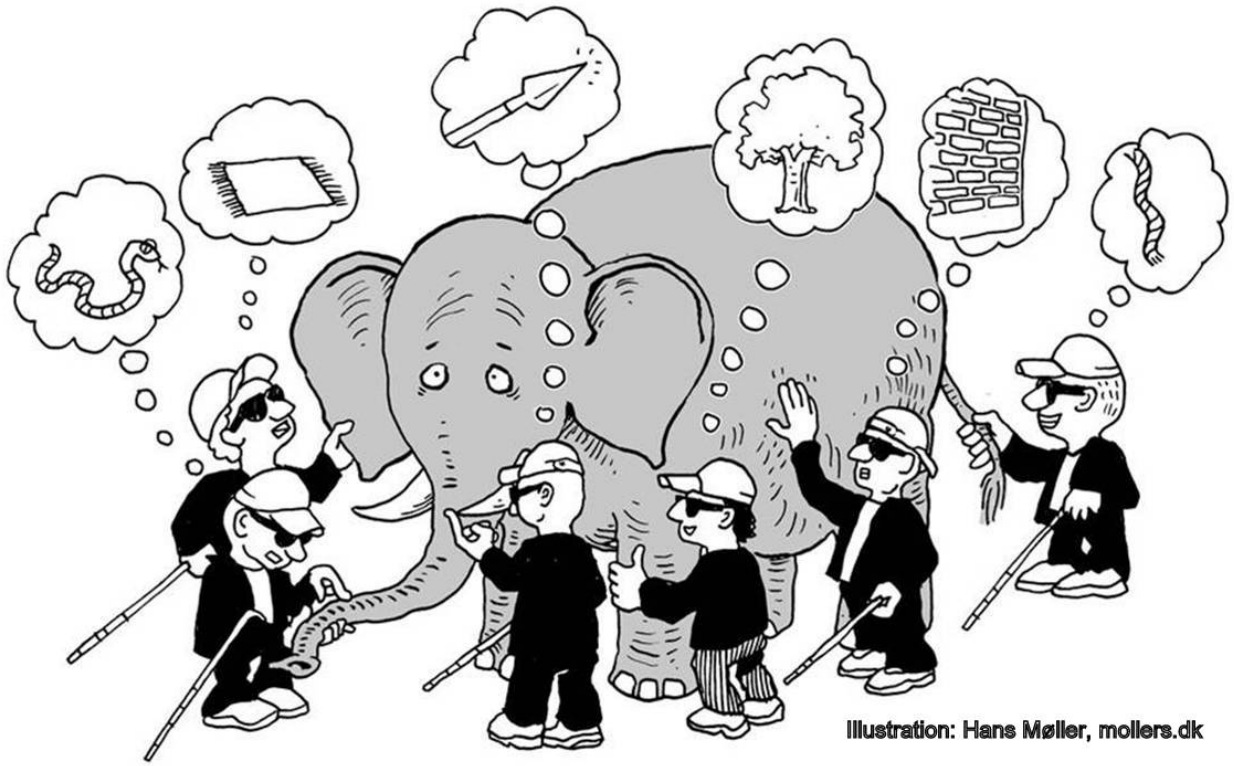


Fig. 4 | The delivery journey of cancer nanomedicine. The journey of nanoparticles once administered into the body. **(1)** Nanoparticles are administered into the blood, where they adsorb blood serum proteins. **(2)** Nanoparticles encounter non-tumour tissues, which sequester the nanoparticles and prevent tumour delivery. In addition to the liver, other organs, such as the spleen and kidneys, clear nanoparticles from the circulation. **(3)** Nanoparticles enter the tumour predominantly via active transport processes such as transcytosis (shown). Other mechanisms include vesiculo-vacuolar organelles and migrating cell effects. Passive transport mechanisms, such as interendothelial gaps, play a minor role. **(4)** Nanoparticles are retained inside the tumour owing to interactions with tumour cells and acellular components. **(5)** Nanoparticles exit the tumour predominantly via the lymphatics. Both lymphatic channels and vesicle-vacuolar organelle mechanisms of exit are shown. Tumour blood vessels contribute a minor role to nanoparticle exit. **(6)** Nanoparticles are transported through the lymphatic circulation, where they encounter immune cells in the lymphatic vessels and lymph nodes, which sequester nanoparticles. **(7)** Nanoparticles are transported back to the blood circulation via the right lymphatic trunks (shown) or thoracic duct. Nanoparticles then repeat this cycle (returning to the first step) until they are cleared from circulation. Nanoparticles, cells and organs are not drawn to scale.

Nguyen 2024, The mechanisms of nanoparticle delivery to solid tumours

Different Interpretation of the Same Data

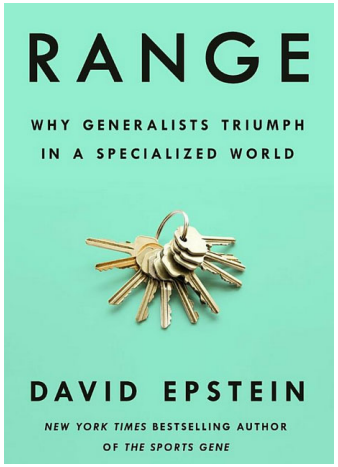
An elephant can be described by many different ways.
But which is the characteristic description of an elephant?

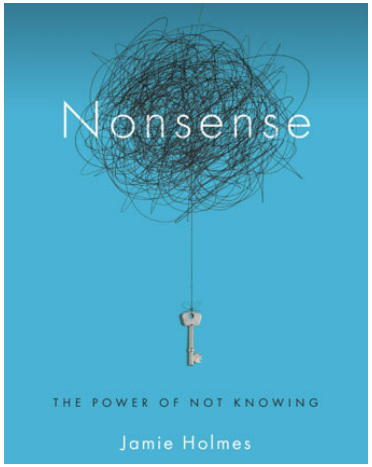


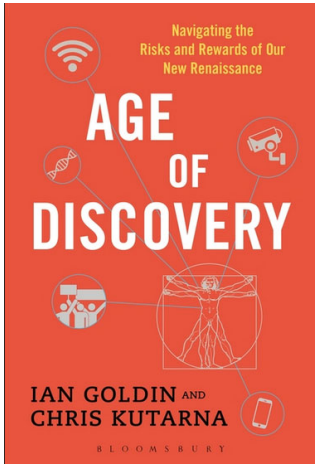
Finding the true answer.

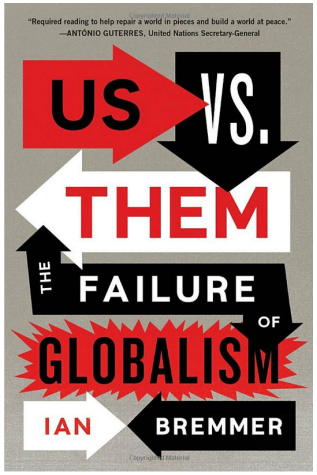
1. Hypothesis
2. Exchange of ideas, critique, and collaboration
3. Data collection and analysis
4. Iterative process of experimentation and analysis
5. Question one's own data to avoid cognitive bias

Science The Endless Frontier









Functional fixedness.
The man with a hammer = The man with nanomedicine, lacking the far transfer ability.

One tidy theoretical formula with a single lens bends every event to fit its ideas. This does not work on ill-defined problems.

The future is uncertain. We must train the next generation of scientists for the uncertain future to **solve problems that have no easy answer**, **to learn failure is a part of progress**, and to keep an open mind and empathize with different viewpoints.

Scientists should be able to navigate the risks and rewards, build the ability to **shift resources and focuses to a completely unexpected direction**, continue relentless improvements by challenging paradigms, and mix ideas to enrich humanity.

History shows that **people give their best when their best is required of them**. That day is here now.

Human beings have evolved to use their natural ingenuity to create the tools they need to survive

Concepts, ideas, and potentials in research articles are just the first step. It is the execution that makes the real difference.
The drug delivery field needs more implementations in clinical applications.

https://www.hiv.gov/hiv-basics/overview/history/hiv-and-aids-timeline

Nanomaterials: From Natural To Synthetic

Microfabrication: Sticky Fingers

Sticky fingers: Novel robotic grippers expand role in fulfillment

These cool gecko-inspired grippers show how the best innovations don't add complexity, but eliminate it. Greg Nichols, 2020.

Robots with gecko-inspired hands are becoming more important during the rise of on-demand-everything. That's prompting a leader in robotic end-of-arm tooling to expand its lineup of the biologically-inspired gripper pads for robots that work in various industries, including fulfillment and logistics.

The company's gripper uses millions of "micro-scaled fibrillar stalks" to stick to smooth surfaces using van der Waals forces, which is the mechanism geckos use to climb. The technology was first developed with space in mind and grew out of a Stanford research project that inspired work at the NASA Jet Propulsion Lab. NASA was exploring van der Waals forces as an effective way to capture orbiting satellites for salvage or repair. Suction cups and vacuum grippers aren't effective in space, and traditional robotic end effectors can push objects away in zero gravity.

OnRobot's Gecko no-mark adhesive gripper seemed like a grippy solution to a sticky situation, and the company's success with its grippers has reinforced the market need for this sort of product. Last year OnRobot won silver at the Edison Awards Gala, which came on the heels of the Gecko Gripper winning the Robotics Award at the Hannover Messe in Germany.

https://www.zdnet.com/article/sticky-fingers-novel-robotic-grippers-expand-role-in-fulfillment/#ftag=CAD-03-10abf5f

Gecko Gripper – SPECIAL ADHESIVE TECHNOLOGY, NO-MARK GRIPPING

No compressed air requirement saves maintenance costs and provides faster payback in as little as 5 months.
Precise, no-mark gripper technology increases productivity in pick-and-place tasks.
Innovative gecko technology enables gripping of flat, porous objects such as PCBs to extend automation capabilities.
https://onrobot.com/en/products/gecko-gripper

Microfabrication: Gecko's Attachment Pads

This review paper discusses design parameters that were found to be instrumental to the adhesive properties of synthetically fabricated adhesive structures, currently available fabrication methods for producing these adhesive structures, as well as the various testing methods that have been used experimentally to characterize adhesion performance.

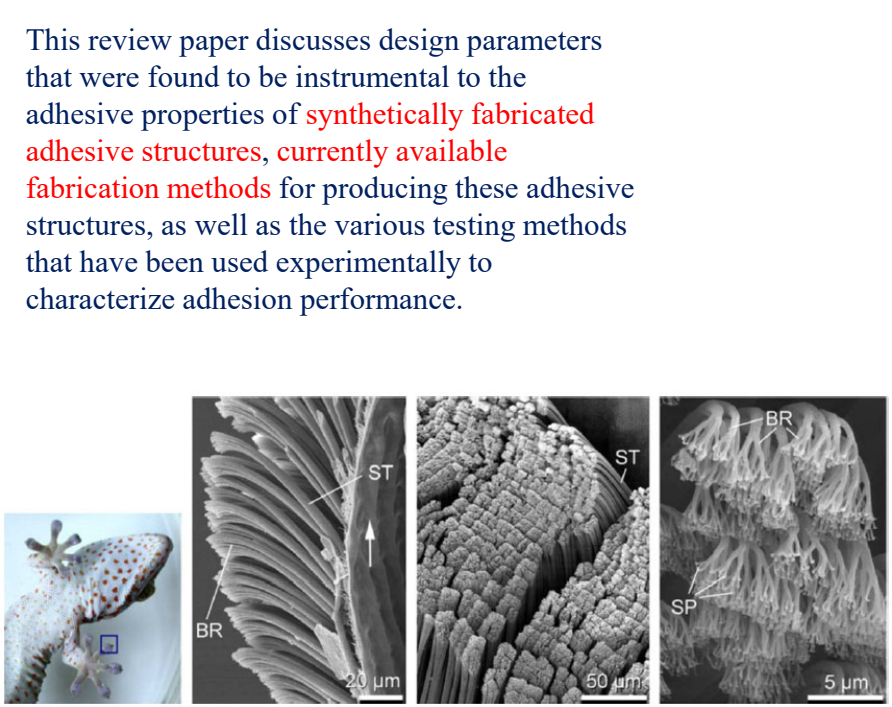


Fig. 2. Adhesion map for spherical tip contacts.

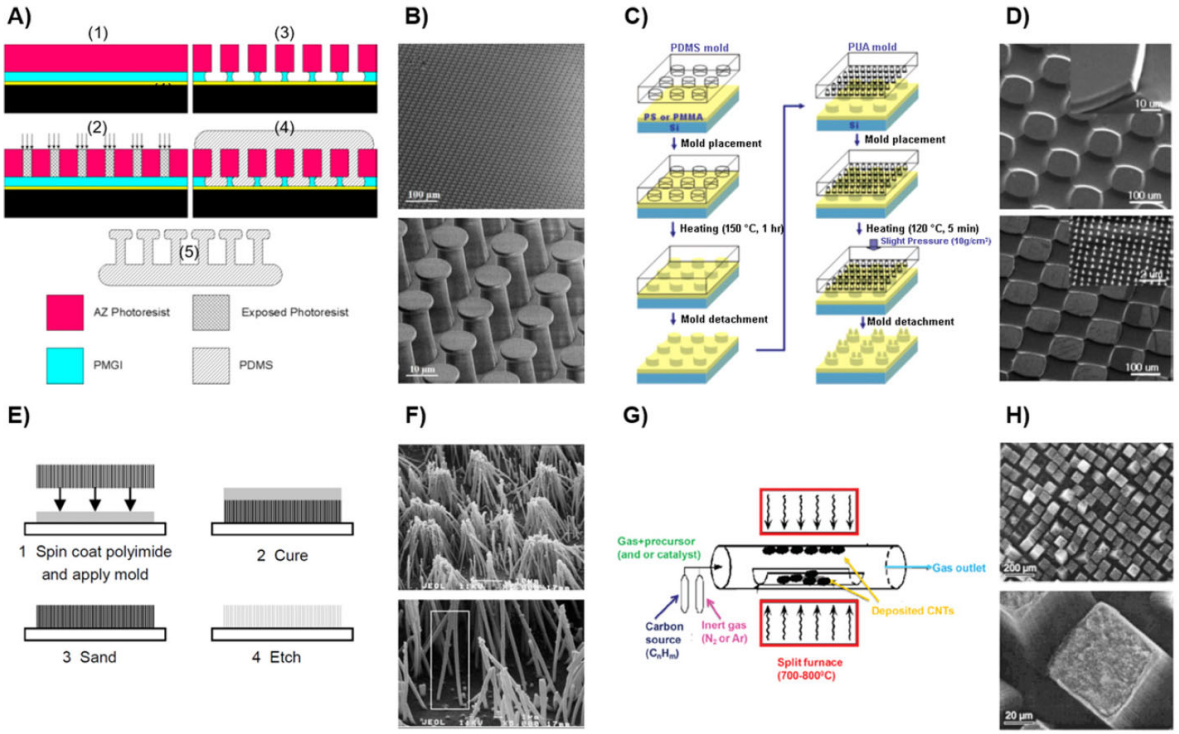
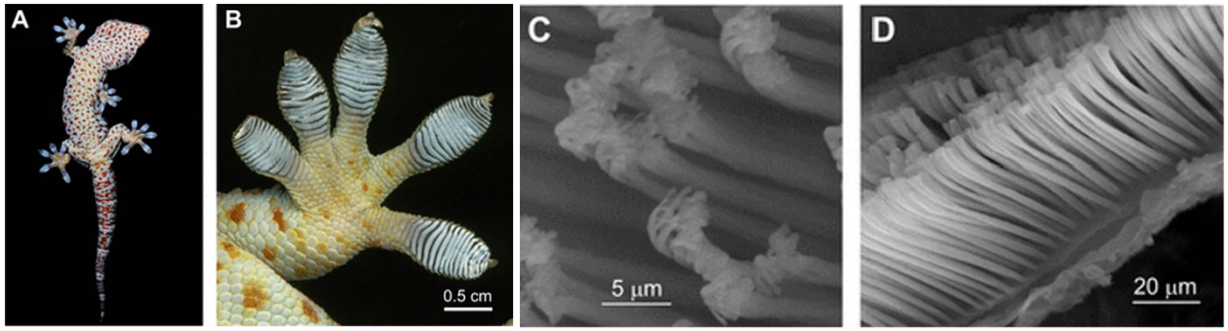


Fig. 3 (A) (1) A silicon wafer is coated with Cr/Au followed by spin-coating and baking PMGI and AZ 9260 photoresists. (2) The AZ 9260 is UV-exposed under the post array mask. (3) Following exposure, the photoresist is developed and dried, leaving undercut areas. (4) Sylgard® 184 is poured onto the mold and cured. (5) The cured silicone is removed by hand, producing the final dry adhesive. (B) SEM images of 10 μm diameter posts with a cap thickness of 1.5 μm and post height of ~ 20 μm. (C) Schematic of the two-step capillary force lithography process. Polymer microstructures were fabricated using a micropatterned PDMS mold followed by nanofabrication on top of the preformed microstructure using a nanopatterned PUA mold. (D) SEM images of PS microstructures and micro/nanoscale hierarchical structures. A microstructure with 120 μm posts and 25 μm spacing was used. The nanostructure is 100 nm in diameter and 400 nm in spacing with a height of 450 nm. (E) Synthetic fiber fabrication by nanocasting. (F) Clumping in an array of 0.6 μm diameter polyimide fibers. (G) Schematic diagram of chemical vapor deposition (CVD) setup. (H) SEM images of MWCNTs deposited on a masked pattern after 10 min of CVD. Reproduced with permission from

Pan 2019, Bioinspired Adhesives, Reference Module in Materials Science and Materials Engineering

Nanostructures in Nature



An overview of the hierarchical nature of the gecko adhesive system. (A) A ventral view of a tokay gecko on glass, showing the toe pads. (B) Lamellae on the gecko toe pads. (C) The setae that make up the lamellae. (D) The flattened tips of branched setae (spatulae). https://jeb.biologists.org/content/219/7/912.figures-only

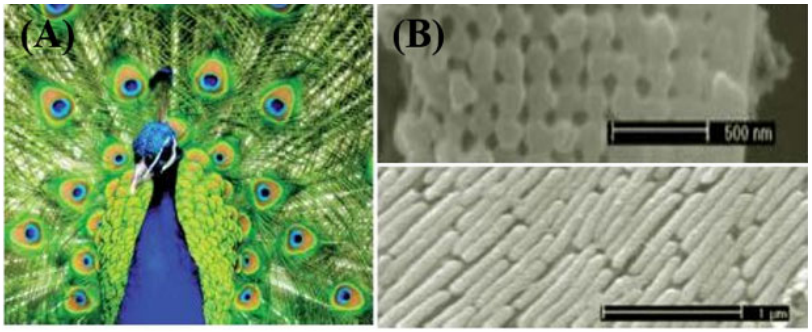


Figure 7: (A) Photograph of peacock feathers showing various colors and patterns. (B) Cross-sectional SEM images of the transverse (top) and longitudinal (bottom) sections of green barbule cortex.

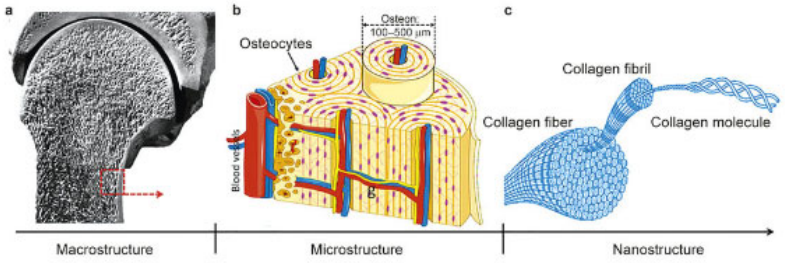


Figure 8: The macro- and microstructure of bone and its components with nanostructured materials employed in the regeneration of bone. (a) Macro-scopic bone details with a dense cortical shell and cancellous bone with pores at both ends. (b) Repeating osteon units within cortical bone.(c) Collagen fibers (100–2000 nm) comprised of collagen fibrils.

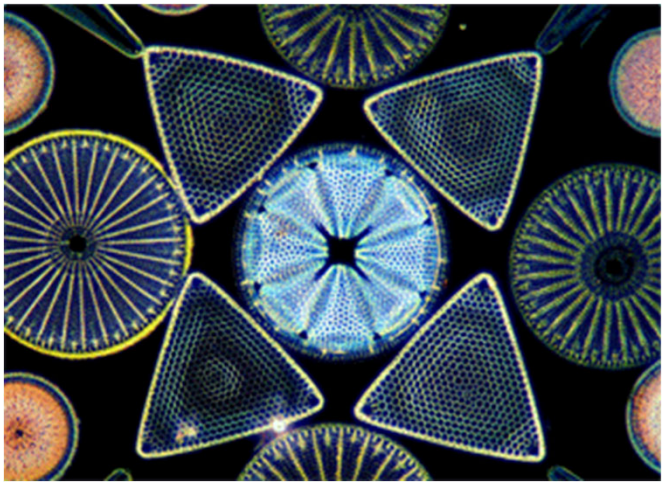
Jeevanandam 2018, Review on nanoparticles and nanostructured materials

Nanostructures in Nature: Planktonic Diatoms

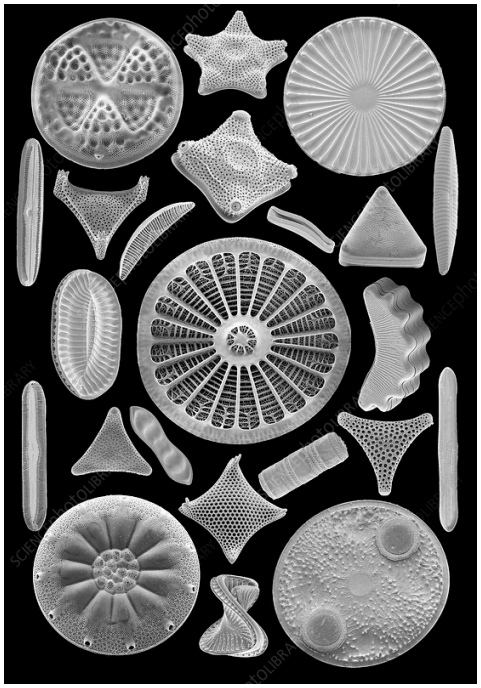
Diatoms are single-celled algae that live in houses made of glass. They are the only organism on the planet with cell walls composed of transparent, opaline silica. Diatom cell walls are ornamented by intricate and striking patterns of silica.

Diatoms turn energy from the sun into sugar.
Diatoms produce 50% of the air we breathe.
Diatoms remove carbon dioxide (CO_2) from the atmosphere.
Diatoms are food for the entire food web.

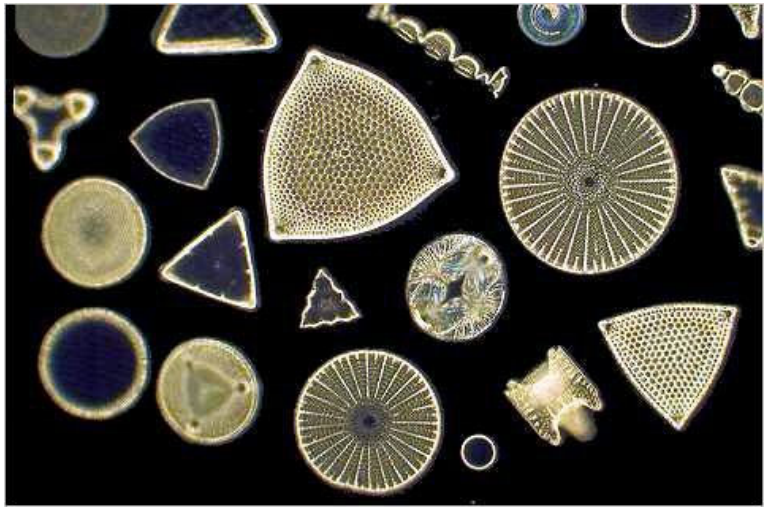
https://diatoms.org/what-are-diatoms



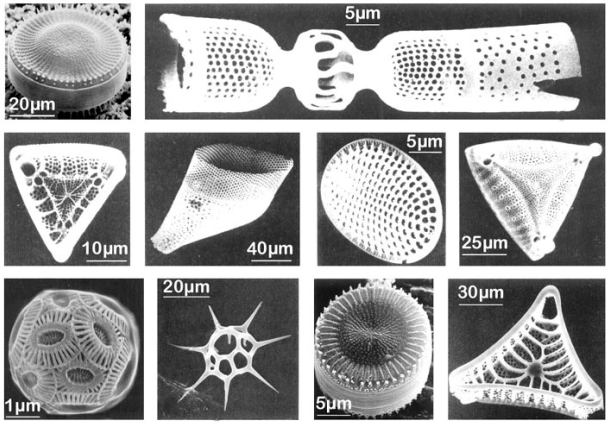
http://www.go-star.com/antiquing/diatoms-victorian-microscope-slides.htm



https://www.sciencephoto.com/media/943455/view/diatoms-sem

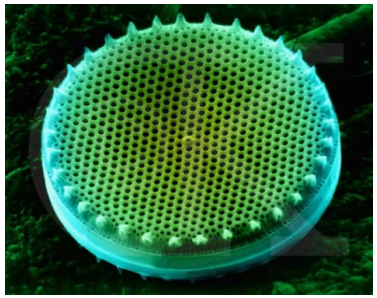


https://bukuipa.co.id/kingdom-protista/



Selection of planktonic diatoms
(not representative for the mediterranian)

https://www.pinterest.com/pin/168814686003330498/



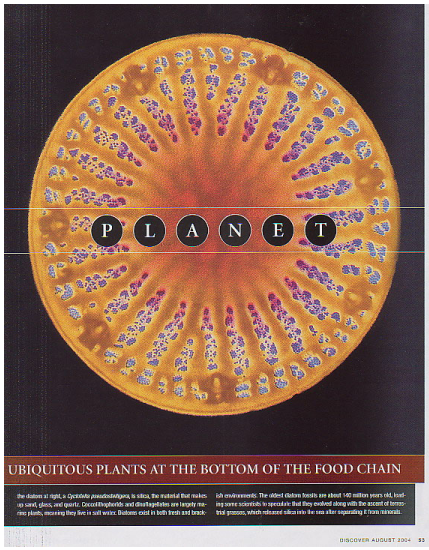
https://wyrdscience.wordpress.com/2011/01/10/205/

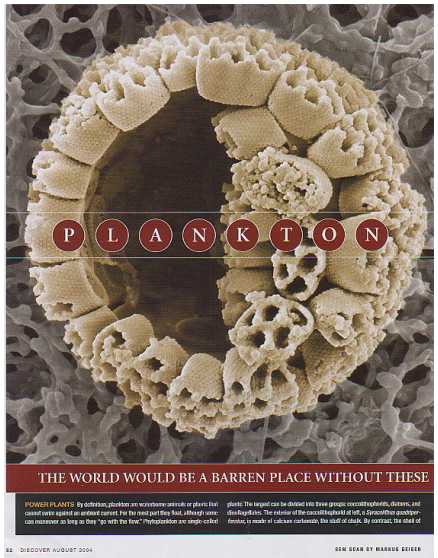
Nanostructures in Nature: Planktonic Diatoms

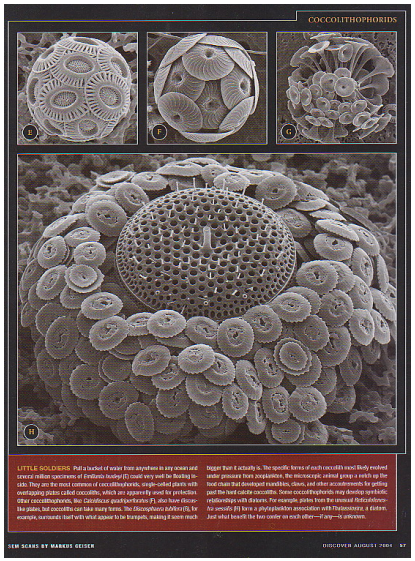
By definition, plankton are waterborne animals or plants that cannot swim against an ambient current. For the most part they float, although some can maneuver as long as they "go with the flow." Phytoplankton are single-celled plants. The largest can be divided into three groups: coccolithophorids, diatoms, and dinoflagellates. The exterior of the coccolithophorid, a Syracolithus quadriperforatus, is made of calcium carbonate, the stuff of chalk. By contrast, the shell of the diatom Cyclotella pseudostelligera is silica, the material that makes up sand, glass, and quartz. Coccolithophorids and dinoflagellates are largely marine plants, meaning they live in salt water. Diatoms exist in both fresh and brackish environments. The oldest diatom fossils are about 140 million years old, leading some scientists to speculate that they evolved along with the ascent of terrestrial grasses, which released silica into the sea after separating it from minerals. | SEM scan courtesy of Markus Geisen.

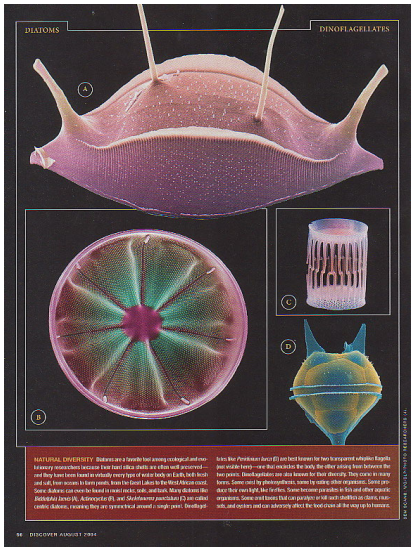
Plankton are literally at the bottom of the food chain, a source of nourishment for virtually every animal in the sea. They are ancestors to terrestrial plants, which seem to have evolved from certain ocean phytoplankton hundreds of millions of years ago.

Scanning electron microscope (SEM) images show that they can be arrestingly beautiful. Coccoliths are not always round, flat plates, like hubcaps; many look like trumpets, cabbage leaves, daisies, or stars.









https://www.discovermagazine.com/environment/plankton-planet

From Nature to Fabrication

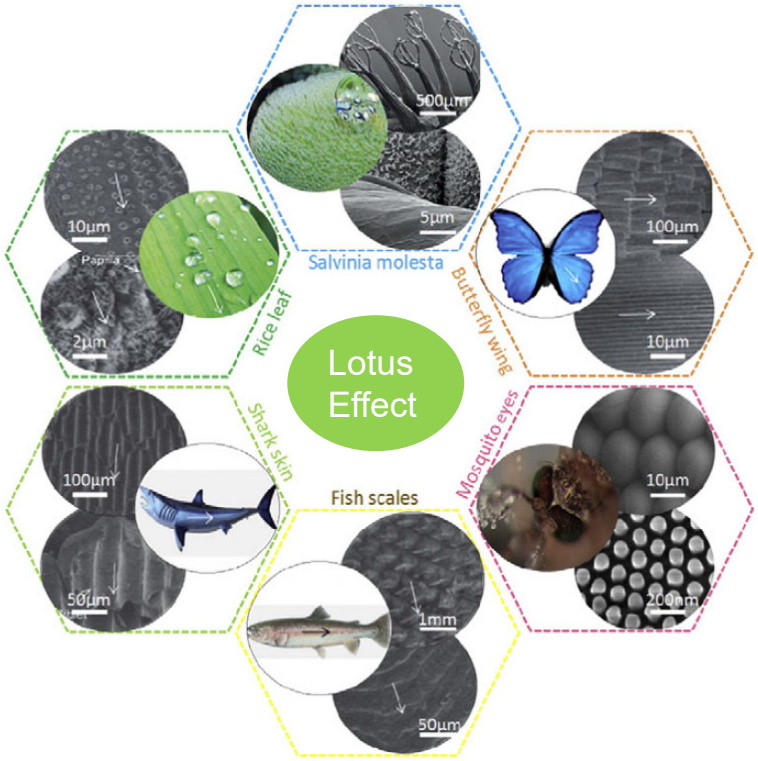


Fig. 1. The typical self-cleaning surfaces in nature and their SEM images. The droplets of water on the surfaces can roll off following a preferential direction dictated by the structural features.

Zhang 2016, Lotus effect in wetting and self-cleaning

From natural

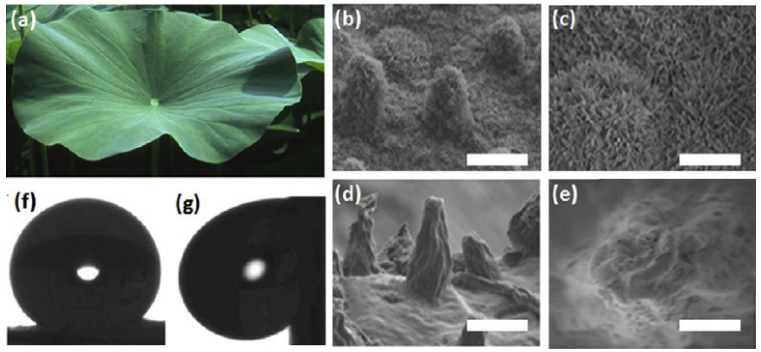


Fig. 2. Image and SEM images of lotus leaf surface. (a) A fresh lotus leaf in nature, (b) the micro-structure of lotus leaf, (c) the nano-structure of lotus leaf, (d) the micro-structure of annealed lotus leaf, (e) the nano-structure of annealed lotus leaf, (f) a droplet placed on an untreated lotus leaf, and (g) a droplet placed on an annealed lotus leaf, then tilted to an angle of 90°. (Scale bar: (b and d) 10 μm, (c and e) 3 μm).

to synthetic surface structures

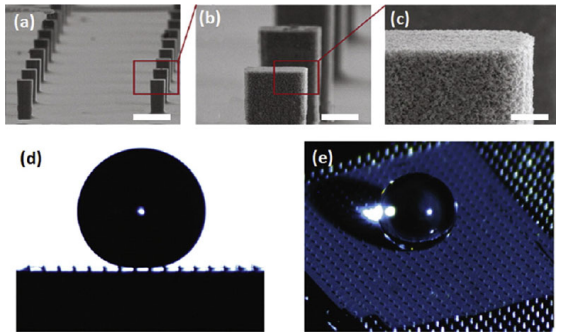


Fig. 6. Droplet on the fabricated micro/nano roughened hierarchical surface. (a-c) Nano-scaled roughness etched by XeF2 gas that conformally covers the micro-scale array of pillars fabricated through deep reactive etching. (d-e) Droplet sitting on the double roughness with the value of the pillar spacing to width ratio at 7.5, supported by only several pillars. The contact angle at this state is 173°. (Scale bar: (a) 50 μm, (b) 10 μm, and (c) 2 μm).

Superhydrophobic Paper

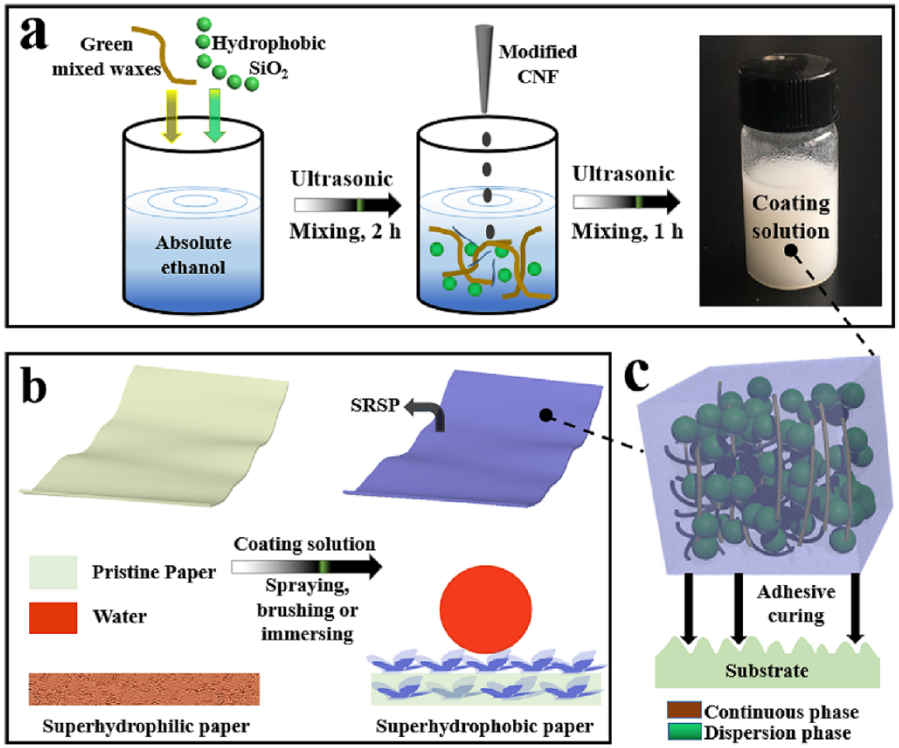


Fig. 1. Design of SRSP. (a) Fabrication process schematic illustration of targeted coating solution, and the building block of SRSP. (b) Schematic illustration of the procedure for coating treatment procedure to obtain the SRSP. (c) Illustration of the superhydrophobic composite coating layer (consisting of the continuous phase: brown part and dispersion phase: green part) was formed on the surface of the pristine paper-based substrate through synergistic reinforcement of cross-linking reaction.

Long 2022, Synergistic reinforced superhydrophobic paper with green, durability, and antifouling function

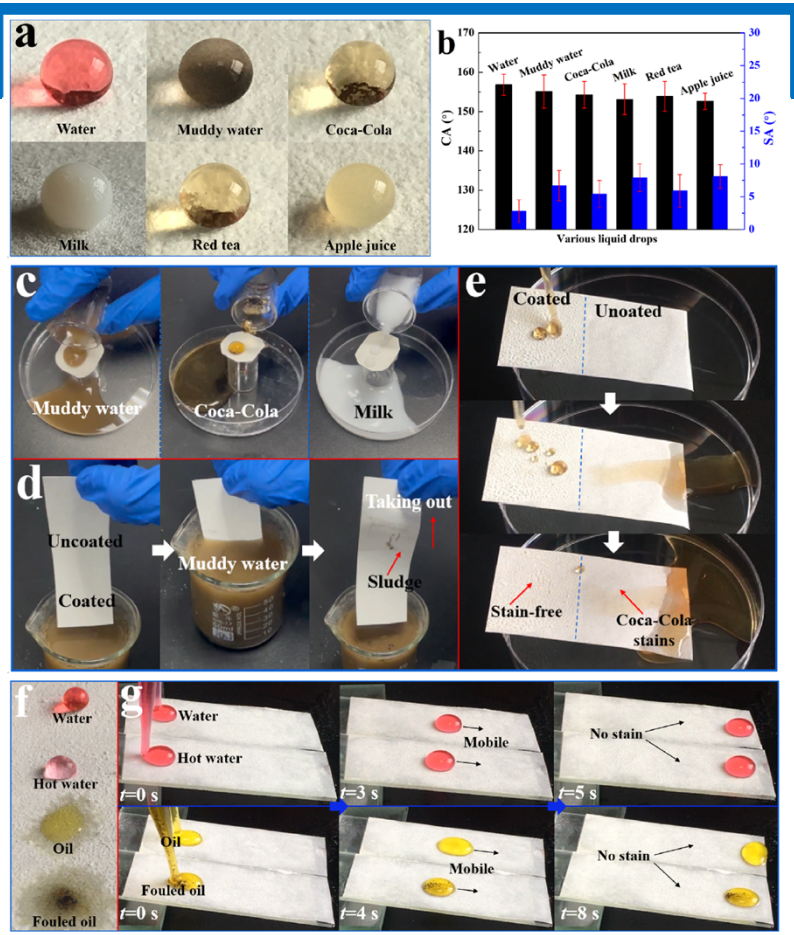
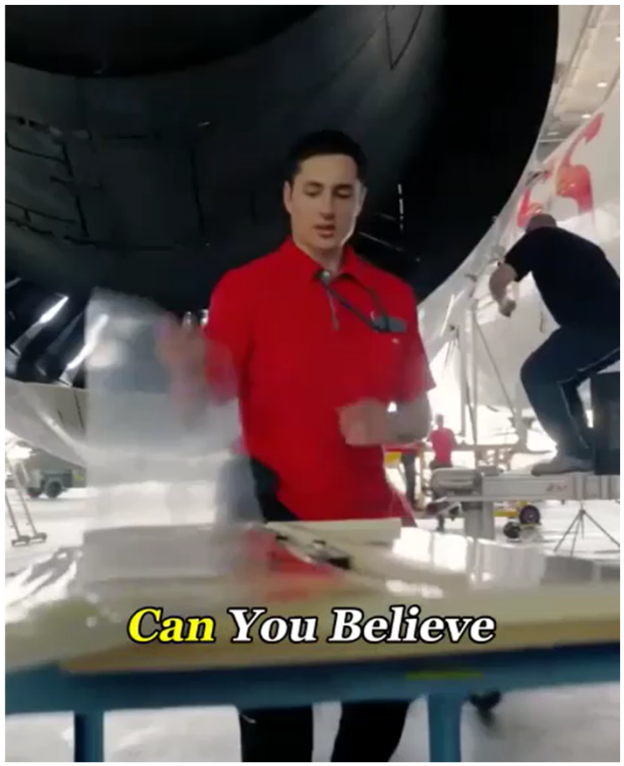
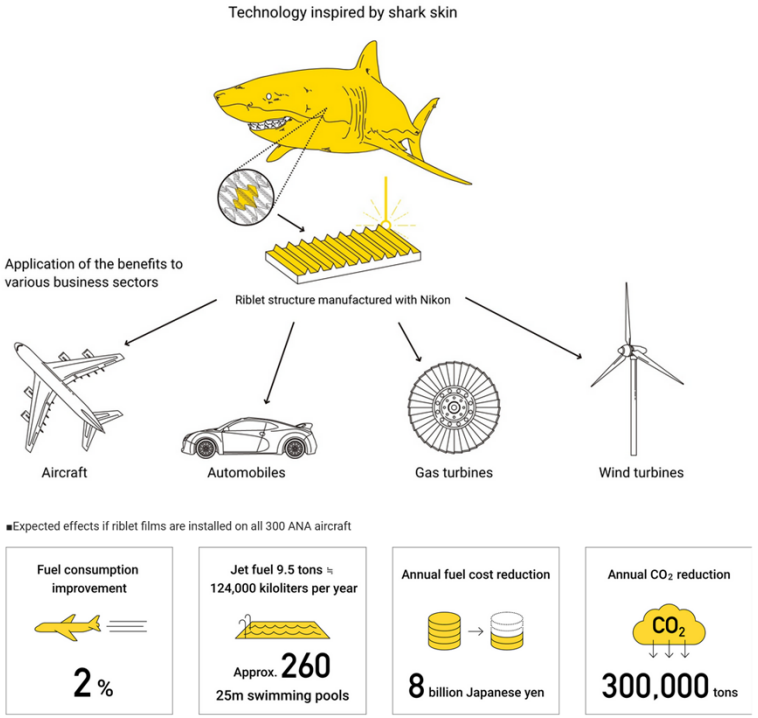


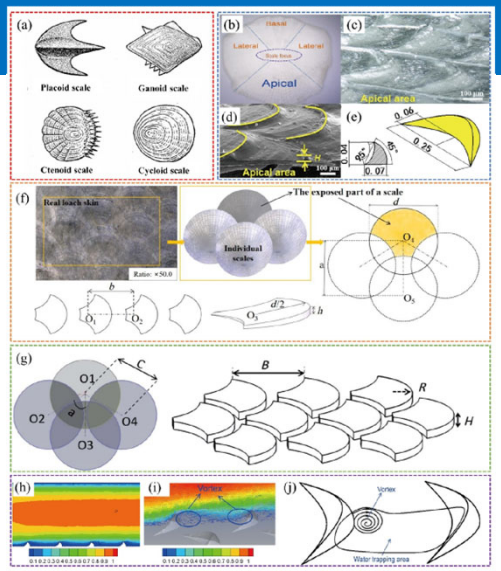
Fig. 6. Direct antifouling ability of SRSP. (a) Different types of liquid droplets with spherical shape on SRSP surface: red-colored water, muddy water, Coca-Cola, milk, red tea, and apple juice. (b) CAs and SAs of different liquids on the SRSP surface. (c) Three water-based liquids including muddy water, Coca-Cola, and milk were poured onto the SRSP surface. (d) Uncoated pristine paper surface (upper image) and SRSP surface (lower image) was dipped into muddy water and brought out. (e) Movement of Coca-Cola on the substrate composed ofuncoated pristine paper surface (right) and SRSP surface (left). (f) Wetting behavior of water, hot-water (~100 ◦C), oil, and foul-oil droplets on SRSP surface. (g) Time-sequence images of the free mobility of water, hot-water, oil, andfoul-oil droplets down along the tilted SLIPS-SRSP surfaces with a tile angle of ~10°.

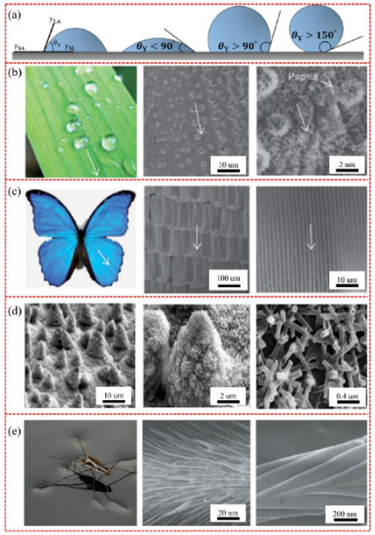
Riblets for Reducing Drag





https://www.nikon.com/company/sustainability/highlight/2306_riblet/



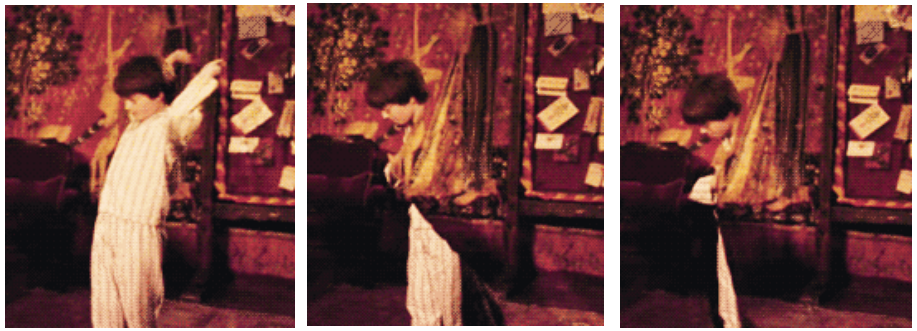


https://www.tiktok.com/@curibeepop/video/7597028578496220447?_r=1&_t=ZP-93gotEB3DYM
https://www.youtube.com/watch?v=vSxNn7uh1so&t=4s
https://newatlas.com/aircraft/aeroshark-aircraft-skin/
https://www.surface-technology.info/topics/topic-area/coatings/sharkskin-for-aircraft-aeroshark-technology-certified

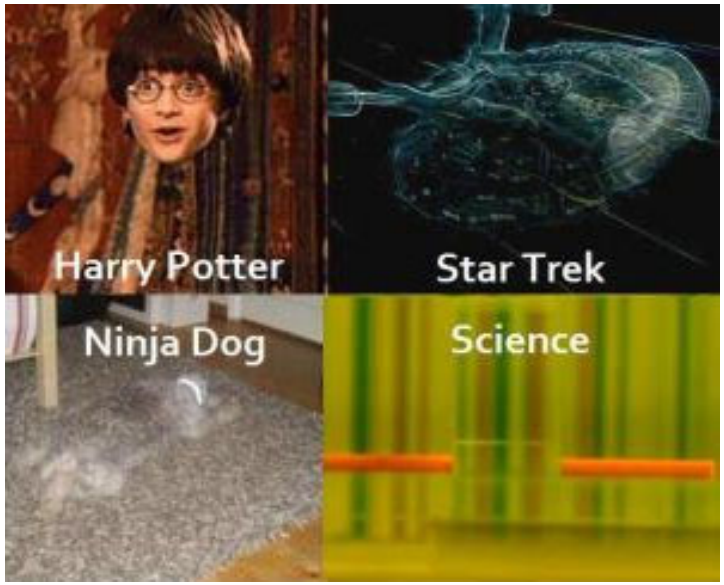
Hu 2025, A review of drag reduction methods and principles in bionic interface

Nano (Maybe Pico) Camouflage Technology

Invisibility in Movies



Harry Porter's Cloak of Invisibility

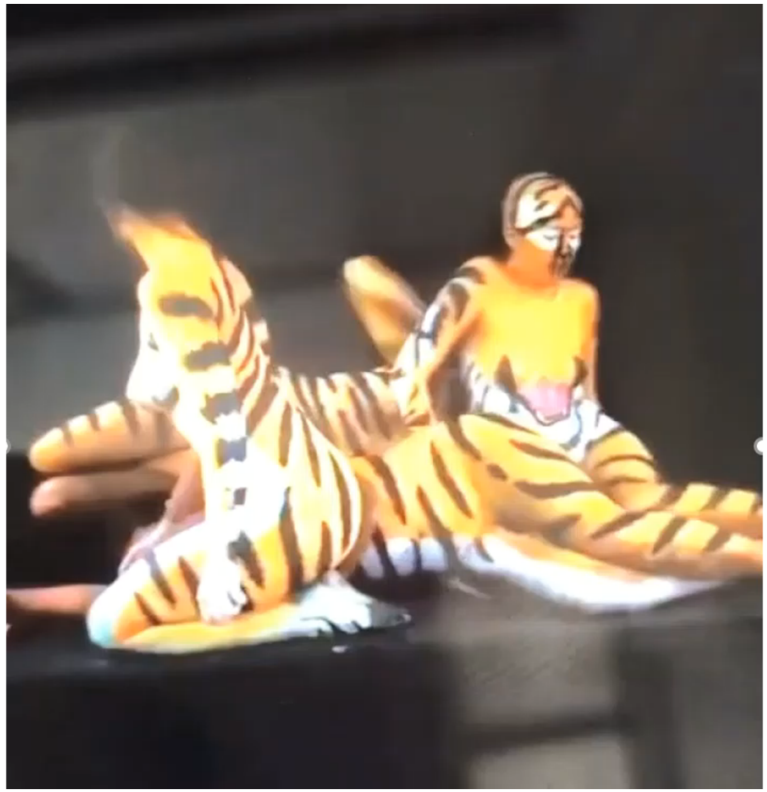


Invisibility — like time travel, teleportation, flying, and super-speed — has been a fixture in science fiction ever since science fiction has existed. The most well-known examples range from the one used by the Romulans in Star Trek, Harry Potter's deathly hallows cloaking device, and the elven cloak Frodo and Sam used to evade Sauron's army at the gates of Mordor.

http://www.aiat.tech/article/215b5c38ac473f65bf2d8d39.html

https://futurism.com/scientists-have-found-a-way-to-interfere-with-light-to-make-objects-invisible

Human Camouflage



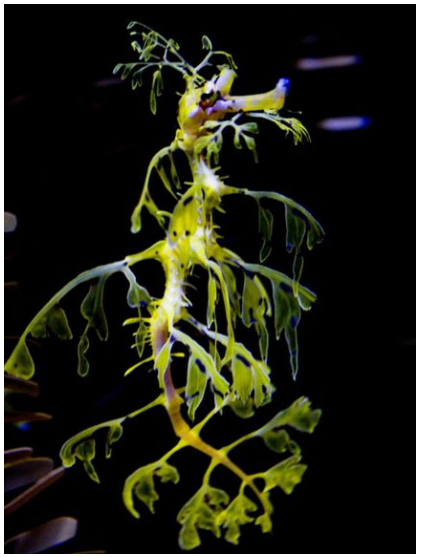
@rody_eug1, TikTok

https://www.proapto-camouflage.com/neuropsychology-of-camouflage

Invisibility in Real World through Camouflage

Tasseled Anglerfish

Cuttlefish



Leafy Sea Dragon

Trumpetfish

Reef Stonefish

http://ocean.nationalgeographic.com/ocean/photos/undersea-camouflage/#/camouflage05-trumpetfish_13511_600x450.jpg

Invisibility in Real World




Octopus Camouflage
An amazing transformation of colors that match with the background in a matter of seconds.

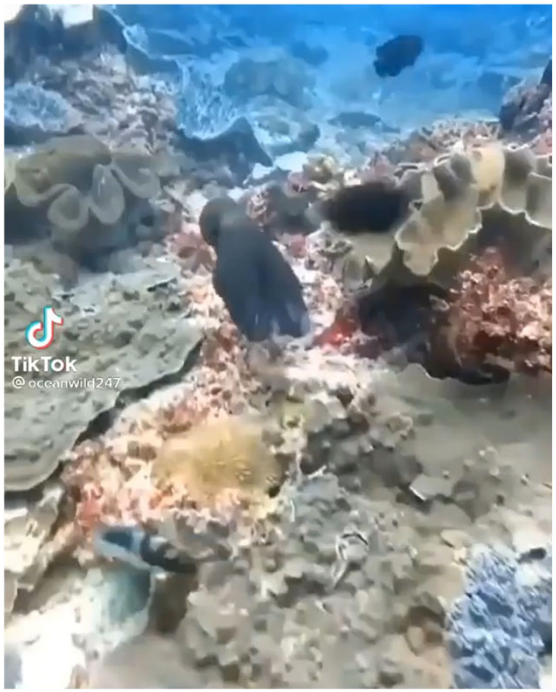
http://www.youtube.com/watch?v=eS-USrwuUfA

Invisibility in Real World

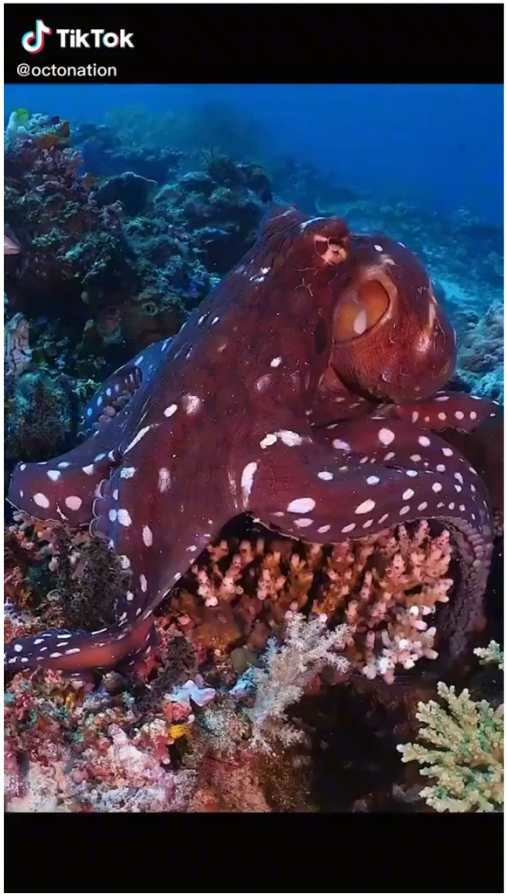
Octopus Camouflage

It is even more amazing that octopus is color blind.

http://www.youtube.com/watch?v=eS-USrwuUfA



Octopus Camouflage



TikTok. @oceanwild247

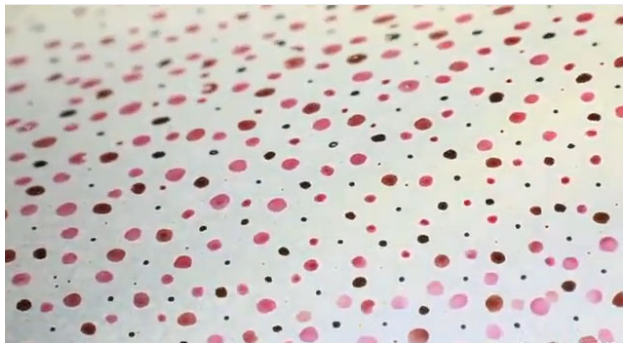
My Octopus Teacher (Netflix 2020)

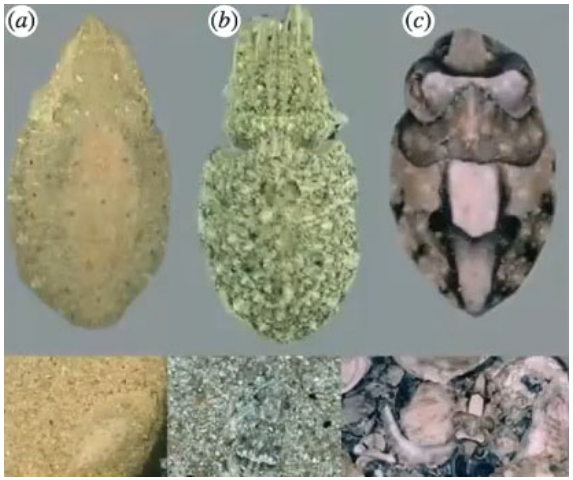
A filmmaker forges an unusual friendship with an octopus living in a South African kelp forest, learning as the animal shares the mystery of her world (1:05:34)

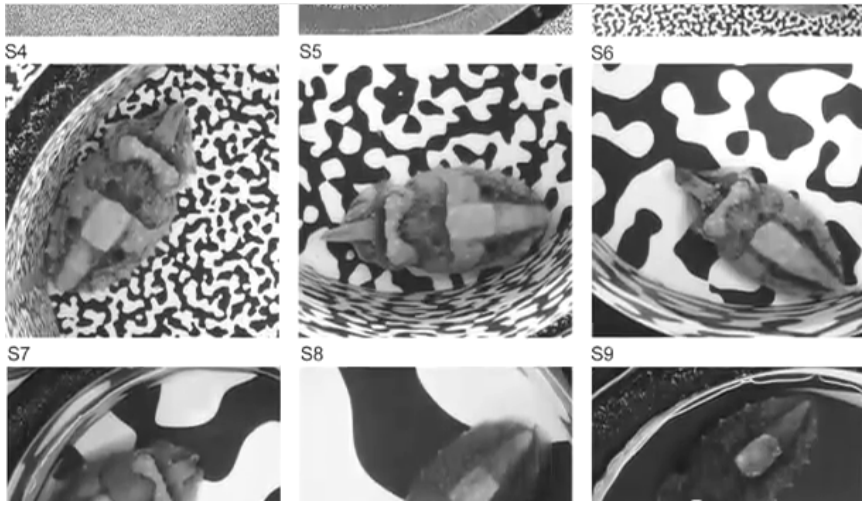
Almost Instant Changes in Color, Pattern, and Shape of the Skin

Cephalopods (Squid, Octopus, Cuttlefish) have several tricks for blending in with their undersea surroundings: they can change color, pattern and even the shape of their skin.

http://www.youtube.com/watch?v=eS-USrwuUfA



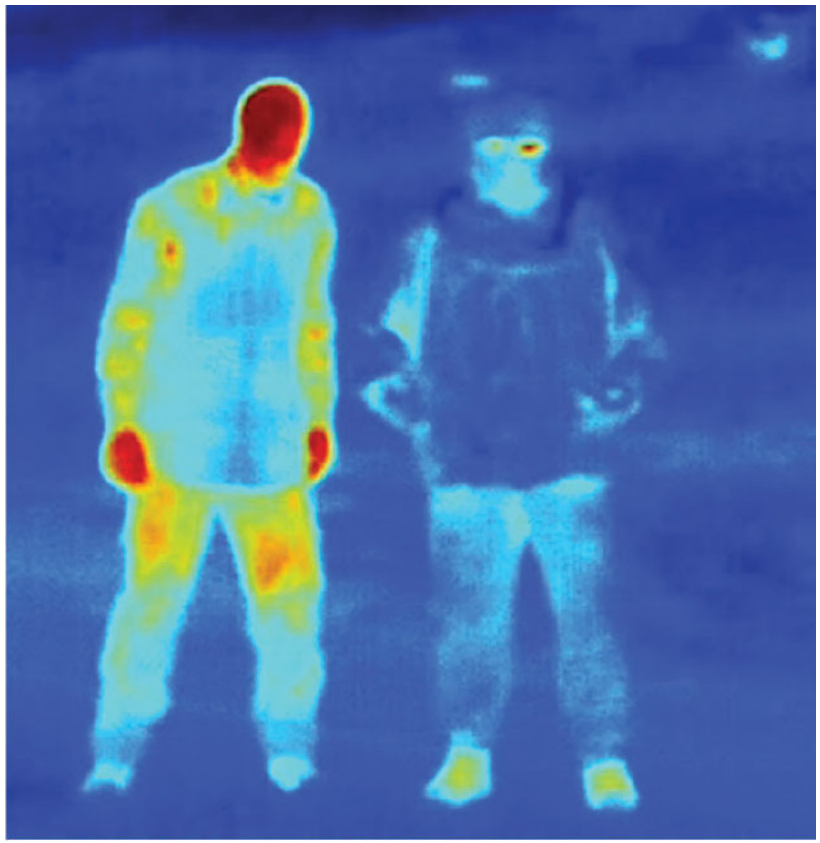




http://www.sciencefriday.com/segment/08/05/2011/squid-octopus-cuttlefish-masters-of-camouflage.html

Smart Camouflage for Soldiers

Army eyes reversible camouflage fabric to enable infantry to hide from infrared sensors



https://digital.militaryaerospace.com/militaryaerospace/20240506/MobilePagedArticle.action?articleId=1983268#articleId1983268

Stealth – Innovative Textile Technology For Thermal Signature Management

https://www.thefirearmblog.com/blog/2024/02/16/innovative-textile-technology-enhances-thermal-signature-management/

Nanopores & Molecular Imprinting

A Nanopore DNA Reader

Since the 1990s, nanopores have been used for sequencing strands of DNA. A voltage is applied across the nanopore, which is embedded in a thin lipid membrane, causing a stretch of DNA to thread through the pore. A helicase enzyme then methodically pulls the molecule back through. As this happens, the nitrogenous bases that make up the DNA affect the ion current flowing through the pore, and by measuring these current changes, researchers can decode the DNA sequence. Now, biophysicist Cees Dekker of Delft University of Technology in the Netherlands and colleagues have repurposed this technology for deciphering amino acid differences among peptides (*Science*, 374:1509–13, 2021).

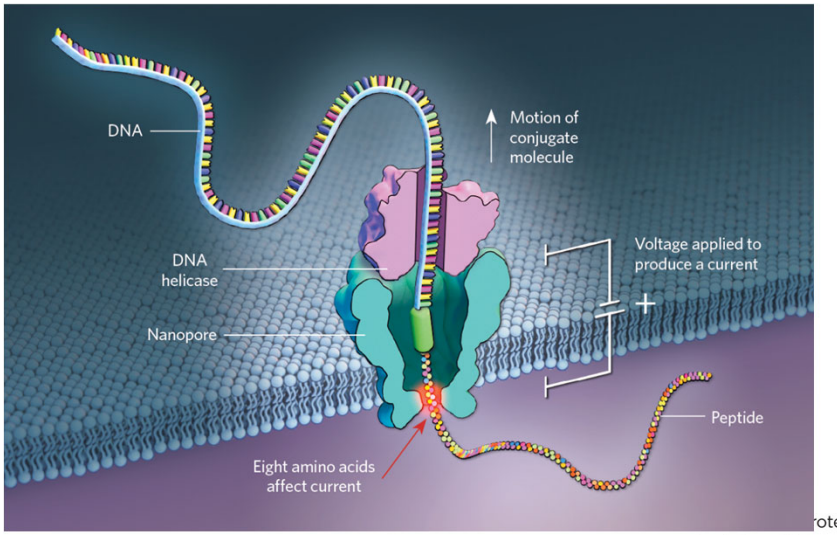
Dekker's team starts by linking a synthetic peptide with the 5' end of a single strand of DNA. After a zap of voltage sends the conjugated molecule through the nanopore, the Hel308 helicase walks on the DNA section, pulling both the DNA and the attached peptide back through the nanopore. As with DNA sequencing, ratcheting the peptide through the nanopore changes the ion current, and the researchers can link the changes to a specific sequence of amino acids in their designed peptide. The target peptide is read in this way multiple times, threading back through the pore as the helicase falls off and being pulled back through again by another, improving the technique's fidelity. In a proof-of-principle study, the researchers were able to distinguish three different 26-amino-acid-long peptides that only varied by a single amino acid.

The method cannot be used to decode protein sequences without a known reference for comparison, however. That's because not only does the amino acid at the pore's entrance affect the ion current, but the eight surrounding amino acids do as well. "Right now, it is not yet a full de novo sequencing tool," Dekker writes in an email to *The Scientist*. "Yet it is very powerful since we showed that by changing even a single amino acid within the chain, we observed dramatic differences in the current step signals." The new method therefore could be useful for detecting amino acid mutations or identifying the presence of a specific peptide of interest within a mixture of proteins, he says.

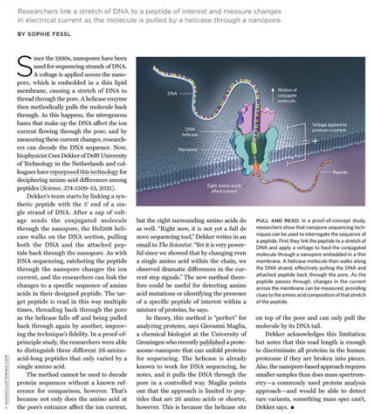
In theory, this method is "perfect" for analyzing proteins, says Giovanni Maglia, a chemical biologist at the University of Groningen who recently published a proteasome-nanopore that can unfold proteins for sequencing. The helicase is already known to work for DNA sequencing, he notes, and it pulls the DNA through the pore in a controlled way. Maglia points out that the approach is limited to peptides that are 26 amino acids or shorter, however. This is because the helicase sits on top of the pore and can only pull the molecule by its DNA tail.

Dekker acknowledges this limitation but notes that this read length is enough to discriminate all proteins in the human proteome if they are broken into pieces. Also, the nanopore-based approach requires smaller samples than does mass spectrometry—a commonly used protein analysis approach—and would be able to detect rare variants, something mass spec can't, Dekker says. ■

Researchers link a stretch of DNA to a peptide of interest and measure changes in electrical current as the molecule is pulled by a helicase through a nanopore (Sophie Fessl).



PULL AND READ: In a proof-of-concept study, researchers show that nanopore sequencing techniques can be used to interrogate the sequence of a peptide. First they link the peptide to a stretch of DNA and apply a voltage to feed the conjugated molecule through a nanopore embedded in a thin membrane. A helicase molecule then walks along the DNA strand, effectively pulling the DNA and attached peptide back through the pore. As the peptide passes through, changes in the current across the membrane can be measured, providing clues to the amino acid composition of that stretch of the peptide.



The Scientist Digest, Feb 2022 (Issue 2)

Dynamics of Driven Polymer Transport through a Nanopore

Molecular transport in confined nanoscale geometries is the basis for many emerging biotechnologies and biological processes. Polymer translocation across a nanoscale pore has been one of the most intensively studied topics in this field. Motivated in part by the goal of DNA sequencing, a rich phenomenology of behaviour has been observed, requiring ideas from polymer physics, surface science and fluid mechanics. Nanopore sensors work by measuring the modulations in ionic current as single molecules are electrophoretically driven through the pore. Ever since the first demonstration of nucleic acid detection, intensive efforts have focused on understanding the physics governing key experimental observables such as the translocation time (τ).

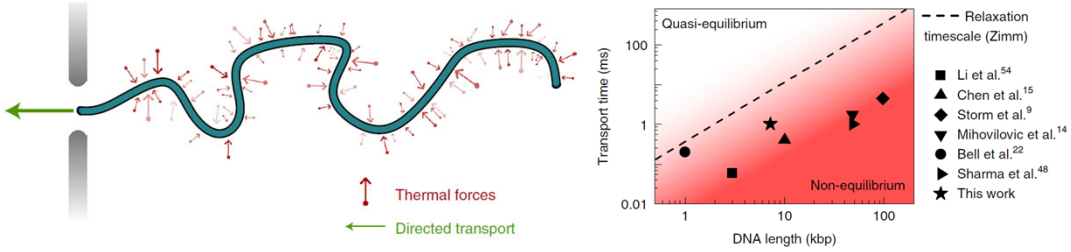


Fig. 1 | Translocation of dsDNA through synthetic nanopores is a non-equilibrium process. Schematic illustrating directed polymer translocation through a nanoscale aperture. The entropic forces due to thermal noise are indicated together with the driving force, for example, an electrophoretic force due to an applied potential difference.

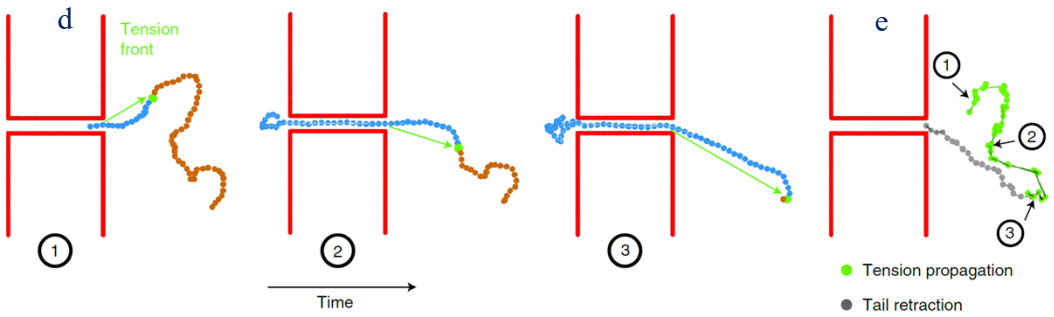


Fig. 5 | Simulations show that correlated motion arises from initial distribution of DNA conformations. d, Three snapshots (time increasing from left to right) of a simulation with the position of the tension front indicated by the bead in green. The chain is coloured blue for the section that has already been pulled taut and orange for the remainder of the chain. Loops in the DNA structure are successively straightened during the translocation as the tension front follows a random path set by the initial conformation of the DNA. e, Overall path of tension front for the translocation illustrated in d, with the green line showing the path traced out during the tension propagation phase and the grey line showing the path of the last bead once the tension reaches the end of the molecule. The numbers highlight the position of the tension front at the three snapshots shown in d.

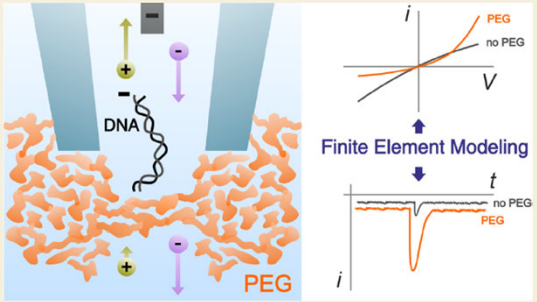
Synthetic nanopores and nanostructured DNA molecules were used to directly measure the velocity profile of driven polymer translocation through synthetic nanopores. The results reveal a two-stage behaviour in which the translocation initially slows with time before accelerating close to the end of the process. Distinct local velocity correlations as the DNA polymer chain passes through the nanopore. Brownian dynamics simulations show that the two-stage behaviour is associated with tension propagation, with correlations arising from the random-walk conformation in which the DNA begins.

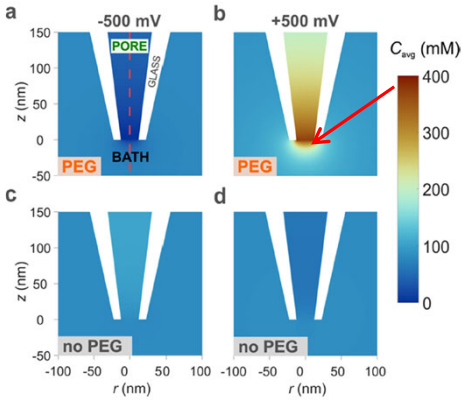
Chen 2021, Dynamics of driven polymer transport through a nanopore

Enhanced Single-molecule Detection in a Nanopore

ABSTRACT: Solid-state nanopores have been widely employed in the detection of biomolecules, but low signal-to-noise ratios still represent a major obstacle in the discrimination of nucleic acid and protein sequences substantially smaller than the nanopore diameter. The addition of 50% poly(ethylene) glycol (PEG) to the external solution is a simple way to enhance the detection of such biomolecules. Here, we demonstrate with finite-element modeling and experiments that the addition of PEG to the external solution introduces a strong imbalance in the transport properties of cations and anions, drastically affecting the current response of the nanopore. We further show that the strong asymmetric current response is due to a polarity-dependent ion distribution and transport at the nanopipette tip region, leading to either ion depletion or enrichment for few tens of nanometers across its aperture. We provide evidence that a combination of the decreased/increased diffusion coefficients of cations/anions in the bath outside the nanopore and the interaction between a translocating molecule and the nanopore−bath interface is responsible for the increase in the translocation signals. We expect this new mechanism to contribute to further developments in nanopore sensing by suggesting that tuning the diffusion coefficients of ions could enhance the sensitivity of the system.

KEYWORDS: *nanopipette, nanopore, finite-element modeling, nanofluidic diode, DNA, poly(ethylene) glycol, PEG*





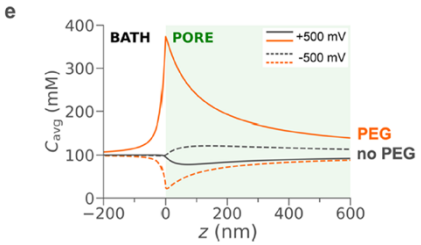
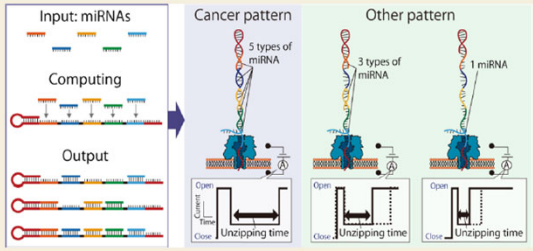


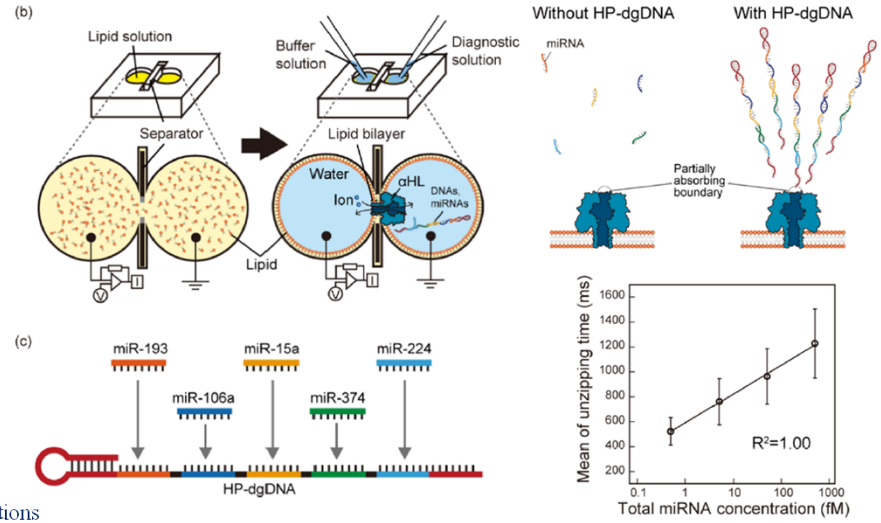
Figure 2. Simulated ion distributions close to the nanopipette tip at ±500 mV in the presence and absence of PEG in the external solution. Average concentration (C_{avg} = 1/2([K^+] + [Cl^-])) with (a, b) and without (c, d) PEG in the external solution for an applied voltage of (a, c) −500 mV and (b, d) 500 mV. (e) Average ion concentrations along the nanopipette axis of symmetry (red dashed line in panel a) in the presence (orange) and absence (gray) of PEG for negative (dashed curves) and positive (solid curves) bias applied. Note that average ion concentrations under different applied potentials and individual cation and anion concentration distributions are included in the Supporting Information (Section S5).

Marcuccio 2023, Mechanistic study of the conductance and enhanced single-molecule detection in a polymer−electrolyte nanopore

ABSTRACT: This paper describes a method for detecting microRNA (miRNA) expression patterns using the nanopore-based DNA computing technology. miRNAs have shown promise as markers for cancer diagnosis due to their cancer type specificity, and therefore simple strategies for miRNA pattern recognition are required. We propose a system for pattern recognition of five types of miRNAs overexpressed in bile duct cancer (BDC). The information of miRNAs from BDC is encoded in diagnostic DNAs (dgDNAs) and decoded electrically by nanopore analysis. With this system, we succeeded in the label-free detection of miRNA expression patterns from the plasma of BDC patients. Moreover, our dgDNA−miRNA complexes can be detected at subfemtomolar concentrations, which is a significant improvement compared to previously reported limits of detection (~10^{-12} M) for similar analytical platforms. Nanopore decoding of dgDNA-encoded information represents a promising tool for simple and early cancer diagnosis.

KEYWORDS: *DNA computing technology, nanopore, microRNA, cancer, membrane*





Takeuchi 2022, Pattern Recognition of microRNA expression in body fluids using nanopore decoding at subfemtomolar concentrations

A Nanopore Protein Reader

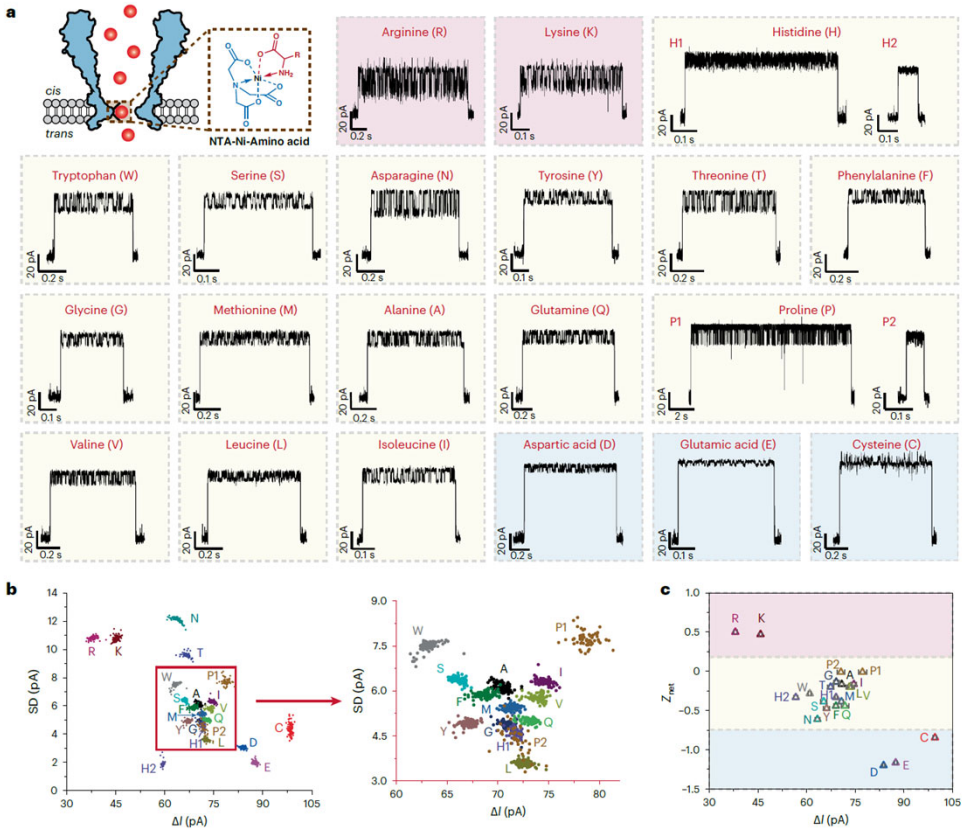


Fig. 2 | Discrimination of 20 amino acids using MspA-NTA-Ni. a, The schematics of amino acid sensing (top left) and representative events generated by different amino acids when measured with MspA-NTA-Ni. The measurements were carried out as described in Methods. A total of 20 proteinogenic amino acids were separately added to *cis* with a final concentration of 2 mM (A, C, F, G, H, K, M, N, Q, R, S, T, V, W, Y), 4 mM (D, E, I, L) or 40 mM (P) (Supplementary Figs. 8–11 and Supplementary Table 4). The final concentration of proline was set higher to compensate for its low rate of event appearance. Histidine and proline both produce two types of nanopore events, defined respectively as H1/2 and P1/2. According to their net charge (Z_{net}), all 20 amino acids were classified into three groups, in which amino acids with positive charge, weak negative charge and strong negative charge were marked with a red, yellow or blue background, respectively. **b**, The scatter plot of Δ*I* versus SD of events acquired with different amino acids. One hundred events acquired with each amino acid were used to generate the plot, according to which, most amino acid events are fully distinguishable. To clarify the detail, the events inside the red box are further zoomed in and shown on the right. Although the events corresponding to P2 and H1 appear to overlap in the plot, their event characteristics are visually different and can be discriminated when other event features such as dwell time, skewness and kurtosis are simultaneously considered. **c**, The correlation between Δ*I* and Z_{net} of amino acids. Generally, the blockage amplitude (Δ*I*) is larger when the net charge of the amino acid is more negative. The color background in the plot is consistent with that in **a**.

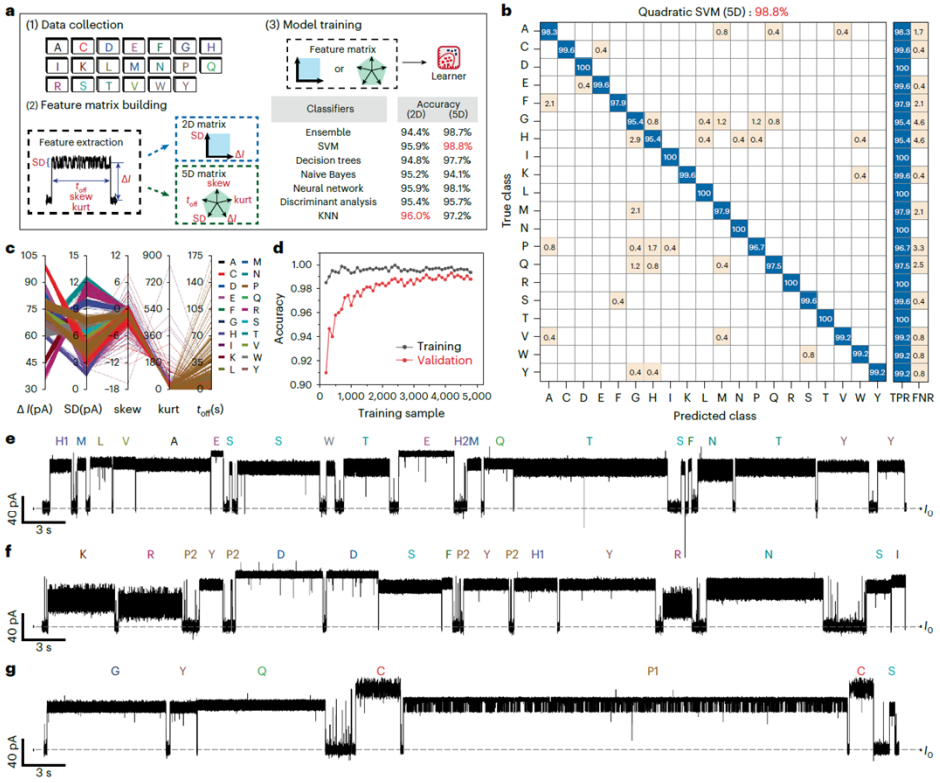


Fig. 3 | Identification of 20 amino acids by machine learning. a, The workflow of machine learning. In brief, sensing events separately acquired with 20 amino acids were collected to form a dataset. Five event features (ΔI, SD, skewness (skew), kurtosis (kurt) and t_{off}) were extracted from each event to form a feature matrix. A 2D feature matrix and a 5D feature matrix were built for machine learning. The 2D matrix contains only two features (Δ*I* and SD), similar to that in a 2D scatter plot (Fig. 2b). The 5D matrix, which contains all five features, includes more information from sensing. Machine learning was performed with the Classification Learner toolbox of MATLAB. Seven classifiers were evaluated with 10-fold cross-validation to screen the best-performing model. For the 2D matrix, the highest validation accuracy is 96.0% (Supplementary Table 6). For the 5D matrix, the highest validation accuracy reaches 98.8%, achieved by the quadratic SVM model (Supplementary Table 7). **b**, The confusion matrix of amino acid classification generated by the quadratic SVM model using the 5D feature matrix. TPR (true-positive rate) and FNR (false-positive rate) represent the correct or false classification of each true class, respectively. **c**, The parallel coordinate plots generated from the 5D feature matrix. **d**, The learning curve of the quadratic SVM model for varying sample size. **e**–**g**, Representative traces acquired during simultaneous sensing of all 20 amino acids. The measurements were performed as described in Methods. All amino acids were simultaneously added to *cis*. The final concentration of H and C was 0.1 mM. The concentration of F, M, N, T, S was 0.5 mM. The concentration of P was 20 mM. The concentration of all remaining amino acids was 1 mM. Zoomed-in views of these traces are shown in Supplementary Figs. 21–23. The events were predicted with the trained quadratic SVM model.

Wang 2024, Unambiguous discrimination of all 20 proteinogenic amino acids and their modifications by nanopore

Molecular Imprinting

Molecular imprinting refers to the creation of specific recognition sites in polymer networks by cross-linking in the presence of a template molecule, which represents the target to be recognized. This process is performed by mixing a solution of one (or several) monomer(s) with the template, thereby forming temporary interactions between the two. Subsequent cross-linking and polymerization, followed by removal of the template, lead to the formation of a polymer structure with embedded complementary cavities for the superstructure of the imprinted molecule. These nanocavities preserve not only the shape and size but also the molecular interactions necessary for the recognition of the target. The resulting molecularly imprinted polymers (MIPs) are thus able to selectively recognize and bind the target via a "lock and key" mechanism similar to those found in biological systems (e.g., antibodies and enzymes). These biomimetic polymeric networks can be prepared by designing interactions between the building blocks of a biocompatible network and the desired specific ligand and stabilizing these interactions by a three-dimensional (3D) structure. These structures are at the same time flexible enough to allow for diffusion of solvent and ligand into and out of the network.

Tour groups at the Chinese Theatre on Feb. 22, 1983 (George Rose/ LA Times)

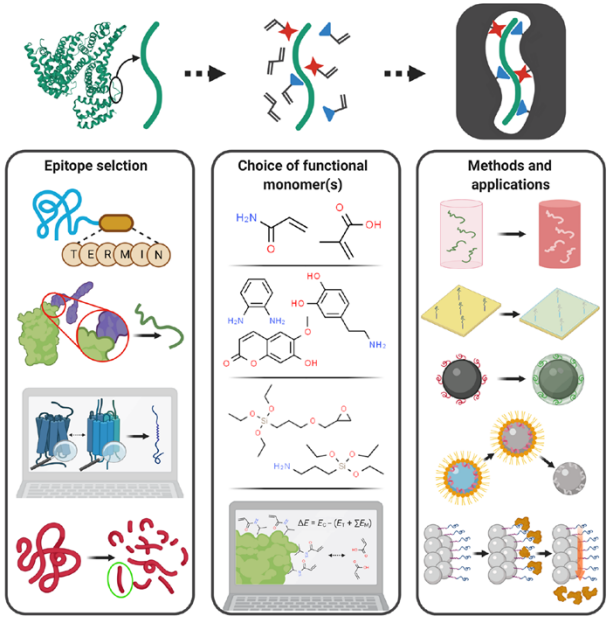


Fig. 2. Major steps in the process of epitope imprinting. Each one presents an array of options that must be carefully considered to optimize MIP efficacy considering the target application.

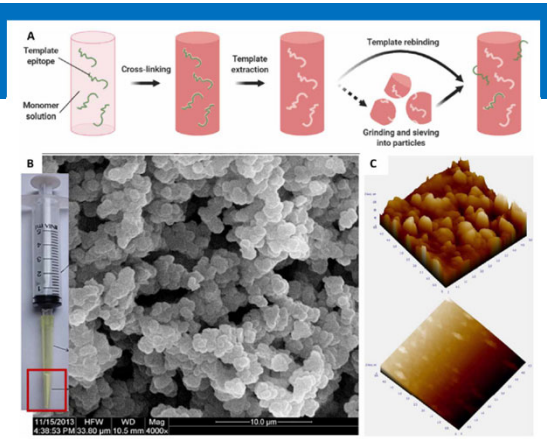


Fig. 6. Bulk molecular imprinting method and representative applications. (A) Bulk imprinting procedure; bulk MIPs can further be processed into microparticles/ nanoparticles by grinding and sieving (dashed arrow). (B) Scanning electron microscopy micrographs of imprinted (MIP C) and nonimprinted (NIP C) poly(2-hydroxyethyl methacrylate-co-N-methacryloyl-l-aspartic acid) cryogels for IgG purification.

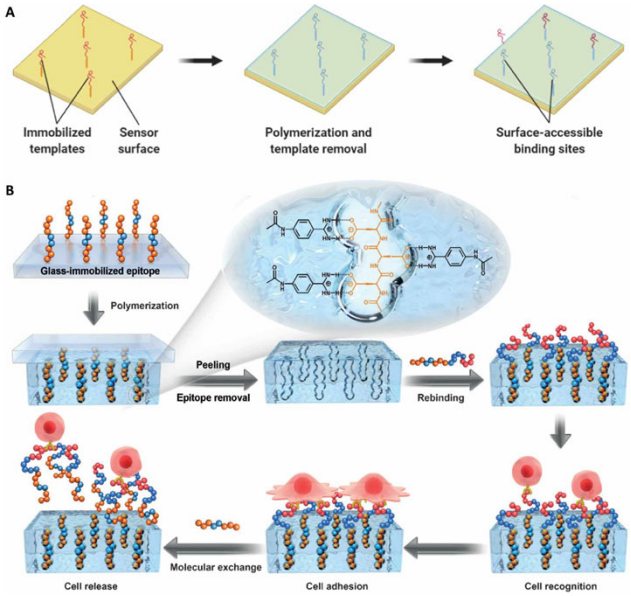


Fig. 7. Surface imprinting on thin flat films. (A) Surface MI procedure, allowing the creation of surface-accessible binding sites for the target molecule. (B) Generation of an epitope-imprinted biointerface for dynamic cell adhesion and harvesting.

Telxelra 2021, Epitope-imprinted polymers-Design principles of synthetic binding partners for natural biomacromolecules

Molecularly Imprinted Polymers

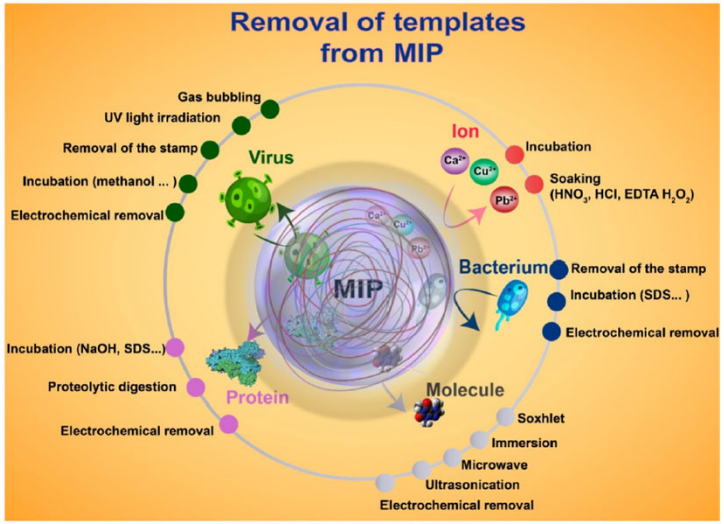


Fig. 2. Summary of selected removal approaches of templates from MIPs.
EDTA: ethylenediaminetetraacetic acid; SDS: Sodium dodecyl sulfate.

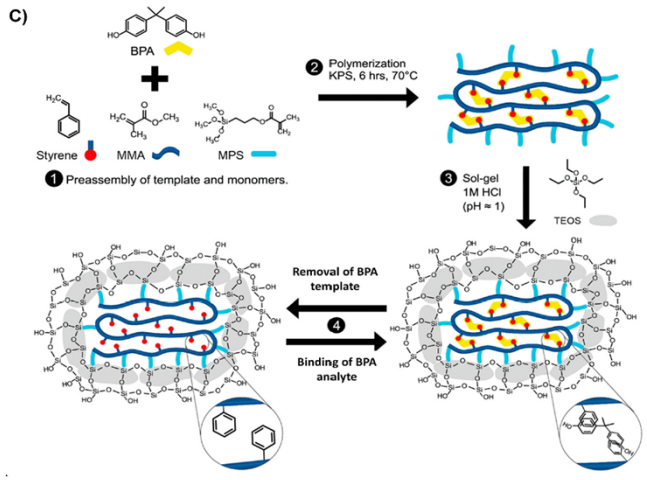


Fig. 9. C): Preparation of MIP and its coating with SiO_2.

Lamaoui 2024, Molecularly imprinted polymers: A closer look at the template removal and analyte binding

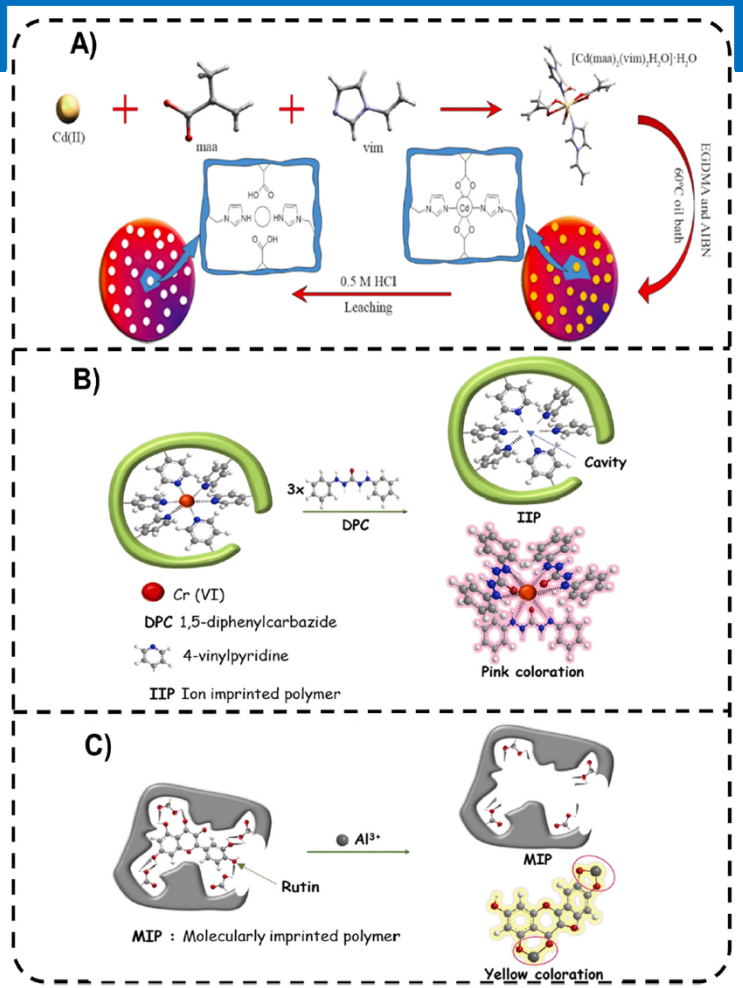
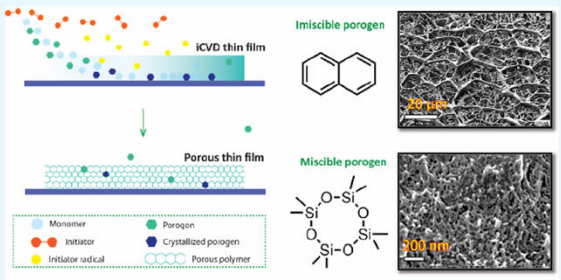
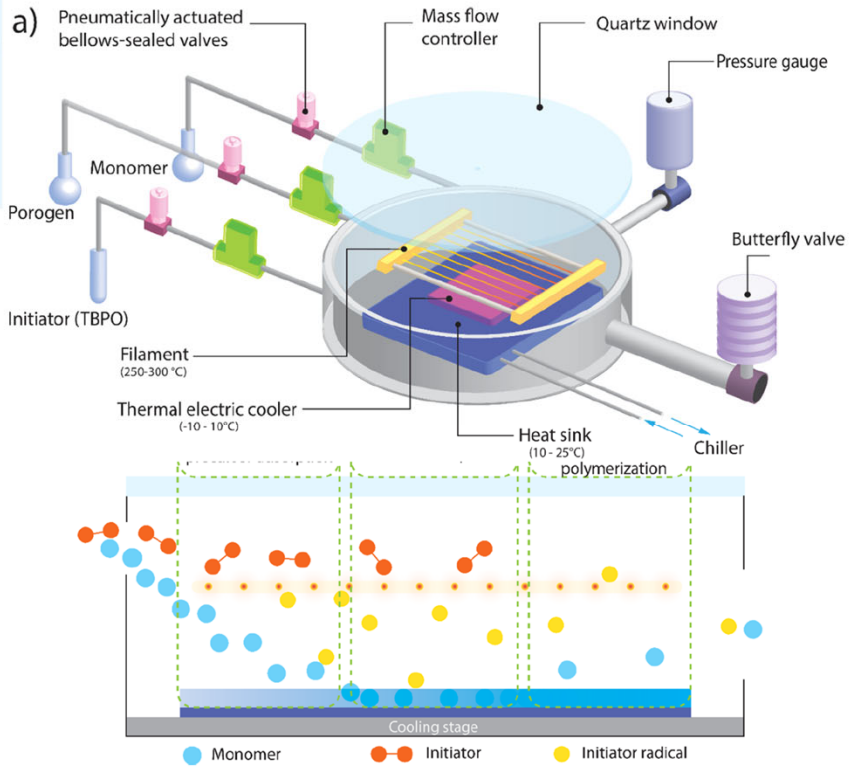


Fig. 3. A) Synthesis of Cd^{+2} imprinted polymer and removal of Cd^{+2} using HCl as a template removal agent. Removal mechanism of B) Cr^{6+} from ion-imprinted polymers (IIPs) and C) Rutin from MIP. MAA: Methacrylic acid; VIM: 1-vinylimidazole; EGDMA: Ethylene glycol dimethacrylate; AIBN: Azobisisobutyronitrile.

Porous Polymer Films with Tunable Pore Size and Morphology

ABSTRACT: The fabrication of porous polymer thin films with precise thickness and morphological control through conventional solvent-based techniques is challenging. Herein, we present a fabrication method for porous polymer thin films based on chemical vapor deposition that provides control over pore size, pore morphology, and film thickness. The porous films are prepared by co-depositing crystallizable porogen molecules with cross-linked poly(glycidyl methacrylate) (pGMA) thin films, which are synthesized by initiated chemical vapor deposition (iCVD). As the porogen is deposited, it crystallizes and phase-separates from the polymer film; simultaneous polymerization of pGMA limits crystal growth, controlling the size of crystals. Using naphthalene as porogen resulted in thin films with pore sizes from 5.9 to 24.2 μm and porosities ranging from 59.4 to 78.4%. Using octamethylcyclotetrasiloxane as porogen, which is miscible with the GMA monomer, drastically reduced the pore dimensions, ranging from 14.4 to 65.3 nm with porosities from 8.0 to 33.2%. The film morphology was highly dependent on the relative kinetics of porogen crystallization, phase separation, and heterogeneous polymerization. The kinetics of these competing processes are discussed qualitatively based on nucleation theory and Cahn−Hilliard theory. Fourier-transform infrared spectroscopy confirmed the retention of the reactive epoxide functionality of glycidyl methacrylate, which can enable further chemical derivatization as required for application in optoelectronics, sensing, separations, and biomedical devices.





Huo 2022, Porous polymer films with tunable pore size and morphology by vapor deposition