Biomedical Polymers (Biomaterials)
Hans Rosling Shows You 200 Years of Global Growth in 4 Minutes
By Aaron Saenz (Dec 09, 2010)

Hans Rosling. A professor of international health in Sweden, Rosling has a long history of exploring the facts and figures that surround our changing world. In the short segment of the BBC series below, Rosling gives one of his most famous lectures with a new twist. Using 120,000+ bits of data and augmented reality, the exuberant professor takes us through the last 200 years of global history and its uneven growth of wealth and health. No one makes statistics sound quite as awe-inspiring as Rosling.

His Gapminder site makes public data easily accessible, colorful, and meaningful to people who would otherwise ignore graphs as boring. In Rosling’s long history of amazing lectures (many of which can be found on YouTube) he has shown the importance of understanding the history of global changes if we want to plan for a better future.

Rosling’s review of the past 200 years leaves me rather optimistic about the years ahead. As he has outlined elsewhere, there are serious problems facing us in regards to exponential population growth and global health. Yet there are also solutions to humanity’s grand challenges of poverty, health, energy, etc. Demonstrations like this one could help broader audiences not only grasp the seriousness of the situation, but have hope that we can improve the world with our policies and technologies. As Rosling shows, the world is always changing and our beliefs must change with it. Perhaps colorful graphs and exciting lectures will help us reshape how we think of the world. At the very least they’ll change the way we think of statistics.
Biomaterials are any (natural or synthetic) materials which are in contact with the body or body components to **protect, support, restore, augment, or replace** damaged tissue or a biological function.

Biomaterials

2002 2011

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**Blood-contacting biomaterials**

**Non-blood-contacting biomaterials**

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**Biomaterials in Current Medical Practice**

- **Medical implants**, including heart valves, stents, and grafts; artificial joints, ligaments, and tendons; hearing loss implants; dental implants; and devices that stimulate nerves.
- **Methods to promote healing of human tissues**, including sutures, clips, and staples for wound closure, and dissolvable dressings.
- **Regenerated human tissues**, using a combination of biomaterial supports or scaffolds, cells, and bioactive molecules. Examples include a bone regenerating hydrogel and a lab-grown human bladder.
- **Molecular probes and nanoparticles** that break through biological barriers and aid in cancer imaging and therapy at the molecular level.
- **Biosensors** to detect the presence and amount of specific substances and to transmit that data. Examples are blood glucose monitoring devices and brain activity sensors.
- **Drug-delivery systems** that carry and/or apply drugs to a disease target. Examples include drug-coated vascular stents and implantable chemotherapy wafers for cancer patients.
The Borg: Half Machine, Half Human

The Borg are cyborgs, having outward appearances showing both mechanical and biological body parts. Individual Borg are referred to as drones. Borg commonly have one eye replaced with a sophisticated ocular implant. Borg usually have one arm replaced with a prosthesis, bearing one of a variety of multipurpose tools in place of a humanoid hand. Since different drones have different roles, the arm may be specialized for myriad purposes such as medical devices, scanners, and weapons. Borg have flat, white skin, giving them an almost zombie-like appearance.

https://en.wikipedia.org/wiki/Borg

Scientists are working on the development of a new equipment, more functional and cheaper, that could be deployed in primary healthcare centers. Detecting SARS-CoV-2 virus...

Engineers Print Wearable, High-Performance Biometric Sensors Directly on Skin

An international team of researchers developed a novel technique to produce precise, high-performing biometric sensors. Wearable sensors are evolving from watches and electrodes to bendable...

New Method of 3D-Printing Soft Materials Could Jump-Start Creation of Tiny Medical Devices for the Body

Researchers at the National Institute of Standards and Technology (NIST) have developed a new method of 3D-printing gels and other soft materials. Published in a...

Bioengineered Membrane to Capture Airborne COVID-19 Droplets – Inspired by Plant That Traps Insects

Team’s inspiration comes from nature — the pitcher plant, with its liquid membrane that traps insects. Detection and analysis of airborne coronavirus droplets using a...

New “Cyborg” Technology Could Enable Merger of Humans and AI

Although true “cyborgs” — part human, part robotic beings — are science fiction, researchers are taking steps toward integrating electronics with the body. Such devices...

Advanced Cryo-EM Reveals Viral RNA Replication Complex Structure in “Game-Changing” Detail

For the first time, scientists at the Morgridge Institute for Research have generated near atomic resolution images of a major viral protein complex responsible for...

Solving a DNA Mystery: “The Bizarre Thing About the Bubbling DNA”

Exposure to enzymes causes peculiar response in liquid droplets formed by DNA; new study explains mechanisms behind it. “A watched pot never boils,” as the...

Seaweed Extract Outperforms Remdesivir in Blocking COVID-19 Virus in Cell Studies

Heparin, a common anticoagulant, could also form basis of a viral trap for SARS-CoV-2. In a test of antiviral effectiveness against the virus that causes...

https://scitechdaily.com/tag/biomedical-engineering/
Synthetic Cells
Lab Grown Blood Vessel
eLegs Exoskeleton

Lab Grown Lungs
3D Bioprinter

Elysium (Matt Damon)
Edge of Tomorrow

http://www.time.com/time/specials/packages/0,28757,2029497,00.html
The Robot Suit

Sarcos Robotics Guardian XO Full-Body Powered Exoskeleton. The Best Inventions of 2020

Decades after RoboCop filled moviegoers’ heads with cyborg-suit fantasies, science has finally delivered: next year, the Salt Lake City firm Sarcos Robotics will release the Guardian XO—one of the first commercially available full-body powered exoskeletons ($8,500 monthly lease). The exoskeleton—an earlier iteration of which was recognized in TIME’s 2010 list of Best Inventions—is effectively a wearable robot shell that enables wearers to lift as much as 200 lb. It’s designed to prevent on-the-job injuries by reducing the strain of manual labor, and boasts as much as six hours of battery life. —J.R. Sullivan

Buy now: Sarcos Robotics Guardian XO

Blood-Contacting Biomaterials
Blood-contacting Soft Tissue Replacements Biomaterials

Heart valve prostheses

Mechanical heart valves:
Caged ball or caged disc type: polished CoCr alloy cage and silicone rubber ball, valve sewing ring made of knitted composite of PTFE and polypropylene cloth.
Tilting disc type: Pyrolytic carbon disc, guiding struts made of titanium or CoCr.
Bileaflet type: Pyrolytic carbon valves
Blood-contacting Soft Tissue Replacements Biomaterials

- Heart valve prostheses
- Vascular prostheses: Dacron, PTFE, Silicone rubber
- Cardiac pacemakers
- Blood oxygenator
- Extracorporeal dialysis
- Blood circulation tubing
- Intravascular catheter
- Cardiovascular stent

http://www.nostalgiacentral.com/tv/drama/sixmillion.htm

Total artificial heart

Polyurethane - Lady's stocking girdle

Scientific American
Left Ventricular Assist Device

Restoring Flow

Although artificial hearts are stymied by complications, left ventricular assist devices (LVADs) are extending lives. Doctors began implanting them a decade ago to keep heart failure patients alive while they waited for weeks or months for an available transplant organ. Today, improved designs are being installed as final fixes. Indeed, the distinction between an LVAD used as a bridge to transplant and as a permanent aid “is disappearing,” says Kiyoto Fukamachi, head of the Cleveland Clinic’s Cardiovascular Dynamics Laboratory.

“Some patients who received an LVAD as a bridge have been living with it for two or three years.”

A healthy left ventricle pumps freshly oxygenated blood through the aorta to the body. LVADs help the ventricle or take over its operations if the chamber is weak or has stopped functioning. First-generation designs, which still exist, are pulsatile: an implanted pump pushes blood in pulses like a natural heart. Second-generation LVADs are smaller, relying on a rotor that continuously streams blood. Engineers are exploring experimental, third-generation devices that use magnetically levitated pumps, reducing moving parts.

Yet “no one approach is necessarily better than the others,” Fukamachi says. “The choice depends on a patient’s circumstances.” The pulsatile machines, including Thoratec Corporation’s HeartMate I and World Heart Corporation’s Novacor, may still provide the best option if a patient needs a full takeover. Continuous-flow models such as MicroMed Cardiovascular’s DeBakey can be smaller and simpler because they do not require valves or a vent tube. Levitation devices may show less wear over time. (In the U.S., HeartMate I is approved for bridge and permanent therapy; Novacor is approved for bridge. Other models are in trials.)

Complications are involved, of course. A wire must protrude from the body to a controller and battery, leading to infection in up to 15 percent of patients. Blood clots can form inside pumps, so patients must live on anticoagulants, which increase the chance for problematic bleeding. Device failure occurs, too. But doctors are likely to implant more LVADs because heart donors remain scarce. Only 2,100 transplants are performed in the U.S. every year, whereas 3,000 to 4,000 people are perennially on the waiting list. —Mark Fischetti
Polycarbonate device that allows access to the blood.

Devices are intended for short-term use while on waiting list.

Often on list for extremely long time.

The air port is the main route of infection.

Improved integration with tissue is anticipated to reduce infection.

Material/tissue mechanical property mismatch.
Interventional Cardiology and Removing Plaque

Heart Attack

When a clot clogs an artery already choked with fatty deposits (atherosclerosis), blood is prevented from reaching part of the heart. Without oxygen, the tissue begins to die (black area, left).

https://www.tourmyindia.com/medical-tourism/blog/balloon-angioplasty-linked-fatal-neurological-events/
Cardiovascular Stents & Drug-Eluting Stents

Drug-Eluting Stents

Figure 5. Representative sections of arteries at site of stent bridges (Paragon stain at 20 and 80 magnification). A, Bridge from bare metal control. Healing is complete with bridge (B) covered by the fibromuscular neointima. B, Bridge from paclitaxel stent. C, Control with polymer but no drug in any part of the stent.  (Finkelstein 2003, Local drug delivery via a coronary stent with programmable release pharmacokinetics. Circulation DOI: 10.1161/01.CIR.0000050367.65079.71)
Hemodialysis

The Filter that Fights Ebola

Hemopurifier Developed by Aethlon Medical

What makes the Ebola virus so frightening is its speed. In a matter of days, it can pump out enough copies of itself to overtake the immune system. But the Hemopurifier, a specially designed cartridge that attaches to a dialysis machine, can tip the balance back in the body’s favor: its lectin filter attracts Ebola viruses and sucks them from the blood as it flows through. It’s been used only once, on a patient in Germany, but it did the trick—effectively curing his Ebola infection. In the future, doctors hope similar tech could be used on viruses like hepatitis.


https://www.sharonmukhi.com/work/home-hemodialysis
Fast Swelling Hydrogels for Aneurysm Treatment

Hydrogel core expands to provide a uniform scaffold for neointimal growth and additional volumetric filling of the aneurysm

https://www.microvention.com/product/hydroframe

Mucoadhesive hydrogel films to cover the ulcer area. Delivery of blood clotting agents.

The procedure called gastroscopy involves the placing of an endoscope (a small flexible tube with a camera and light) into the stomach and duodenum to search for abnormalities. Tissue samples may be obtained to check for *H. pylori* bacteria, a cause of many peptic ulcers. An actively bleeding ulcer may also be cauterized (blood vessels are sealed with a burning tool) during a gastroscopy procedure.

Bioinspired Hydrogels as Biomaterials

Zhu 2021, Recent Advances in Bioinspired Hydrogel-Materials, Devices, and Biosignal Computing
Non-Blood-Contacting Biomaterials
### Non-blood-contacting Soft Tissue Replacements Biomaterials

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### Hard Tissue Replacements Biomaterials

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<td>Bone repair and joint implants</td>
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<td>Metallic alloys, biodegradable polymers (PLA, PGA) for treating minimally loaded fractures.</td>
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<td>Surgical wires</td>
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<tr>
<td>Used to reattach large fragments of bone, to provide additional stability in long-oblique or spiral fractures of long bones.</td>
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<tr>
<td>Pins</td>
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<tr>
<td>Used primarily to hold fragments of bones together and to guide large screws during insertion.</td>
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<td>Screws</td>
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<td>Plates</td>
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Implantable Nanogenerators

The implantable nanogenerators (i-NGs) technology to cardiac implantable electronic devices (CIEDs)

Figure 1. Cardiac conduction system and self-powered CIEDs. (a) The schematic of cardiac conduction system. (b) The evolution of cardiac NGs and self-powered CIEDs based on TENG (top left) and PENG (bottom right) technologies. TENG: i-NGs based on the principle of triboelectricity PENG: i-NGs based on the principle of piezoelectricity

Li 2021, Materials perspectives for self-powered cardiac implantable electronic devices
A prosthesis can replace a lost limb but not the muscles in it... until now

You’ve heard of artificial hips, knees and limbs. But what about artificial muscles? Think about it: if you lose the lower part of your leg, you can replace the bone with a piece of titanium or even carbon fibre. But how do you replace the muscles that powered that leg?

In most cases, you don’t. The prosthesis isn’t powered at all, except by the energy the rest of the leg puts in. A Paralympic sprinter doesn’t use a battery to power their blade, so the blade must be made in such a way that the materials can utilise as much of the energy transferred from the rest of the body as possible.

Now, though, researchers are working on artificial muscles to power the next generation of artificial limbs, and not just for amputees – for robots as well. The difficulty they have in doing this is getting a lot of power out of something the size and weight of a real muscle. Traditionally, robots capable of lifting heavy loads have weighed in pretty heavily themselves and if you’re already carrying around a prosthesis, you don’t want to be dragging along a power pack the size of a car battery to run it.

To solve the problem, scientists have been taking inspiration from nature. Many are now using soft materials, such as electroactive polymers, which change shape and size in response to an electric current but don’t weigh a huge amount. There have also been slow-twitching prototypes based on twisting together slender synthetic threads in such a way that they contract and relax in response to temperature changes and are capable of lifting up to 7 kg. Most recently, researchers at Harvard University used very thin, very strong materials called elastomers to create artificial muscles that contracted as fast as natural muscles when supplied with electricity.

By Hayley Bennett (@gingerbreadlady)
Artificial Bone

Build a better bone
3D-printed bone may offer an alternative to metal skeletal implants

Bone is one of the few tissues that can regenerate, so most fractures heal nicely. But in some cases – more serious breaks, for example, or bone loss or deformity caused by diseases such as cancer, accidents and other traumatic injuries – the body needs help rebuilding bone. A handful of researchers are working to create materials that can be placed directly into damaged areas to provide structural support and eventually get absorbed by the body as new bone forms.

Traditionally, orthopaedic surgeons in these cases have used metal implants – a material that doesn’t quite gel with the body. “The problem is, we don’t get tight integration of the bone to the implant, simply because it’s metal,” says Hala Zreiqat, professor of biomedical engineering at the University of Sydney. Instead, she looked to ceramic to create an artificial material that is, like bone, both highly porous and extremely strong.

She and her colleagues made a ceramic-based scaffold infused with zinc, strontium and other substances to bolster its biological and mechanical strength. They also developed the technology for producing it using a 3D printer. When they tested the material in sheep tibia bones, which are relatively close to the size of human tibias, they found that the material not only spurred native bone formation and fixed bone defects, but was also fully integrated within a year.

The material is being developed by an Australian company called Allegra Orthopaedics. It’s on track for testing in humans in 2020, after another round of animal tests, Prof Zreiqat says. She envisions being able to print material based on a patient’s CT scan, so as to tailor it precisely to their injury. Eventually Prof Zreiqat plans to test whether her material can replace a whole mandible of the jaw. “It’s beautiful,” she says. “The idea is, we can get enough bone growth and the doctors don’t have to go back in.”

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 Alla is science writer who specialises in biology, health, medicine and technology.

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BBC SCIENCE FOCUS MAGAZINE COLLECTION
ABSTRACT: Implant surface modification by nanopatterning is an interesting route for enhancing osseointegration in humans. Herein, the molecular response to an intentional, controlled nanotopography pattern superimposed on screw-shaped titanium implants is investigated in human bone. Compared to those adherent to the machined (M) implants, the cells adherent to the nanopatterned (MN) implants demonstrate significant upregulation (1.8- to 2-fold) of bone-related genes (RUNX2, ALP, and OC). Controlled nanotopography, in the form of hemispherical 60 nm protrusions, promotes gene expressions related to early osteogenic differentiation and osteoblastic activity in implant-adherent cells in the human jaw bone.

Figure 1. SEM evaluation: (A) Low-magnification overview of the mini-implant; (B) intermediate-magnification image of an implant with a machined surface; and (C) an implant with a nanopatterned surface. (D) High-magnification image of semispherical profiles on the nanopatterned surface. Images (B) and (C) were taken at the root of the implant thread. Image (D) was taken at the flank of the implant thread. All analyzed implants were sputter-coated with 30 nm titanium film and heat-treated.
Sutures

Transition from Silk to Nylon

1950s: Polymeric Vascular Prostheses
-Nylon, Orlon, and Dacron
-Orlon and Dacron found to be superior
Both had high patency rates in large arteries
Biomedical Polymers

Current: Existing polymers
Find application.
(e.g., Teflon - nuclear bomb)

Future: Find problems and needs
Develop new polymers

Teflon was used in various biomedical devices, but it is not used as widely anymore due to many unjustified lawsuits against the company.

Zipper Band-Aids speed up healing and does not leave a scar.
TikTok, @cooltechnology2021
Polymers for Wound Healing

Figure 3. A–C) Schematic of the smart wound bandages with wound markers sensing capabilities and on-demand delivery of therapeutic molecules for the treatment of chronic wounds. A) Conceptual view of the automated smart bandage. The bandage comprised a multilayer flexible pH sensor and a flexible heater for on-demand release triggering thermoresponsive drug carriers containing antibiotics in the wound site with wireless communication capabilities to smartphones. B) Schematic view of integrated drug-releasing microparticles within the dressing. a–c) Optical image of the temperature-responsive microparticles at different temperatures. d–f) Fluorescence images of embedded drug microcarriers inside the smart microheater attached hydrogel dressing. Rhodamine B was used for better visualization of drug carriers inside the dressings. g) Release profile of cefazolin as a model antibiotic drug in different temperatures. h) Controlled release profile of cefazolin.

Figure 8. A–H) Schematic demonstration of a smart hydrogel-based wound dressing. A) An intelligent hydrogel wound dressing for the early detection of wound infection. B) Schematics of the stages of the smart wound dressing fabrication process. C) A close-up view of the final prototype of the smart wound dressing. D) Assessment of the function of treated dressing by using Triton under UV light exposure.

Farahani 2021, Would healing. From passive to smart dressings
Continuous Glucose Monitoring and Insulin Delivery

Records glucose levels every five minutes. Replace the sensor after three days of use. Required to take finger sticks twice a day to calibrate the glucose sensor.

Sensor-Augmented System

Computer-controlled diabetes
Managing diabetes means an ever-changing daily regime of multiple, self-administered insulin injections. But what if there was a device that could do the managing for you? (SARA RIGBY)

For someone living with type 1 diabetes, monitoring and maintaining glucose levels can be a chore, requiring, on average, an injection of insulin between two and six times a day. A team at Imperial College London is aiming to make their lives easier by developing a device dubbed the ‘bionic pancreas’. “It will be a revolution both in terms of glucose control and quality of life for people living with diabetes,” says Dr Pau Herrero-Vinas, an engineer on the team. The pancreas is a small, pear-shaped organ that controls blood sugar levels. The cells responsible for this job, beta cells, respond to spikes in glucose levels by simultaneously releasing and manufacturing the hormone insulin, which allows glucose to be absorbed into tissue. When not enough insulin is produced, glucose builds up in the bloodstream and, past a certain point, can lead to coma and death. High blood sugar levels, also known as hyperglycaemia, can cause blindness, heart disease and nerve damage over the long-term.

TECHNOLOGY STEPS IN

In people with type 1 diabetes, the pancreas contains only 20 to 30 per cent of the regular number of beta cells, meaning that insulin levels are dangerously low unless treated with regular injections of insulin. The bionic pancreas, or the Bio-inspired Artificial Pancreas for the Home, is designed to act like a replacement organ. The process of regulating blood sugar levels is fully automated, so the device is constantly monitoring glucose levels and making small changes to keep them under precise control.

The device is comprised of a glucose sensor, an insulin pump and a microchip. The microchip’s algorithm calculates the precise amount of insulin needed, mimicking the behaviour of beta cells. By embedding all the software onto a microchip, the team created a device that not only requires small amounts of power, but is also compatible with other medical devices the user might need. “We focussed on developing a system that’s very low-power so that it can calculate the correct insulin dose. When the user isn’t eating, though, the MiniMed works happily on its own – meaning it is most effective overnight. “Overnight control is a problem that’s already been solved, so it’s not very challenging anymore,” says Dr Herrero-Vinas. “But daytime control, especially after meals, that’s still a problem. So that’s what we’re focussing on: to have a system that works at night and through the day.” The bionic pancreas is currently being clinically tested. Once these tests are complete, says Dr Herrero-Vinas, the team will look at licensing the product to make it available to patients, which he estimates will happen in a couple of years. by SARA RIGBY Sara is BBC Science Focus Magazine’s online assistant.

A scientific guide to the human body
Figure 1. Design and characterization of the NICE device including mechanical properties, permeability, and cell compatibility. (A) Schematics of the device showing the islet-laden hydrogel core surrounded by the nanofibrous skin that prevents cell penetration while allowing maximum mass transfer, along with a photo of nanofibrous tubes with different diameters (from left to right: 0.5, 1, 1.5, 2, and 3 mm) and a scanning electron microscope image of the nanofibers. (B) Tensile test (stress-strain curves) of the nanofibrous tubes (n = 4). (C and D) Photographs showing the device being stretched more than three times in length (C) and bent without kink (D). (E) SI of mouse islets (the ratio of insulin secretion in the buffers of high- and low-glucose concentrations) encapsulated in the device, compared to that of free-floating islets after 1 and 7 days of culture; mean ± SD (n = 3). (F) Live (green) and dead (red) staining of free-floating islets and islets encapsulated in device after 1-day culture. The data were compared using the two-tailed Student’s t test. Scale bars, 3-mm (A) macroscopic image and 100-μm (F) and 5-μm (A) microscopic images. n.s., nonsignificant.

Wang 2021, A nanofibrous encapsulation device for safe delivery of insulin-producing cells to treat type 1 diabetes.
Biomaterials for Encapsulation of Cells

Yang 2021, A therapeutic convection–enhanced macroencapsulation device for enhancing β cell viability and insulin secretion

Fig. 1. Design of a ceMED for increasing mass transport, β cell viability, and insulin secretion sensitivity. (A) Illustration comparing diffusion-based versus convection-enhanced approaches. Expanding MEDs from a typical two-dimensional (2D) wafer static system to a 3D MED brings forth mass transport limitations and cell death. These limitations motivate the introduction of a HF in a 3D expanded MED to allow increased nutrient delivery by perfused flow in the ceMED. (B) Simulation showing the gradient of oxygen (millimolar), glucose concentration (millimolar), and insulin secretion rate (nanomolar per second) as a function of position inside a static macroencapsulation with multiple layers of islets. The color bars indicate the concentration of each variable. White arrows indicate the hypoxic regions in the islet due to diffusion-limited transport of the oxygen in the device. (C) Scheme of the ceMED, consisting of an EqC, a CC, and a connecting HF. EqC captures glucose and oxygen from the surroundings; HF transports these solutes to the encapsulated cells in the CC. Inside the CC, positive pressure facilitates flow and improved mass transport to and from the encapsulated cells. The CC is enclosed by a PTFE membrane for protection from immune attack while allowing for nutrient transfer. (D) Gross view of a fully assembled, transplantable ceMED and its components. The ceMED can be connected to various pump systems, exemplified here by an osmotic pump.
Nanofiber-Hydrogel Composite for Angiogenesis

Fig. 1. Engineering a nanofiber-hydrogel composite with interfacial bonding between nanofiber surface and hydrogel network. (A) Schematic of the synthesis and structure of PCL nanofiber-HA hydrogel composite. (B and C) Scanning electron microscopy images of rat native fat tissue (B) and PCL nanofiber-HA hydrogel composite (C) showing that fibers are embedded into the HA hydrogel network (arrowheads). (D) Image showing a PCL nanofiber-HA hydrogel composite (G’ = 250 Pa, left) and an HA hydrogel [oscillatory shear storage modulus (G’) = 80 Pa, right] constructed from the same 80-Pa HA hydrogel. (E) Image showing that the composite can be injected through a 30-gauge needle. (F and G) G’ of HA hydrogels and nanofiber-hydrogel composites with different PEGDA cross-linker concentrations.

Fig. 2. Enhanced cell migration and vascular-like network formation inside composite. (A) hASC migration from 200-μm spheroids embedded in the 80- and 150-Pa HA hydrogels and the 150-Pa composite. (B) Quantitative analysis of cell migration distance inside the hydrogels and the composite (n = 4 to 7). (C) hASCs formed 3D connected networks in the 150-Pa composite. (D) Vascular-like network formation in the 80- and 150-Pa hydrogels and the 150-Pa composite. (E) Quantitative analysis of vascular-like network formed inside the hydrogels and the composite (n = 6). Cell morphology was visualized by staining for actin with Alexa Fluor 568 Phallolidin shown in red. Cell nuclei were stained with 4’,6-diamidino-2-phenylindole (DAPI) shown in blue. Nanofibers were labeled with FB78 shown in green. Scale bars, 100 μm. Statistical significance was calculated by one-way ANOVA with the Dunnett’s post hoc test. Comparison was performed between groups. **P < 0.01, ****P < 0.0001. Data are presented as means ± SEM.

Li 2019, Nanofiber-hydrogel composite–mediated angiogenesis for soft tissue reconstruction
Tissue Expander

Manual delayed expansion.
Predefined size and shape.
No ability to reshape by surgeons.

Hydrogel Tissue Expanders

Copolymers of methyl methacrylate and N-vinylpyrrolidone
The volume increase of 3-12 folds.
Hydrogel in silicone shell to reduce the swelling speed.

Predefined size and shape.
No ability to reshape by surgeons.

http://www.osmed.biz/html_e/produkte/produkte.html
A hydrogel expander normal and being flexed between fingers. Note its elasticity.

Restiex® (Re-Shapable Tissue Expanding Hydrogel)

http://polyscitech.com/currentResearch/restiex/
Hard Tissue - Soft Tissue Interface
Figure 1. Structure of bone-to-soft interfaces in the human knee joint. (a) Human knee (from Servier Medical Art) illustrating a blue box for the osteochondral interface (OI) and a red box for the enthesis (E). (b) Schematic of the osteochondral interface divided into the morphology and distribution of the cells (left) and the matrix organization (right) within the different zones in the OI. Panel b is reproduced with permission from ref 72. Copyright 2021 MDPI. (c) Diagram showing the gradients observed in the OI. (d) Histological image of the osteochondral unit showing the different zones in the OI. The subfigure corresponds to a picrosirius red stained sample, imaged with a polarized light filter that shows the collagen distribution (aligned in orange and random in green). Panel d is reproduced with permission from ref 137. Copyright 2021 Elsevier. (e) Schematic of the ligament/tendon interface (enthesis, E) showing the predominant type of collagen and its orientation, and the type and morphology of the cells present in each zone. Panel e is reproduced with permission from ref 83. Copyright 2021 MDPI. (f) Diagram showing the gradients observed in the enthesis. (g) Histological image of the enthesis showing the different zones connecting the tendon and bone. The subfigure corresponds to a fluorescence microscope image showing the fibers of collagen type II in bright orange. Subfigure g is from ph.tum.de/latest/news/tendon-boneinsertion and reproduced with permission from ref 5. Copyright 2021 Nature.

Kruize 2021, Biomimetic Approaches for the Design and Fabrication of Bone-to-Soft Tissue Interfaces
Figure 3. Schematics of different fabrication methods that can be used for bone-to-soft interfaces, from highly organized interfaces (left) to randomly organized interfaces (right). (a) Digital light processing-based 3D/bioprinting showing that sequential input of different digital masks can be used to generate patterns with interfaces of different materials. Panel a is reproduced with permission from ref 186. Copyright 2021 National Academy of Sciences. (b) Extrusion-based 3D/bioprinting showing that the combination of multiheads containing different bioinks can be used to generate scaffolds with gradients (in this example, cell gradients mimicking articular cartilage cell density. Panel b is reproduced with permission from ref 187. Copyright 2021 MDPI. (c) Electrospinning setup with two spinnerets creating a transitory region. Reproduced with permission from ref 212. Copyright 2021 John Wiley and Sons. (d) Iterative freeze-casting (or ice-templating) can be combined with freeze-drying to achieve bilayered structures with a defined interface.

Kruize 2021, Biomimetic Approaches for the Design and Fabrication of Bone-to-Soft Tissue Interfaces
Other Biomaterials
Approved the use of the device under the emergency-use exemption

written informed consent was provided by the patient’s parents

The splint was manufactured from polycaprolactone

Polycaprolactone

N. Engl. J. Med. 368: 21
Commonly Found Degradable Biomaterials in FDA Approved Devices

Devices are approved by the FDA

Polymers are not approved by the FDA

Polydioxanone: suture clips and bone pins
poly(caprolactone): contraceptives and as a suture
Poly(PCPP-SA anhydride): Gliadel Wafer

poly(glycolic acid) (PGA)
poly(lactic acid) (PLA)
copolymer (PLGA)
degradable sutures, bone pins, and drug delivery vehicles
About SonarMed™ Airway Monitoring System

The SonarMed™ airway monitoring system includes a bedside monitor and single-use sensor. The SonarMed™ sensor fits any brand of standard endotracheal tube (ETT) in sizes ranging from neonatal to pediatric populations (2.5 mm–6.0mm ID) and attaches by replacing the 15-mm connector at the end of the ETT, placing the sensor between the ETT and the ventilator circuit. The SonarMed™ monitor incorporates an easy-to-read color screen that continuously displays any change in ETT depth within the trachea.

In 1990, Purdue University Professor George Wodicka conceived of a medical device that gives clinicians vital information to make more informed, life-saving decisions for their smallest patients.

https://www.purdue.edu/newsroom/releases/2021/Q2/every-newborn-on-a-ventilator-can-now-be-better-protected,-thanks-to-technology-that-helps-prevent-a-common-breathing-tube-incident.html
Biomaterials for Sensors

Purdue Biomedical engineer Professor Chi Hwan Lee specializes in sticktronics and custom-printed soft medical sensors. Electronic stickers to streamline large-scale 'Internet of Things'


An electronic glove that simulates the sense of touch for prosthetic hands.

A sensor that can be placed on an over-the-counter contact lens and then used to detect glaucoma in patients.
Biomaterials for Sensors

Baumgartner 2020, Resilient yet entirely degradable gelatin-based biogels for soft robots and electronics

Fig. 1 | A resilient yet fully degradable biogel. a,b. Naturally derived ingredients, such as gelatin and citric acid, enable an elastic and stable, but fully degradable, biogel. Together with cellulose fibres and zinc, soft and durable pneumatic actuators (a) and multifunctional e-skins (b) are realized.

Extended Data Fig. 3 | Assembly of sensor skins. Assembly process of the sensor skin consisting of degradable e-skin and reusable PCB. 1, Gels of different mechanical properties are joined by laser assisted rapid healing (LARH). 2–3, A zinc metal sheet is then applied to the gel and structured by a fiber laser. 4, After the structuring process the zinc residues are peeled off. 5, A flexible reusable PCB is mounted on the gel and soldered to the zinc foil of the e-skin. In the last fabrication step a temperature sensitive paste is placed on the gel to finalize the temperature sensor.

Biogel preparation. Citric acid (1 g) and glycerol (8 g) were dissolved in deionized water (8 g) and heated to 60 °C. Sugar syrup (7 g) was heated to 60 °C to reduce its viscosity and mixed to the presolution. After cooling to room temperature, gelatin powder (4 g) was added and allowed to soak for 1 h. The mixture was heated in an oven at 70 °C for 1 h and stirred in a planetary mixer (DAC 600.2 VAC-P, Hauschild Engineering) under vacuum (2,350 r.p.m., 450 mbar) for 4 min to achieve a homogeneous precursor ready for moulding. Gel recipes with varying compositions used here are listed in Supplementary Table 3.

Biogel foam. E471 powder was dissolved in deionized water (ratio 1:2) for 2 h under vigorous stirring. The dissolved E471 (8 g) was mixed with the biogel presolution and gelatin powder (4 g) and allowed to soak for 1 h. The mixture was heated at 65 °C for 1.5 h and mixed with a hand blender for 30 s at 5,000 r.p.m., which resulted in a microfoam, which was cast into acrylic glass moulds.

Biogel thin films. The prepared warm liquid biogel was poured on a Teflon plate and distributed via doctor blading. The films were left to dry for 1 h, which resulted in a thickness of 0.58 mm. Coating with talcum powder rendered non-sticky films.

Biogels with biodegradable encapsulation. Shellac solution was prepared according to Luangtana et al.46. Schellac (36 g) was dissolved in ethanol (100 g). PEG 400 (7.2 g) was added to the shellac solution and stirred for 10 min. G2430 biogel samples were dip coated in the shellac solution four times, followed by 30 min of heating at 50 °C in an oven and a final heating at 70 °C for 1 min. We repeated this procedure to achieve a homogeneous encapsulation of thickness ~200 μm.
PSYONIC Announces Launch of Revolutionary New Bionic Hand: Ability Hand™
Leader in Advanced Prosthetics Releases the First Commercially Available, Accessible and Affordable Bionic Hand
September 1, 2021 - (Champaign, IL) - PSYONIC, the world’s leading advanced prosthetic device company, released their revolutionary new Ability Hand™ to potential users and clinicians nationwide today. Fast, tough, and intuitive, the Ability Hand is the first and only bionic hand with multi-touch sensory feedback on the market.

The Ability Hand system includes a multi-articulated prosthesis that is robust, lightweight and offers touch feedback, as well as being the fastest operating hand on the market with a 200ms closing speed.

About the Ability Hand:
Lightweight. The Ability Hand weighs in at 470 grams – about 20 percent less than the average human hand. And it comes in two sizes, so it fits a much broader range of people than the typical prosthetic.
Multi-articulated. All five fingers flex and extend, and the thumb rotates.
Easy to charge. The Ability Hand charges using USB-C in about an hour. A charge lasts all day. You can even charge your phone from your arm!
Cross-compatible. The Ability Hand works with most third-party EMG pattern recognition systems, EMG direct control systems, linear transducers, and force-sensitive resistors.
Tough. The Ability Hand is lightweight, water-resistant, and each finger can handle blunt force impact without breaking.
Bluetooth compatible. You can connect your hand to our iOS and Android mobile apps, so your prosthetist can fine tune your Ability Hand and you can make constant improvements to its grips and functionality.
Over-the-air updates. We’ll continually update the Ability Hand’s software, and you’ll be able to download those over-the-air from our app.

The Ability Hand works with most third-party myoelectric pattern recognition systems, myoelectric direct control, linear transducers, or force sensitive resistors. Prosthetists work with their patients to determine which system is best to integrate with the Ability Hand. Each hand is equipped with patent-pending high-performance motor control, compliant finger joint technology, a 7.4V 2200mAh battery pack, Bluetooth connectivity, and sensory touch feedback. The hand is compatible with most commercially available third-party wrist rotators and elbows.

The Ability Hand is covered by Medicare and most insurance companies. Currently, about 10% of people with an upper-limb difference in the U.S. can afford a bionic hand. PSYONIC predicts that number will increase to 75% with the release of their bionic hand.

Clinicians can purchase the Ability Hand by contacting sales@psyonic.co. For more information, visit https://www.psyonic.io

About PSYONIC:
PSYONIC is an advanced prosthetic company developing affordable and accessible devices. The Ability Hand is the first product for the company. Founded out of the University of Illinois at Urbana-Champaign, and grown in partnership with some of the best incubators and accelerators industry, PSYONIC is focused on bringing better prostheses to the market. The team at PSYONIC believes that everyone should have access to the best available prosthetic devices. For more information about PSYONIC visit www.psyonic.co or connect with PSYONIC on Facebook, Twitter, Instagram, and LinkedIn.

https://www.psyonic.io/ability-hand
The stark performance gap between living organisms and artificial machines arises from their bodies’ different material compositions and physicochemical behaviors. Living organisms bypass many shortcomings of modern robots due to their soft matter construction and the distributed nature and complexity of biological sensorimotor systems.

The key elements of robotic functionality: actuation, perception, power, and control.

Figure 1. A paradigm for robotic materials design. (a) Inspired by design approaches in materials science and engineering, robotic materials couple robotic behaviors in self-contained material systems through considerations of material processing-structure-properties-function relationships. (b) Opportunities for robotic innovations via robotic materials are illustrated through relevant processing methods for target robotic functions in emerging applications.

Truby 2021, Designing Soft Robots as Robotic Materials
Bionic Touch

TOUCH THIS: A motorized tactor developed by Kinea (bottom right) mechanically stimulates an alternative body surface (bottom left) to “playback” the sensations picked up by fingertip sensors (top left) of a prosthetic hand. The Modular Prosthetic Limb (top right and featured image), developed by the Johns Hopkins Applied Physics Laboratory, uses the Kinea sensors in its fingertips.

HDT Global; Johns Hopkins University Applied Physics Laboratory
http://the-scientist.com/2012/09/01/missing-touch/

If you can’t feel anything, your hand is pretty close to useless. That is basically the problem with prosthetic hands for the last century—no touch.

—Gerald Loeb, University of Southern California
Skin-Inspired Healable Conductive Elastomers

Stretchable conductive elastomers play an irreplaceable role in flexible electronic devices. However, stretchable conductive elastomers are usually soft and susceptible to damage. Highly stretchable and elastic conductive elastomers integrated with damage resistance, damage tolerance, and healability are fabricated by loading ionic liquids (ILs) within the polyurethane (PU) elastomers of the multiblock polymers of poly(dimethylsiloxane)/polycaprolactone (PDMS/PCL) coordinated with Zn$^{2+}$ ions.

Figure 1. Fabrication process of the conductive elastomer. (a) Synthesis process of PU and the molecular structure of the loaded [EMIM][TFSI]. (b) Schematic illustration of the fabrication of the PU–Zn–IL elastomer. The digital image in (b) shows a piece of the PU–Zn–IL elastomer. (c) Digital images of the PU–Zn–IL elastomer at (i) ~20% strain and (ii) ~400% strain connected in a circuit with an LED bulb.

Figure 3. (c) Schematic illustration of the structure of the PU–Zn–IL elastomer.

Wang 2021, Skin-Inspired Healable Conductive Elastomers with Exceptional Strain-Adaptive Stiffening and Damage Tolerance
Next year marks the 50th anniversary of Dr. William Hillenbrand’s then anonymous donation of $500,000 to establish biomedical engineering research at Purdue. That initial seed investment brought us Drs. Leslie Geddes, Willis Tacker, Joe Bourland, and Charles Babbs to Purdue who put Purdue BME on the map with more than 30 inventions, many of which focused on implantable electronic devices including and energy-efficient implantable defibrillator and the automatic pacemaker.

Established in 2010, the Center for Implantable Devices (CID) established at Purdue University strives to continue this legacy of our founding faculty who focused on the translation of their applied research for real clinical impact. Over the past several years, CID emerged as the new powerhouse in bioinstrumentation with substantial extramural support from NIH, DARPA, Cook, Samsung, and others. With a renewed institutional commitment to excellence in biomedical instrumentation research at Purdue BME, we are expanding our capability with the focused hiring of a senior faculty in bioinstrumentation. We are uniquely positioned with a network of stellar clinical collaborators at Indiana University School of Medicine, Goodman Campbell Brain and Spine, and the Purdue University College of Veterinary Medicine. With ongoing research on clinical-needs driven projects including closed-loop peripheral neuromodulation, smart catheter for intraventricular hemorrhage and hydrocephalus, stretchable epicardial sensors for cardiac electrophysiology, automatic drug delivery system for opioid overdose, and many others, CID at Purdue BME is well-poised to reach the pinnacle of excellence at clinical scale for the future of biomedicine.

https://engineering.purdue.edu/BME/AboutUs/News/2021/2021-Center-For-Implantable-Devices
Implantable Nanogenerators

Figure 3. Packaging materials for i-NG and CIEDs.
(a) Foreign-body reaction schematics.
(b) H&E staining images of PCBMA zwitterionic hydrogel and PHEMA hydrogel implanted for 1 week and 3 months in rats.
(c) Super-repellent surface bringing hemocompatibility by creating nanoscale textures with trapped air pockets.
(d) Bioadhesive made of hydrogel material and its stable adhesion on a beating rat heart in vivo.

Li 2021, Materials perspectives for self-powered cardiac implantable electronic devices
Biomaterials for Chips

Biomaterials are used in microfabricated devices to replicate the physiological microenvironment in studies using so-called “organ-on-chip,” “tissue-on-chip” or “disease-on-chip” models, which can reduce the use of animal models with their inherent high cost and ethical issues, and due to the possible use of human cells can increase the translation of research from lab to clinic.
Biomaterials for Chips

Figure 1. Schematic of the LOM. (a) Different sensors embedded in the PDMS. (b) Comparison of Young’s modulus based on PCB, skin, and PDMS. (c) Scheme of the different parts of the LOM on skin. Embedded in PDMS, the Young’s modulus of the system is more similar to that of our skin. (d) Strain–stress curve of and Young’s modulus of PDMS and the nonwoven fabric of the mask.

Figure 2. Recorded data from the LOM. (a) Scheme of the different parts of the system on the mask. (b–e) HR, SpO₂, T, and BP, compared with data collected from commercial products. (f) Remote real-time monitoring of a person using the mask for HR, SpO₂, T, and BP.
Nature-Inspired Biomaterials

Fig. 1 Examples of nature-inspired bulk and surfaces: (a) Cu nanostructure for high wavelength absorption generated through plasma-assisted etching of Cu plate. (b) Optical fibre with different angles inspired by Steller’s jay feather. (c) Cu nanostructure generated with ion beam structure from south. (d) Boiling plant-inspired nodal structure. (e) Hierarchical graphene plates inspired from potato skin. (f) Soft robotic thermally driven paper inspired by folding of cattleya leaf. (g) 3D printed corallinear for superhydrophobic action inspired by a rose leaf. [Selected from ref. 10 (2020 NPG); b from ref. 11 (2019 Wiley-VCH); c from ref. 12 (2020 Wiley-VCH); d from ref. 13 (2019 NPG). e from ref. 14 (2019 Wiley-VCH); f from ref. 15 (2019 Springer) and g from ref. 16 (2019 Wiley-VCH).]

Fig. 2 Classification scheme. Arrow direction shows a generic classification of nature inspiration, mimetics and mimicry.

Katiyar 2021, Nature-inspired materials

Fig. 5 Different nature-inspired examples: (a) Enhanced wall strength construction mimicry of interlocking weaver ants. (b) Full-scale generation using 3D printing. (c) Enhanced glass toughness inspired by tooth enamel. (d) Fiber-reinforced armor strength polymer inspired by fish scales. (e) The alignment of carbon nanotubes in nanocomposites inspired by wood grain. [Selected from ref. 7 (2016 NPG); c from ref. 8 (2015 NPG); c from ref. 9 (2014 NPG); b from ref. 10 (2014 NPG); d from ref. 7 (2014 NPG); e from ref. 10 (2013 NPG); e from ref. 11 (2013 NPG).]

Fig. 8 Another example of an electrical gel inspiring the novel design of hydrogel. (a) The biomimetic strategy for the plant-inspired catechol thermally-based self-adhesive, tough, and antibacterial NP-PEA hydrogel. Adapted from ref. 17 (2014 NPG).

Define
Naturalise
Discover
Abstract
Emulate
Evaluate

Fig. 12 The concept of design spiral. The figure shows the concept of a spiral adopted from the Biomimicry research institute.
Bio-Sommelier (Bimetallic Tongue)

Fig. 1 Comparison of mono- and bimetallic LSPR sensors. (a) SEMs showing (i) monometallic Al, (ii) monometallic Au, and (iii) bimetallic Al/Au regions. (b) Transmission response of arrays of Al-only (dotted-blue), Au-only (dotted-red), and bimetallic Al/Au (black solid) in water.

Fig. 2 Effect of surface chemistry on the sensitivity of Au, Al, and Au/Al sensor arrays. (a) Surface chemistry combinations used: (i) native Al, Au (ii) Al-HMDS, Au-DT, and (iii) Al-PEG, Au-PFDT. (b) The shift in plasmonic response from water for monometallic arrays in 10%, 20%, and 30% solutions (v/v) of (i) acetone and (ii) ethanol. (c) The shift in plasmonic response from water for bimetallic arrays in 10%, 20%, and 30% solutions (v/v) of (i) acetone and (ii) ethanol. The different surface chemistries (native Al, Al-HMDS, Al-PEG, native Au, Au-DT, and Au-PFDT) alter the plasmonic peak of the nanostructures when exposed to the same organic solvent. This results in different peak-shifted curves. The RIU values for acetone and ethanol solutions were obtained from S. S. Kurtz, et al. (1965) and T. A. Scott (1946), respectively. For (b) and (c), the lines are present to guide the eye and the error bars are one standard deviation from the average.

Macias 2019, Whisky tasting using a bimetallic nanoplasmionic tongue
Biocompatibility
The appropriate biological performance, either local or systemic, of a given implant in a specific application.

Desirable host response depends on the type of materials implanted and their intended use. It may be total inertness and no interaction with tissues surrounding the implanted materials or positive interaction resulting in active participation of the cells surrounding the materials.

Biocompatibility is a dynamic two-way process that involves the time-dependent effects of the host on the material and the material on the host. The performance of a biomaterial should not be affected by the host and the host should not be negatively affected by the implanted biomaterials.

No clear, absolute definition of biocompatibility exists yet mainly due to the fact that the biomaterials area is still evolving.

Potential side effect:
Toxic, carcinogenic, immunogenic, and inflammatory responses.
Foreign Body Reaction

Composed of foreign body giant cells, macrophages, fibroblasts and capillaries

Surface topography will dictate the extent of the foreign body reaction

- smooth surfaces have a foreign body reaction composed of macrophages and foreign body giant cells at the surface.
- rough surfaces have foreign body giant cells, macrophages, and granulation tissue sub-adjacent to the surface response.

High surface-to-volume implants have a higher ratio of macrophages and foreign body giant cells at the implant sight, increasing fibrosis.

The foreign body reaction may persist for the entire life of the implant.
Immune Response to an Implanted Biomaterial

**Fig. 1.** The inflammasome in the immune response to an implanted biomaterial. (A) Biomaterial implantation: The process of implantation of a biomaterial causes injury to cells. Danger signals released from injured cells (such as alarmins, HMGB1, ATP and UTP) results in the recruitment and activation of polymorphonuclear leukocytes (PMNs), monocytes and resident macrophages, via pattern recognition receptor (PRRs) engagement. Well-known damage associated molecular patterns (DAMPs) include ATP, nucleic acids, HSP, monosodium urate, HMGB1 and inflammatory cytokines. The adsorption of blood proteins to material surface will further recruit immune cells. (B) Acute inflammatory response to biomaterials: Immune cells secrete proteolytic enzymes and reactive oxygen species (ROS) that will degrade the biomaterial surface and ECM components. Endogenous danger signals are usually released from stressed or necrotic cells and also damaged ECM during acute inflammation. (C) Inflammasome activation: Activation of NLRP3 inflammasome, composed of NLRP3, ASC, and pro-caspase-1, is regulated by two-step signals: The first signal (signal 1) can be danger signals released from injured tissues and immune cells that will enhance the expression of inflammasome components and target proteins via activation of NF-κB. The second “activation” signal (signal 2) promotes the assembly of inflammasome components, that involves three major mechanisms, including generation of ROS, lysosomal damage (phagocytosis of biomaterial degradation products), and the potassium efflux. Inflammasome assembly leads to caspase-1 activation that in turn cleaves the pro-forms of cytokines IL-1β and IL-18 as well as gasdermin D that induce the pyroptotic inflammatory cell death. The perpetuation of the inflammatory cascade culminates either in resolution of inflammation, return to homeostasis and tissue healing or in chronic inflammation and biomaterial encapsulation.

**Fig. 5.** Wear particles released from loose implants lead to inflammasome activation. Wear particles are recognized as such or after phagocytosis (lysosomal rupture), by PRRs including TLRs and NLRs leading to the assembly of NLRP3 inflammasome. Once assembled the NLRP3 inflammasome cleaves pro-IL-1β into the active IL-1β. Secreted IL-1β can promote the maturation of osteoclasts into bone-resorbing cells increasing bone resorption and consequently impairing implant function.

Vasconcelos 2019, The inflammasome in host response to biomaterials—Bridging inflammation and tissue regeneration
FIGURE 1 | Timeline of the events leading to the development of the foreign body reaction to a material following its implantation into the body. The composition of the cell population adhered to the surface of the implant evolves over time following the initial implantation. Factors released by cells (indicated by blue text) contribute to the recruitment of further cells and progression of FBR. ROS, reactive oxygen species.

FIGURE 6 | Bioresorbable electronic patch (BEP) implant for controlled drug release. Reproduced under the terms of the Creative Commons Attribution License (Lee et al., 2019). (A,B) The patches are fabricated from a drug-loaded (doxorubicin) oxidized starch (OST) reservoir, and an electronics-containing compartment made from Mg (conductor), PLGA (dielectric), and PLA (encapsulation) which is bound to it. (C) Wireless control mediates drug delivery into neural tissue. (D-F) Doxorubicin release into tissue occurs over a period of days. (G) The entire implant becomes fully resorbed within 10 weeks of implantation, leaving no adverse reaction in the nearby tissue.
### Failure of Biomaterials and Biomedical Devices

1. Tissue Biocompatibility (Inflammation and Wound Healing)
2. Thrombosis (Blood Clotting)
3. Infections

**Biomaterials-Tissue Local Interactions** (at biomaterial-tissue interface)

<table>
<thead>
<tr>
<th>Effect of material on host tissues</th>
<th>Effect of environment on materials</th>
<th>Systemic Interactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Blood material interactions</td>
<td>• Physical-mechanical effects</td>
<td>• Embolization</td>
</tr>
<tr>
<td>• Modification of healing</td>
<td>• Wear</td>
<td>• Hypersensitivity (itchy/redness)</td>
</tr>
<tr>
<td>• Inflammation</td>
<td>• Fatigue</td>
<td>• Elevation of implant elements in blood</td>
</tr>
<tr>
<td>• Infection</td>
<td>• Corrosion</td>
<td>• Particle transport to distal tissues</td>
</tr>
<tr>
<td>• Tumorigenesis</td>
<td>• Stress-corrosion cracking</td>
<td></td>
</tr>
</tbody>
</table>

**Biological Effects**

- Adsorption of tissue constituents by implant
- Enzymatic degradation
- Calcification

**Device Associated Complications**

- Thrombosis/thromboembolism
- Infection
- Exuberant or poor healing
- Biomaterial failure
- Adverse local tissue reaction
- Adverse systemic effect
Fibrosis/Fibrous Encapsulation

- Fibrosis surrounds the biomaterial with an interfacial foreign body reaction
- Consists of connective tissue
- Isolates the biomaterial from the local tissue environment
- End stage healing response
- Exceptions to the rule

- Implant site repair involves 2 processes:
  - regeneration, replacement of injured tissue by parenchymal cells of the same type
  - replacement by connective tissue (fibrous capsule)
- Extent of the injury and framework of the tissue (bone vs nervous system) determines process
  - cells are labile (stem cells), stable (can replicate, but not typical), or permanent (static)
  - all injuries to permanent cells give rise to fibrosis/loss of tissue function

Description of fibrous capsule formation around the implanted biomaterial. Activated polymorphonuclear leukocytes (PMN) release enzymes to remove dead cells, and macrophages (Mφ) participate in the phagocytosis of foreign and cellular debris. Mφ also stimulate fibroblasts (FB) to secrete collagen and other extracellular matrix components to form a fibrous capsule around the implanted biomaterial.
More women have been diagnosed with a deadly lymphoma caused by breast implants, according to a report released
Wednesday from the Food and Drug Administration.

In a statement, the FDA’s Dr. Binita Ashar said there are now 457 women in the U.S. diagnosed with breast implant-
associated anaplastic large cell lymphoma (BIA-ALCL), up from 414 cases in the last report. There have been more than 600
cases of BIA-ALCL, a cancer of the immune system, reported worldwide. Sixteen women have died, nine in the U.S.

“We hope that this information prompts providers and patients to have important, informed conversations about breast
implants and the risk of BIA-ALCL,” Dr. Ashar said in the statement.

The new report comes one day before French regulatory authorities are scheduled to meet to discuss the safety of textured
implants, which are used in cosmetic and reconstructive surgeries and account for 85 percent of the French market. The
majority of ALCL cases have been linked to the textured devices. In December, France’s National Agency for the Safety of
Medicines and Health Products (ANSM) asked Allergan to recall its textured implants after the agency pulled its safety
approval.

That recall followed an NBC News investigation, in conjunction with the ICIJ, finding that ALCL could be more common
than previously thought.

The FDA, which first alerted women to the risks from the textured breast implants in 2011, also announced today that for the
first time, they are sending letters to doctors, specifically primary care physicians and gynecologists, urging them to learn
about ALCL so they can better diagnose and treat women who may be at risk.

ALCL patients, who have been fighting to raise more awareness of disease, applaud the FDA’s efforts to better inform
physicians.

“Letters to these health care providers, like OB/GYNs, ER Doctors are critical to the diagnosis of this disease. They are some
of the first physicians to treat patients symptomatic for BIA ALCL and these patients are often missed and mistreated for
mastitis, shingles and other conditions,” said Michelle Forney, a California mother of two, diagnosed with ALCL last year.

“This disease is not rare. It’s emerging and should not belong in the hands of plastic surgeons.”

The FDA is meeting next month to review safety of all breast implants.
Failure of Biomaterials and Biomedical Devices
Thrombosis & Blood Compatibility
Failure of Blood-contacting Biomaterials and Biomedical Devices

Problems Associated With Biomaterials

Surface-induced thrombosis with blood-contacting biomaterials

Exposure of biomaterial to blood

Protein adsorption
(Type of blood proteins)

Platelet adhesion

Platelet spreading & platelet activation

Thrombus formation

Thrombus aging & embolization

Short-term surface passivation

Vroman effect

- Proteins rapidly adsorb onto the surface ~10 μsec.
- Then competitive displacement of earlier adsorbed proteins with a higher affinity for the surface occurs.
- Protein adsorption can alter the protein conformation and overall function.

Hydrophobic materials:
Fast adsorption which is largely irreversible
Most change in protein conformation (reduced bioactivity)

Hydrophilic materials:
Slower adsorption, with significant desorption
-Protein exchange
Least change in protein conformation (maintains bioactivity)

Slow progress in blood-compatible materials
Control of platelet aggregation by drugs, e.g., Plavix (clopidogrel), Eliquis (apixaban), and Warfarin (Coumadin).
Surface-Induced Thrombosis

Platelet adhesion

Platelet spreading and platelet activation

Thrombus formation

Short-term surface passivation
Schematic description of steric repulsion exerted by the surface-grafted linear polymers such as poly(ethylene oxide) or heparin (A) and globular proteins such as albumin (B).

Prevention of (Platelet-Activating) Protein Adsorption

Steric repulsion by surface-grafted PEO chains

Pluronics®: PEO-PPO-PEO triblock copolymers
PEO: poly(ethylene oxide)
PPO: poly(propylene oxide)

Fibrinogen adsorption to glass surfaces grafted with various Pluronic® surfactants (L, P, and F series). The control surface was trichlorovinylsilane-modified glass. The three numbers in parentheses indicate the numbers of repeating units of ethylene oxide (EO) and propylene oxide (PO) in the poly(EO)/poly(PO)/poly(EO).
Cells interact with blood constantly, yet do not typically induce a thrombotic event unless there is an injury. 

**Glycocalyx** - Glycoprotein, glycolipid, and proteoglycan based covering on one side of the epithelium.

It helps to mitigate non-specific protein adsorption and inhibits cell adhesion.

It is also found in bacteria, and helps to shield bacteria from the immune response.

**Glycocalyx Mimics**

Glycocalyx mimics can bind carbohydrates which are found in the glycocalyx to the surface of a material, can reduce protein binding. Dextran and Maltose among others have been used.

Low density coverage- PEG is superior because the conformational variability allows it to spread and cover more defect areas.

High density coverage- Carbohydrates are theoretically better, because PEG tends to aggregate at higher concentrations.
Successful long-term applications of implantable materials requires prevention or minimization of surface-induced thrombosis and/or fibrous encapsulation (or isolation) of implants by the body.

While the surface modification of biomaterials with PEO, heparin, albumin, and other hydrophilic polymers appears to be promising, further systematic studies on the long-term effects of surface modification of biomaterials are necessary for the development of truly biocompatible materials.
Sterilization
Sterilization vs Sanitation vs Disinfection

Sterilization kills all forms of microbial life (bacteria, spores, fungi, viruses)
Disinfection destroys organisms in a non-sporing vegetative state
Sanitizing reduces organisms on a surface to make them safe for contact

Steam Sterilization (Autoclave)
Process: Steam at 125 °C at 3 atmospheres
Advantages: Simple and quick (~20 min)
Effective
Great to use with non-organics, metals, glass
Disadvantages: Not for use with all polymers (can melt or soften)
Poor penetration throughout the polymer
May potentially lead to degradation of the polymer

Ethylene Oxide Vapor
Process: Pre-conditioning of sample, Gassing/exposure, Evacuation, Aeration (air wash)
Advantages: Can be used with many polymers
Disadvantages: Ethylene Oxide is toxic and potentially explosive
Can have chemical reaction
Need complete removal of the residual gas
Need to optimize the conditions

Gamma Radiation)
Process: Transmission of energy by EM waves that breaks DNA strands, Sterilization is proportional to the amount of radiation absorbed (1 Rad = 100 erg = 1x10^5 Joules absorbed energy/gram of material), γ rays have the highest penetration in air
Advantages: No residual radiation, Can use the sample immediately, Low temperatures can be used, High penetration of the device
Disadvantages: Often times initiates degradation of polymer (changes the molecular weight), Can initiate crosslinkings, Need special equipment and safety precautions