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Mr. Holland's Opus



Top Gun Maverick: AI-Generated Voice



AI for Paper Writing

AI *et al.*: Machines Are About to Change Scientific Publishing Forever

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Supporting Information

Artificial intelligence (AI)-powered text generation will change scientific publishing fundamentally. In the past year, multiple AI systems have showcased production of visual and textual content increasingly indistinguishable from human-generated work, creating almost overnight new possibilities for intellectual workers, and at the same time raising similarly potent concerns. While artists and journalists are more evidently at the forefront of this incipient revolution, it is not hard to imagine a researcher looking away from the frustratingly sparse draft of a research article and wondering: “Could a machine write it for me?” (Figure 1).

This question might have passed for a flight of fancy until recently, as machine-generated scientific arguments were easily distinguishable from human output, and paper-generating software mainly highlighted the permeability of the peer-review process to nonsensical papers.¹ However, these technologies have progressed so rapidly that we have likely entered a new phase, one in which machine-generated text can be integrated in human-generated scientific articles in a seamless fashion. To help illustrate the point in concrete terms, let’s directly ask one of the involved parties:

Question: Can AI write a scientific paper? Answer in two paragraphs.

ChatGPT’s answer:

Yes, AI can write a scientific paper. In fact, there are already AI systems that can write scientific papers by using advanced natural language processing techniques to analyze existing scientific literature and generate text that is similar to human-written scientific papers. This allows AI to quickly and efficiently generate a large amount of text based on a given topic or research area, which can be useful for researchers who want to quickly generate a draft of a paper or for organizations that need to produce a large number of papers on a particular topic.

However, it is important to note that these AI-generated papers are typically not original research, but rather are based on existing research in a particular field. This means that they may not contain any new insights or findings, and are not likely to be published in academic journals. Additionally, the accuracy and validity of the information in the paper may not be as high as a human-written paper, so it is important for a human researcher to review and verify the information before it is published.

This well-structured answer makes reasonable points on both the potential and limitations of its author. As we write, the “assisted-driving” approach suggested by ChatGPT (AI-



Figure 1. Artificial Intelligence assisting the writing process, as imagined by the Midjourney text-to-image generator.

generated text with human supervision) seems to be employed by a growing number of researchers,² promising to free researchers’ time from the burden of scientific writing and get them back to the science. As a matter of fact, ChatGPT’s answer appears conservative, downplaying the role that AI could play in providing scientific insight. With their ability to take into account large swathes of scientific literature and condense them into concise chunks, AI language models could be used by researchers to familiarize themselves with new topics and double-check the completeness of their literature overviews. Since AI models have already made their way into scientific literature search engines,³ it is easy to imagine their evolution

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While current AI language models do not produce statements reaching beyond the content of their training sets, we should ask ourselves whether this is a fundamental feature of the technology or just a temporary limitation.

into brainstorming tools, leveraging their extensive literature knowledge to produce suggestions based on recurrent scientific themes.

Additionally, while current AI language models do not produce statements reaching beyond the content of their training sets, we should ask ourselves whether this is a fundamental feature of the technology or just a temporary limitation. Recent breakthroughs in the use of AI in complex strategic games have highlighted the surprising ease with which AI can outcompete humans in problems considered intractable with computational approaches.^{4,5} Similar breakthroughs in the use of AI for scientific progress might come from the combination of (i) precise goals, i.e., a clear definition of what we consider a successful scientific observation, (ii) algorithms capable of efficiently optimizing its output for these goals, and (iii) structured and accessible scientific data. In this line of thought, we can imagine AI systems proposing new experiments and new descriptions of observed phenomena and arranging data in figures to support their conclusions. An AI system capable of producing original scientific work could revolutionize the whole scientific endeavor—for example, by being less tied than humans to the boundaries of scientific disciplines, bringing multidisciplinary science to new heights.

However, as we take the first steps down the slope of the AI revolution, it is worth envisioning the risks awaiting us at the bottom.

Probably the most immediate concern is that the sandwich paper⁶ and paper-mill systems could become supercharged when coupled with advanced AI language models. A text-generation system combining speed of implementation with eloquent and structured language could enable a leap forward for the serialized production of scientific-looking papers devoid of scientific content, increasing the throughput of paper factories and making detection of fake research more time-consuming. The proliferation of these practices has already had an impact on the publishing world despite the lack of sophisticated approaches,¹ and the problem will likely get worse if AI joins the fray. Scaling up efforts to automatically detect AI content might play an important role in tackling the issue.⁶ However, it is clear that these approaches would require the establishment of clear definitions for fraudulent and legitimate use of AI content. AI can already write articles that would, in the opinion of the authors, pass peer review for a Perspective article (see the Supporting Information for a paper on lead toxicity in perovskite devices, generated by AI). This ability makes the urgent need for a code of conduct for the use of AI-generated text in scientific literature abundantly clear.

On a more abstract level, there are questions regarding the originality of AI-science. Is an AI-generated scientific text original, despite being the product of training over human-made original work? Who is the intellectual owner of the content? These questions echo the ongoing debate surrounding AI-generated art, and suggest similar concerns on who stands to benefit from AI intellectual production. If an AI system is able to gather its information from the entire literature, will it be able to trace its conclusion back to the most relevant scientific work and acknowledge it? Or does the production of scientific content from delocalized literature sources push toward a new paradigm with a decreased emphasis on human authorship? Can we apply straightforwardly the current model of scientific publishing, based on individual contributions and intellectual property transfer from authors to journals, to an increasingly automated environment?

Increased AI-automation might also encroach on the originality of writing styles, supplanting the idiosyncrasies of human authors with a homogeneous style. Is the loss of individual stylistic traits, often culturally influenced, a step closer to mutual comprehension or the removal of a desired feature? This aspect might depend on the degree to which AI systems operate a “regression to the mean” of their training content, flattening potentially valuable deviations. Managing the amount of randomness utilized in the generation of content might offer ways to prevent the homogenization of AI production, but it is worth pondering whether these systems can replicate the diversity of voices and viewpoints provided by human scientists.

While current AI language models do not produce statements reaching beyond the content of their training sets, we should ask ourselves whether this is a fundamental feature of the technology or just a temporary limitation.

Finally, concerning the long-term consequences of the integration of AI in scientific publishing, it is worth considering the vulnerability of AI models to biases. Human researchers are far from being free of biases, but the presence of a plurality of voices helps in restricting the impact of individual biases, and traceability of authorship makes it possible to actively tackle biases in the system. Using a small number and diversity of AI systems for scientific production has the potential to amplify the scale of biases, propagating them efficiently on a global level and avoiding the mechanism of individual scrutiny often used to identify these biases. Since the behavior of these systems depends strongly on their training, it is crucial to understand the composition of the training sets and ensure they are constantly updated with all accepted forms of scientific production. And even if the AI models would be able to gather all the available literature, what would their approach toward consensus-defying reports be? Are they poised to stand on the side of commonly held position and silence singular points of view? Finally, would an AI-centric system of scientific content production be vulnerable to deliberate biasing by malicious actors? These prospects suggest that it is crucial to consider and potentially regulate the openness of the AI models and training sets used, and to start worrying about the emergence of malicious strategies to amplify the relevance of selected opinions.

Some of these concerns might be mitigated with small adjustments, others might require systemic changes, and others still might prompt us to restrict the use of these new technologies. What appears clear is that AI will make its way into the practice of scientific publishing soon, if it has not already done so (how would we know?). In doing so it will change science appreciably and permanently. When computers made their appearance, they entirely changed the way science is performed and communicated—such changes required adjustment and adaptation. The appearance of advanced AI promises to ratchet up the degree of change and, at the same time, the amount of adaptation required. Like our forest-dwelling ancestors that discovered fire, we need to be mindful of the unwanted consequences of our exciting advances, to reap their benefits without setting our homes ablaze.

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AI-Generated Papers and Proposals

NIH has recently observed instances of Principal Investigators submitting large numbers of applications, some of which may have been generated with AI tools. While AI may be a helpful tool in reducing the burden of preparing applications, the rapid submission of large numbers of research applications from a single Principal Investigator may unfairly strain NIH's application review processes. The percentage of applications from Principal Investigators submitting an average of more than six applications per year is relatively low; however, there is evidence that the use of AI tools has enabled Principal Investigators to submit more than 40 distinct applications in a single application submission round.

NIH will continue to employ the latest technology in detection of AI-generated content to identify AI generated applications, but it is imperative that all NIH research applications are consistent with the NIH Grants Policy Statement (GPS) Section 2.1.2's expectation that institutions and affiliated research teams propose original ideas for funding. AI tools may be appropriate to assist in application preparation for limited aspects or in specific circumstances, but researchers should be aware that using AI comes with its own risks. AI use may result in plagiarism, fabricated citations, or other kinds of research misconduct. As a reminder, NIH oversees research misconduct investigations and acts on non-compliance (see GPS Section 4.1.27).

Policy: NIH will not consider applications that are either substantially developed by AI, or contain sections substantially developed by AI, to be original ideas of applicants. If the detection of AI is identified post award, NIH may refer the matter to the Office of Research Integrity to determine whether there is research misconduct while simultaneously taking enforcement actions including but not limited to disallowing costs, withholding future awards, wholly or in part suspending the grant, and possible termination.

NIH will only accept six new, renewal, resubmission, or revision applications from an individual Principal Investigator/Program Director or Multiple Principal Investigator for all council rounds in a calendar year.

<https://grants.nih.gov/grants/guide/notice-files/NOT-OD-25-132.html>



PUBLISHING

Far more authors use AI than admit it

Study by cancer publisher highlights promise of AI detectors and the challenges they pose

JEFFREY BRAINARD

After ChatGPT debuted in late 2022 and wowed users with its humanlike fluency, many academic journals rolled out policies requiring authors to disclose whether they had employed artificial intelligence (AI) to help write their papers. But new evidence from one

Earlier studies tried to quantify the use of AI in papers and peer reviews. But the new study, presented at the International Congress on Peer Review and Scientific Publication earlier this month, is one of the first to assess the reliability of author disclosures. "Disclosures on

Brainard 2025, Far more authors use AI than admit it

AI-Generated Review Papers

The evolution of large language models (LLMs) is reshaping the landscape of scientific writing, enabling the generation of machine-written review papers with minimal human intervention. This paper presents a pipeline for the automated production of scientific survey articles using Retrieval-Augmented Generation (RAG) and modular LLM agents. **Although current iterations produce promising drafts, they fail to meet top-tier publication standards, particularly in critical analysis and originality.**

Let us now dwell upon the advantages of having such a review-generating tool. The first obvious advantage is to **speed up the preparation of review papers**, particularly considering that the proposed methodology is applicable to any subject. There are also **significant advantages regarding the topic's breadth of coverage**. Rather than a limited number of papers from the literature, an automatic generation process can consider thousands or tens of thousands of papers. Here, we have exploited citation networks only to select relevant papers, but additional useful information can be extracted from the networks and their topology.

Furthermore, **generating several distinct versions of a review paper may contribute to reducing the inevitable human bias**. Besides, the future generation of LLM-based tools will likely address currently unsolved issues, such as **fact-checking and attaining high accuracy**. Indeed, we mentioned that we did not check all the references from all the versions individually. Usually, even human experts spend limited time on this type of verification. As for fact-checking, the limited human text processing capability hampers extensive in-depth analyses of large quantities of text. AI will likely handle these issues in the future, contributing to improved reliability of science and technology documentation.

However, several important issues must be considered, in line with the concerns already expressed in the introduction of this paper. First, **the issue of authorship arises**: who should receive credit for the review paper? This also raises concerns about **accountability, intellectual ownership, and proper citation**. A shift in authorship criteria should perhaps be discussed shortly. Moreover, **the training corpus may include flawed or retracted papers, leading the system to learn from incorrect sources**. Identifying who should be held accountable for factual errors or omissions in AI-generated reviews will be challenging. Given the overwhelming volume of literature published daily, manual verification may be virtually impossible. As mentioned above, we anticipate that, in the future, new AI tools will be developed specifically for fact-checking, as only such tools will be capable of processing the vast amounts of text in the scientific literature. Other ethical challenges include the potential for **"review spam,"** in which AI mass-produces papers, **flooding the literature with superficial or redundant content**. Publishing models would also be affected, particularly for journals specializing in review articles. The impact of tools capable of automatically generating papers with original content—which are also under development—is more difficult to assess. For one, it will be challenging to determine whether the ideas introduced are truly original. Ensuring that the research methodology and results are sound and accurate is even more difficult. In fields such as applied materials, these AI agents are unlikely to have a major impact, given the experimental nature of most research in the area. Instead, **they may serve as assistants for literature surveys and data analysis, without replacing human expertise in most aspects of the research process**. Nevertheless, relying on such agents will still require accounting for previously discussed ethical concerns.

Writing Research Articles

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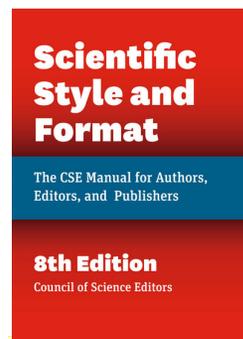
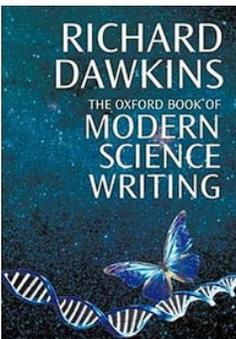
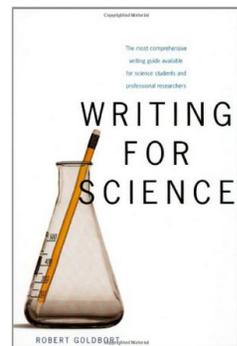
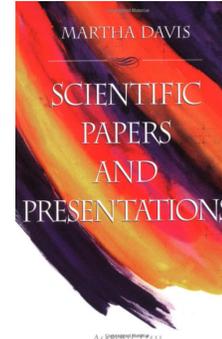
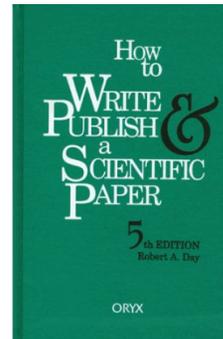
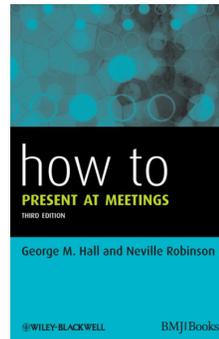
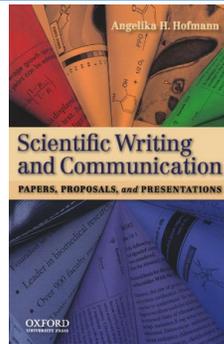
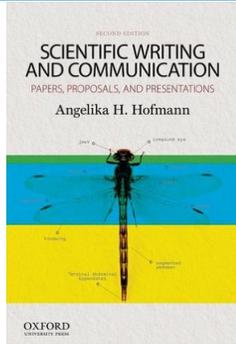
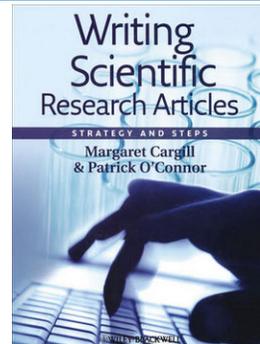
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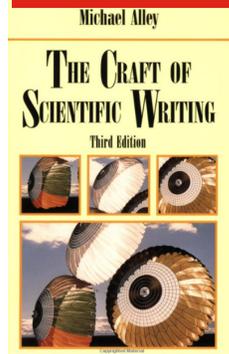
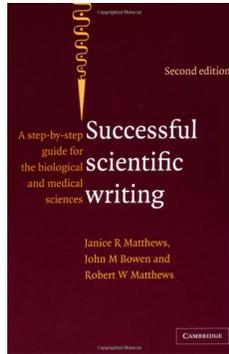
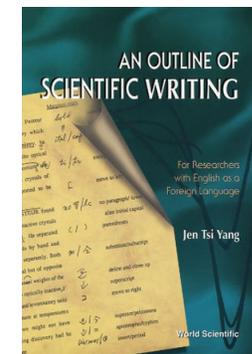
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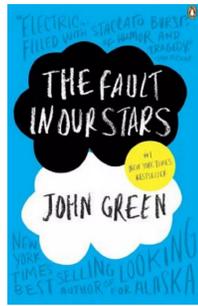
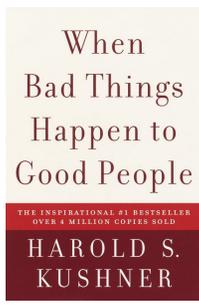
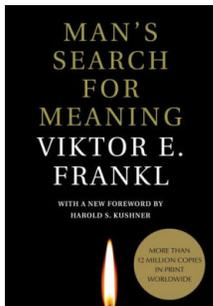
I made use of the college library by borrowing books other than scientific books, such as all of the plays by George Bernard Shaw, the writing of Edgar Allan Poe. The college library helped me to develop a broader aspect on life.

— Linus Pauling —

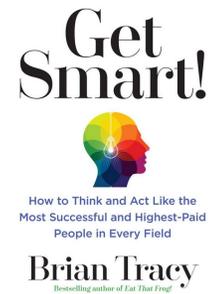
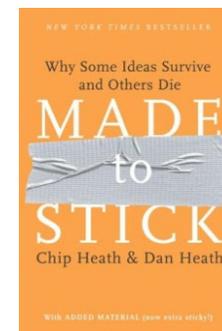
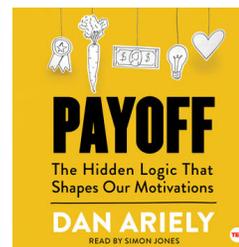
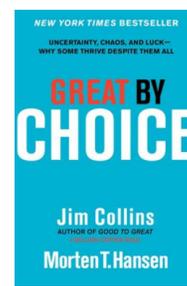
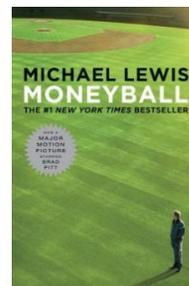
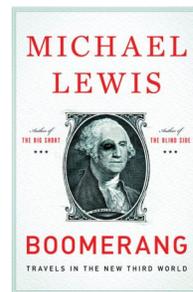
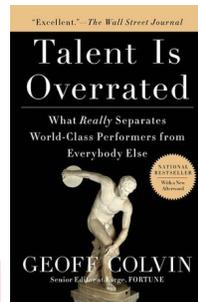
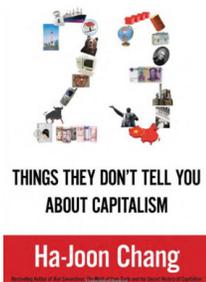
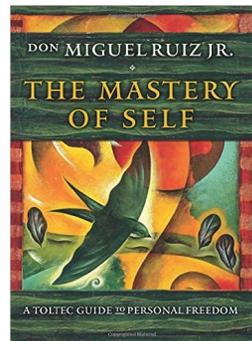
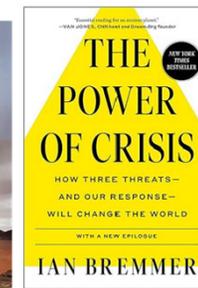
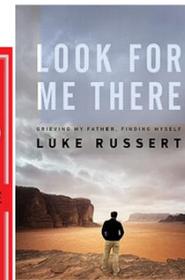
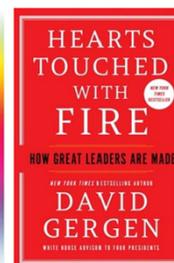
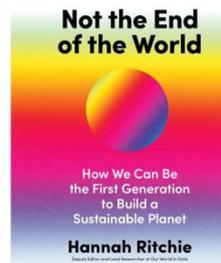
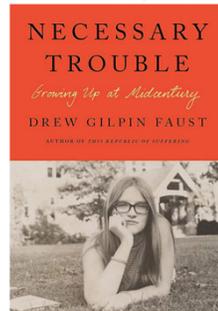
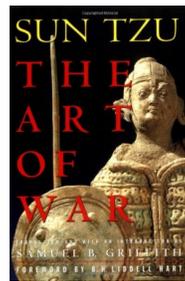
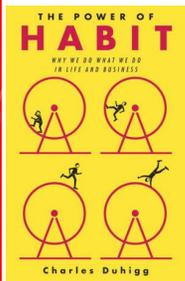
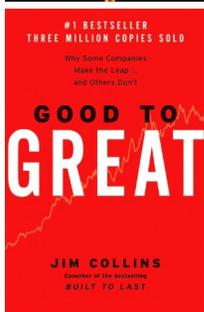
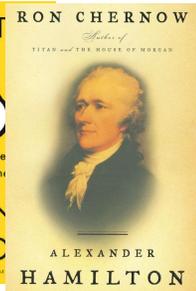
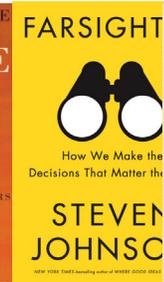
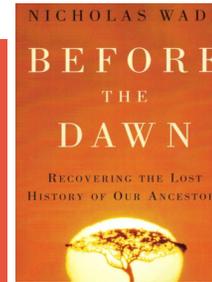
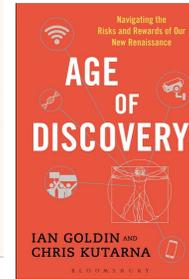
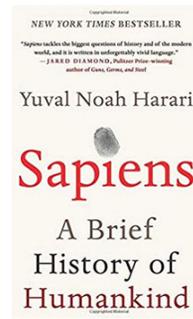
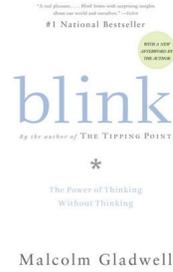
AZ QUOTES



Scientific Research Articles: Storytelling

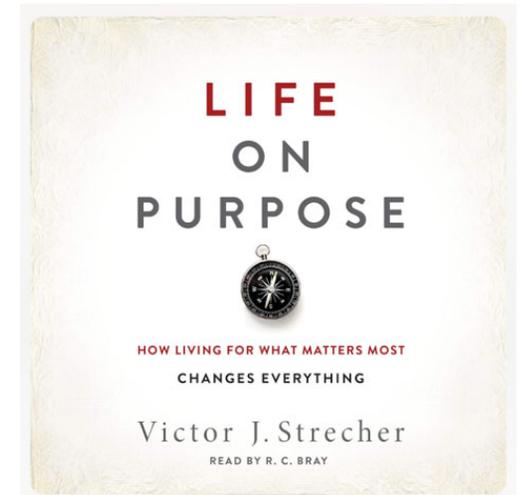
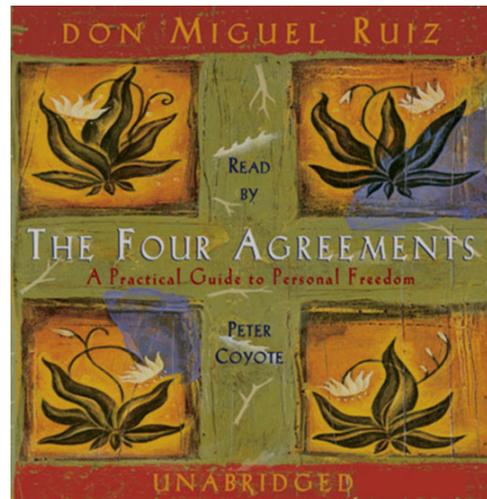
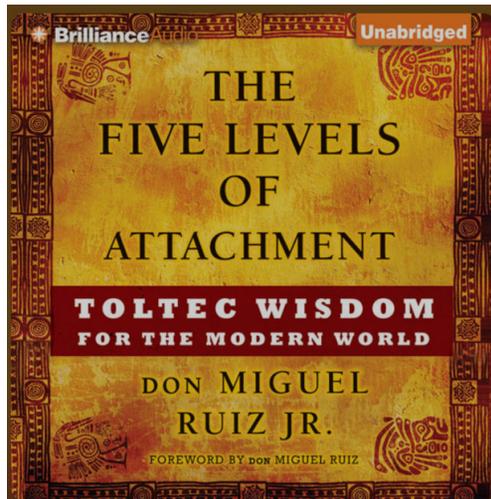
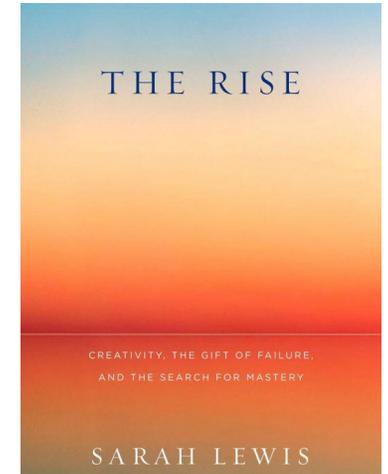
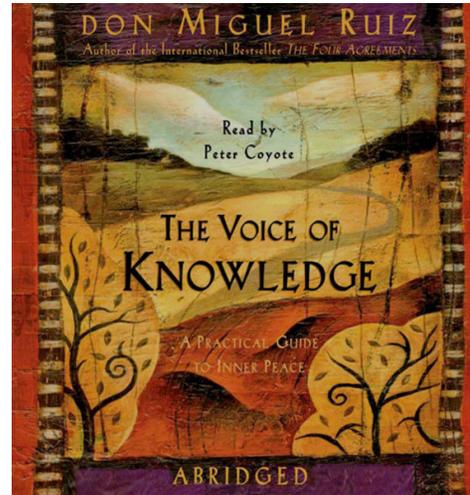
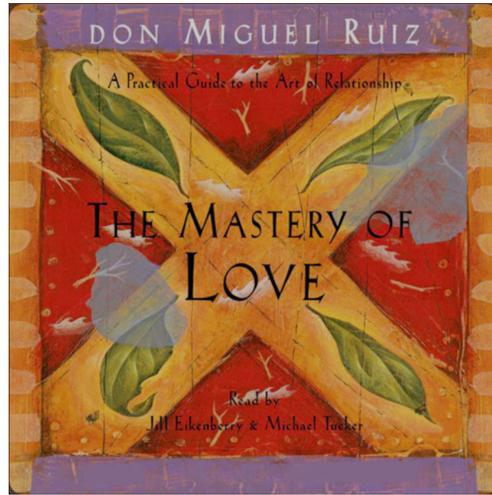
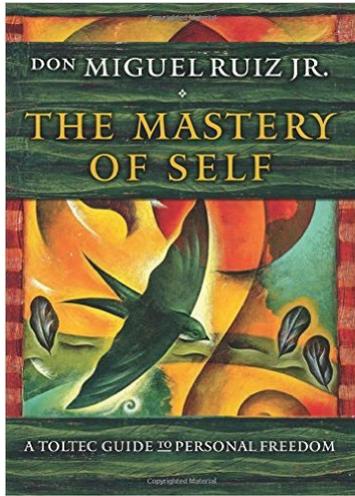


Talking to Strangers
WHAT WE SHOULD KNOW ABOUT THE PEOPLE WE DON'T KNOW
Malcolm Gladwell



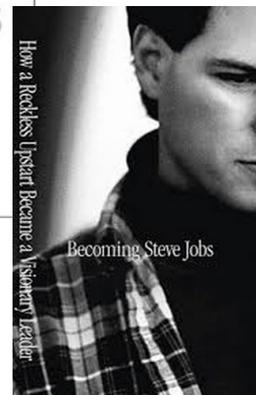
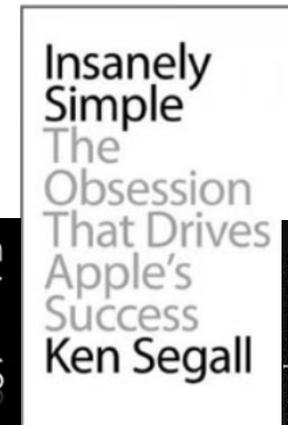
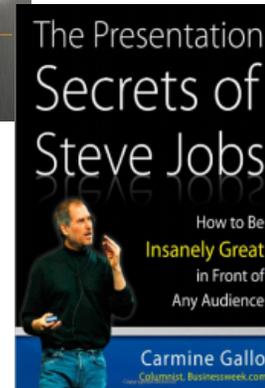
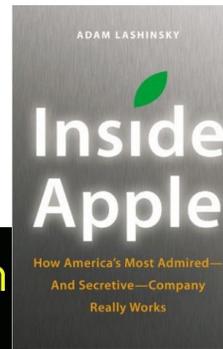
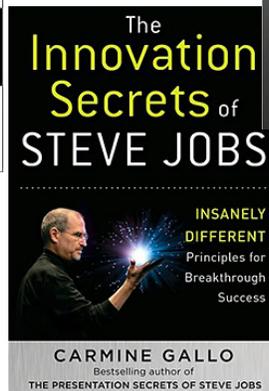
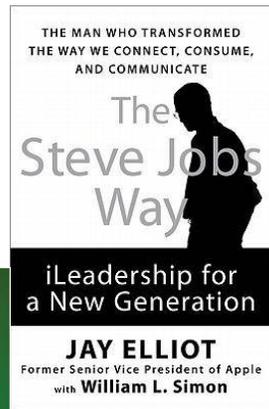
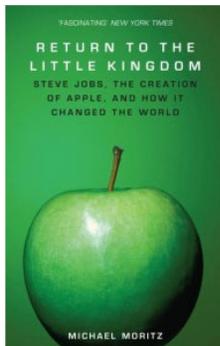
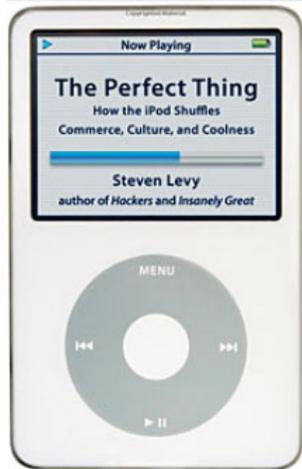
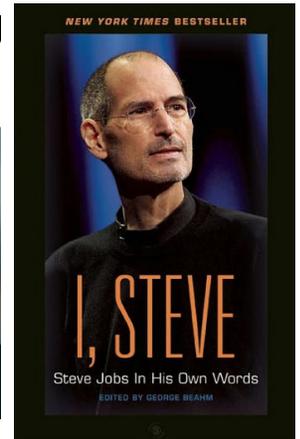
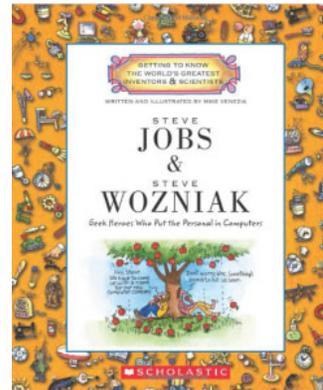
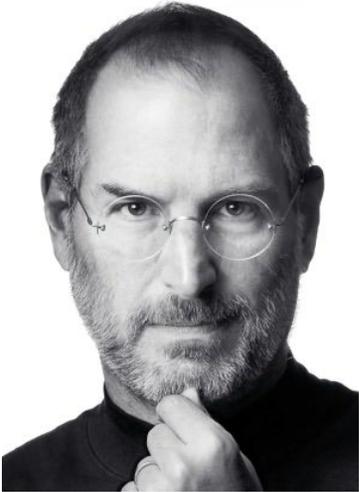
Great Books: Nurturing Your Mind First

Don Miguel Ruiz & Don Miguel Ruiz, Jr.



Steve Jobs: One of the Most Interesting Subjects

Steve Jobs by Walter Isaacson



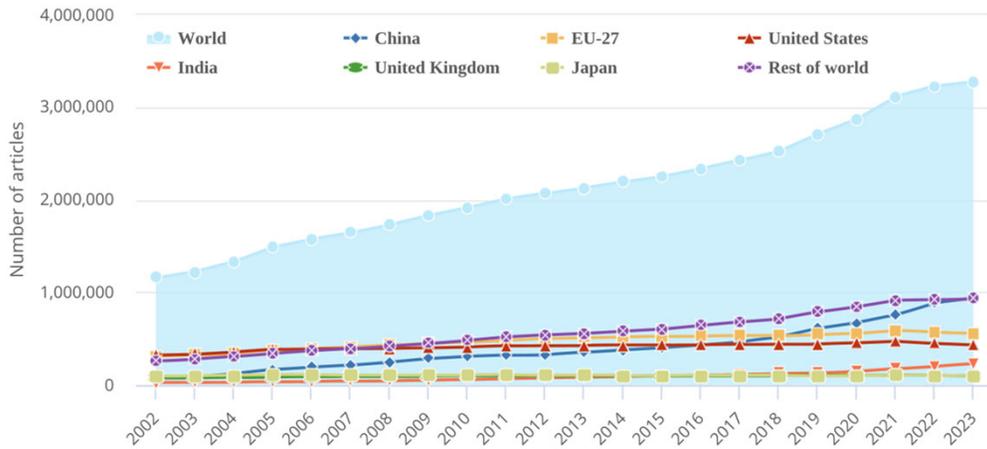
Steve Jobs' 2005 Stanford Commencement Address

https://www.youtube.com/watch?v=Hd_ptbiPoXM



Scientific Papers Published

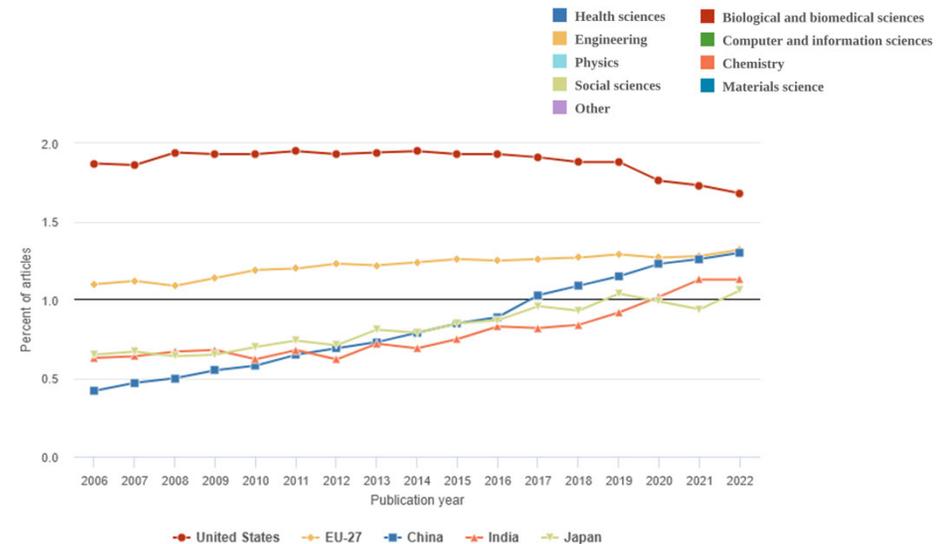
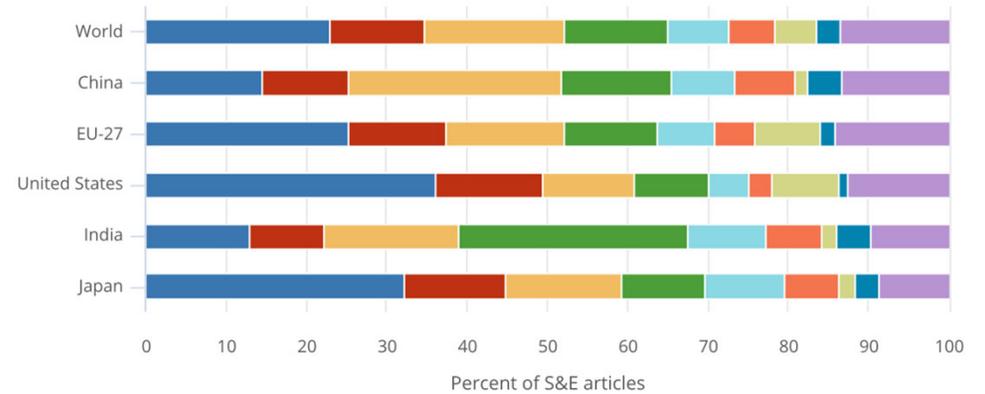
Distribution of national S&E research portfolios across S&E fields, 2023



(Number and percent)

| Rank | Region, country, or economy | 2013 | 2023 | 2023 world total (%) |
|------|-----------------------------|-----------|-----------|----------------------|
| na | World | 2,129,076 | 3,275,079 | na |
| 1 | China | 351,526 | 932,712 | 28.48 |
| 2 | United States | 427,373 | 430,843 | 13.16 |
| 3 | India | 80,195 | 228,174 | 6.97 |
| 4 | Germany | 104,396 | 108,782 | 3.32 |
| 5 | United Kingdom | 98,613 | 97,536 | 2.98 |
| 6 | Japan | 106,968 | 96,543 | 2.95 |
| 7 | Russia | 38,167 | 85,558 | 2.61 |
| 8 | Italy | 66,221 | 82,771 | 2.53 |
| 9 | South Korea | 56,751 | 71,724 | 2.19 |
| 10 | Canada | 59,396 | 63,720 | 1.95 |
| 11 | France | 71,475 | 62,180 | 1.90 |
| 12 | Spain | 53,215 | 60,304 | 1.84 |
| 13 | Brazil | 45,991 | 58,292 | 1.78 |
| 14 | Iran | 31,025 | 55,085 | 1.68 |
| 15 | Australia | 50,403 | 54,589 | 1.67 |

S&E publications, by selected region, country, or economy and rest of world: 2002–23



<https://nces.nsf.gov/pubs/nsb20257/publication-output-by-geography-and-scientific-field#>

S&E publications in the top 1% most-cited journal articles as a share of all S&E journal articles

Scientific Papers Published -

A trend is transient

More Than 87,000 Scientific Papers Already Published on COVID-19.

By Robert Preidt, HealthDay Reporter. March 1, 2021

The world's researchers have worked at a breakneck pace during the COVID-19 pandemic.

Through October 2020, more than 87,000 papers about the new coronavirus were published worldwide. That's a remarkable number even given the significance of the pandemic, according to the researchers who tallied them all up. "It is an astonishing number of publications --- it may be unprecedented in the history of science," said study co-author Caroline Wagner, an associate professor of public affairs at Ohio State University. "Nearly all of the scientific community around the world turned its attention to this one issue," she noted in a university news release.

Wagner and her colleagues analyzed scientific databases and found that 4,875 articles on the coronavirus were produced between January and mid-April of 2020. That number rose to 44,013 by mid-July and to 87,515 by the start of October, according to findings published online recently in the journal *Scientometrics*. The rate at which papers on the coronavirus are being produced far outstrips anything in history. For example, though nanoscale science was one of the hottest topics in science during the 1990s, it took more than 19 years for the number of scientific papers on that topic to rise from 4,000 to 90,000, according to Wagner. "Coronavirus research reached that level in about five months," she said.

This study updates one published in July in the journal *PLOS ONE*. It showed that China and the United States led the world in coronavirus research during the pandemic's early months. The new study found a large decrease in China's contributions after its infection rates fell. Chinese scientists were involved in 47% of papers released worldwide between Jan. 1 and April 8, 2020, compared to 16% of all papers between July 13 and Oct. 5, 2020. "That surprised us a bit," and government funding may be a factor, Wagner said. "At the beginning of the pandemic, governments flooded scientists with funding for COVID research, probably because they wanted to look like they were responding," she said. "It may be that when the threat went down, so did the funding." Also, work by Chinese researchers was slowed by a requirement that all COVID-19 articles be approved by government officials, Wagner noted.

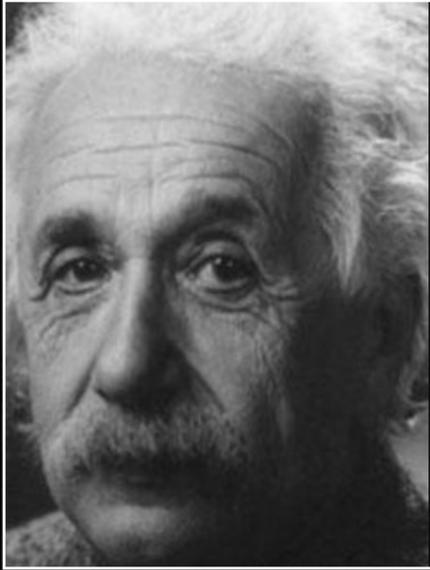
COVID Research

Lipid Nanoparticle

Government Funding dictates research direction

Stable funding for all research topics

Explaining Your Work to Your Grandparents or Family Members



You do not really understand something unless you can explain it to your grandmother.

— *Albert Einstein* —

<https://www.azquotes.com/quote/413120>



Describe What You Found Out & What You Feel!



Range, China. "Huangshan—meaning yellow mountain—is a mountain range in southern Anhui Province in eastern China. The area is well known for its scenery, sunsets, peculiarly shaped granite peaks, Huangshan pine trees, hot springs, winter snow, and views of the clouds from above. Huangshan is a frequent subject of traditional Chinese paintings and literature, as well as modern photography. It is a UNESCO World Heritage site and one of China's major tourist destinations.



Antonio Vivaldi

Though composers of the distant past would often enjoy nature, very few overtly wrote about it. Vivaldi, however, wrote four violin concerti entitled “The Four Seasons”, with each concerto detailing a season.

Music that evokes nature with specific sounds is called Program Music, and this set by Vivaldi was one of the earliest examples of it.

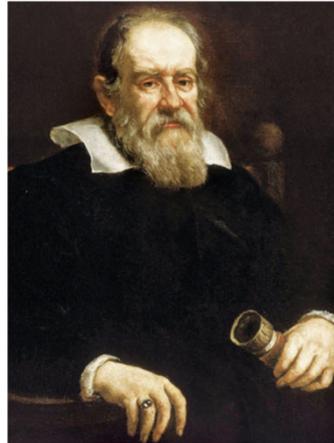
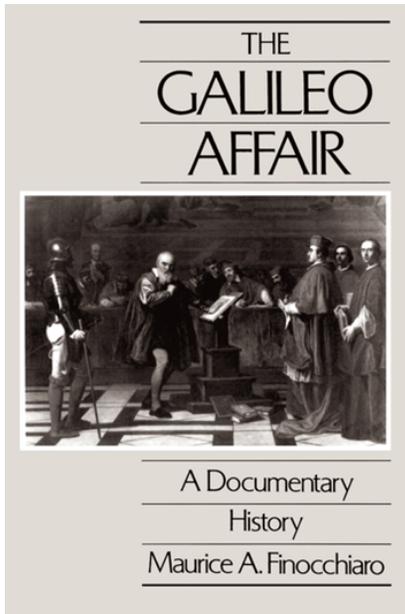
Antonín Dvořák in America

Dvořák spent three years in America as the director of National Conservatory of Music in New York. During this time, he was fascinated by the music of America, especially that of African Americans and Native Americans, resulting in no other than the New World Symphony. He spent the summer of 1893 in the Czech farming village of Spillville, Iowa with his family which proved to be inspirational for him, producing his “American” Quartet and his Quintet in E-flat major, all with unmistakable American themes. Going' Home from Symphony No. 9, From the New World.

Publishing Research Articles

The Galileo Affair

Galileo Galilei: the Father of Modern Science



Discovered a new instrument called the spyglass in 1609

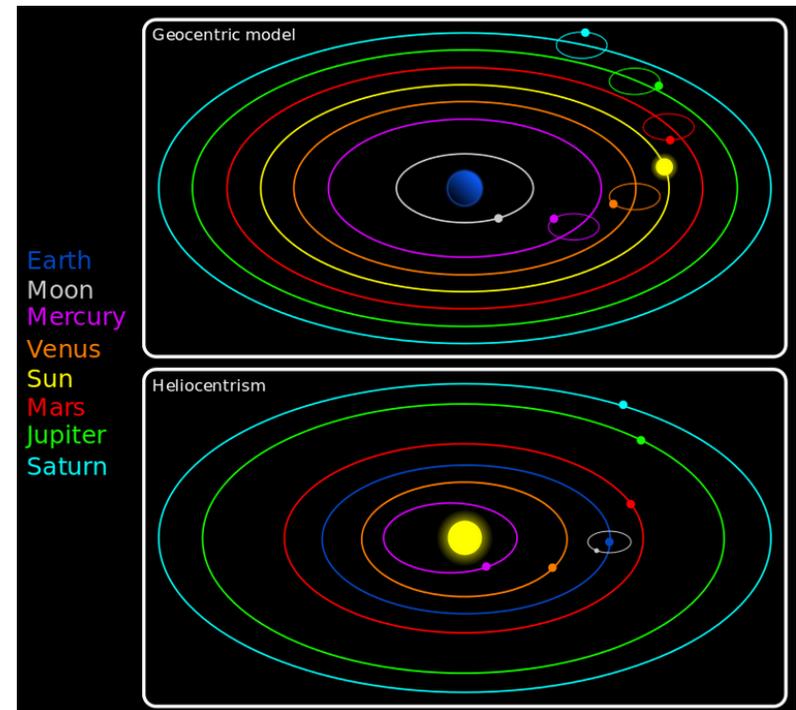


An 1857 painting of Galileo being investigated for his heliocentric beliefs. (How It Works, Issue 179, 2023)

sketch of a philosophical approach to its study. By the “Galileo affair”¹ is meant the sequence of developments which began in 1613 and culminated with the trial and condemnation of Galileo Galilei by the Roman Catholic Inquisition in 1633. Galileo Galilei is the Italian scientist and philosopher whose contributions to astronomy, physics, and scientific instrumentation and methodology in general were so numerous and crucial that, of the several founders of modern science, he is usually singled out as **the “Father of Modern Science.”** The approach to be

Copernicus’s challenge to traditional ideas. Copernicus was able to demonstrate that the known details about the motions of the heavenly bodies could be explained **more simply and more coherently if the sun rather than the earth is assumed to be at the center** and the earth is taken to be the third planet circling the sun. --- Copernicus was able to explain many phenomena in detail by means of **his basic assumption of a moving earth, without having to add artificial and ad hoc assumptions**; the phenomena in question were primarily the various known facts about the motions and orbits of the planets.

On the other hand, in the previous **geostatic system**, the thesis of a motionless earth had to be combined with a whole series of unrelated assumptions in order to explain what is observed to happen. Galileo believed not only that the **geokinetic theory** was simpler and more coherent than the geostatic theory (as Copernicus had shown), not only that it was more physically and mechanically adequate, but also that it was empirically superior in astronomy.



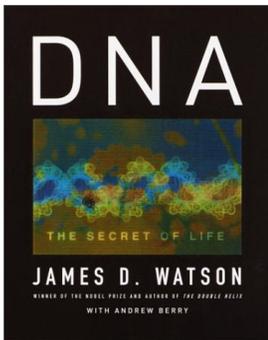
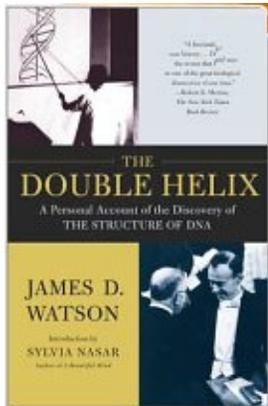
<http://origins.osu.edu/milestones/february-2016-400-years-ago-catholic-church-prohibited-copernicanism>

Scientific Writing

The goal of scientific writing is to

disseminate new scientific information.

Brevity is a cardinal virtue.



MOLECULAR STRUCTURE OF NUCLEIC ACIDS

A Structure for Deoxyribose Nucleic Acid

WE wish to suggest a structure for the salt of deoxyribose nucleic acid (D.N.A.). This structure has novel features which are of considerable biological interest.

A structure for nucleic acid has already been proposed by Pauling and Corey¹. They kindly made their manuscript available to us in advance of publication. Their model consists of three intertwined chains, with the phosphates near the fibre axis, and the bases on the outside. In our opinion, this structure is unsatisfactory for two reasons: (1) We believe that the material which gives the X-ray diagrams is the salt, not the free acid. Without the acidic hydrogen atoms it is not clear what forces would hold the structure together, especially as the negatively charged phosphates near the axis will repel each other. (2) Some of the van der Waals distances appear to be too small.

Another three-chain structure has also been suggested by Fraser (in the press). In his model the phosphates are on the outside and the bases on the inside, linked together by hydrogen bonds. This structure as described is rather ill-defined, and for this reason we shall not comment on it.

We wish to put forward a radically different structure for the salt of deoxyribose nucleic acid. This structure has two helical chains each coiled round the same axis (see diagram). We have made the usual chemical assumptions, namely, that each chain consists of phosphate di-ester groups joining β -D-deoxyribofuranose residues with 3',5' linkages. The two chains (but not their bases) are related by a dyad perpendicular to the fibre axis. Both chains follow right-handed helices, but owing to the dyad the sequences of the atoms in the two chains run in opposite directions. Each chain loosely resembles Furberg's² model No. 1; that is, the bases are on the inside of the helix and the phosphates on the outside. The configuration of the sugar and the atoms near it is close to Furberg's 'standard configuration', the sugar being roughly perpendicular to the attached bases. There is a residue on each chain every 3.4 Å, in the z-direction. We have assumed an angle of 36° between adjacent residues in the same chain, so that the structure repeats after 10 residues on each chain, that is, after 34 Å. The distance of a phosphorus atom from the fibre axis is 10 Å. As the phosphates are on the outside, cations have easy access to them.

The structure is an open one, and its water content is rather high. At lower water contents we would expect the bases to tilt so that the structure could become more compact.

The novel feature of the structure is the manner in which the two chains are held together by the purine and pyrimidine bases. The planes of the bases are perpendicular to the fibre axis. They are joined together in pairs, a single base from one chain being hydrogen-bonded to a single base from the other chain, so that the two lie side by side with identical z-co-ordinates. One of the pair must be a purine and the other a pyrimidine for bonding to occur. The hydrogen bonds are made as follows: purine position 1 to pyrimidine position 1; purine position 6 to pyrimidine position 6.

If it is assumed that the bases only occur in the structure in the most plausible tautomeric forms (that is, with the keto rather than the enol configurations) it is found that only specific pairs of bases can bond together. These pairs are: adenine (purine) with thymine (pyrimidine), and guanine (purine) with cytosine (pyrimidine).

In other words, if an adenine forms one member of a pair, on either chain, then on these assumptions the other member must be thymine; similarly for

This figure is purely diagrammatic. The two ribbons symbolize the two phosphate-sugar chains, and the horizontal rods the pairs of bases holding the chains together. The vertical line marks the fibre axis.



guanine and cytosine. The sequence of bases on a single chain does not appear to be restricted in any way. However, if only specific pairs of bases can be formed, it follows that if the sequence of bases on one chain is given, then the sequence on the other chain is automatically determined.

It has been found experimentally^{3,4} that the ratio of the amounts of adenine to thymine, and the ratio of guanine to cytosine, are always very close to unity for deoxyribose nucleic acid.

It is probably impossible to build this structure with a ribose sugar in place of the deoxyribose, as the extra oxygen atom would make too close a van der Waals contact.

The previously published X-ray data^{5,6} on deoxyribose nucleic acid are insufficient for a rigorous test of our structure. So far as we can tell, it is roughly compatible with the experimental data, but it must be regarded as unproved until it has been checked against more exact results. Some of these are given in the following communications. We were not aware of the details of the results presented there when we devised our structure, which rests mainly though not entirely on published experimental data and stereochemical arguments.

It has not escaped our notice that the specific pairing we have postulated immediately suggests a possible copying mechanism for the genetic material. Full details of the structure, including the conditions assumed in building it, together with a set of co-ordinates for the atoms, will be published elsewhere.

We are much indebted to Dr. Jerry Donohue for constant advice and criticism, especially on interatomic distances. We have also been stimulated by a knowledge of the general nature of the unpublished experimental results and ideas of Dr. M. H. F. Wilkins, Dr. R. E. Franklin and their co-workers at King's College, London. One of us (J. D. W.) has been aided by a fellowship from the National Foundation for Infantile Paralysis.

J. D. WATSON
F. H. C. CRICK
Medical Research Council Unit for the
Study of the Molecular Structure of
Biological Systems,
Cavendish Laboratory, Cambridge,
April 2.

¹ Pauling, L., and Corey, R. K., *Nature*, **171**, 346 (1953); *Proc. U.S. Nat. Acad. Sci.*, **39**, 84 (1953).
² Furberg, S., *Acta Chem. Scand.*, **6**, 634 (1952).
³ Chargaff, E., for references see Zamenhof, S., Braverman, G., and Chantoff, E., *Biochim. et Biophys. Acta*, **9**, 402 (1952).
⁴ Wyatt, G. R., *J. Gen. Physiol.*, **38**, 203 (1952).
⁵ Astbury, W. T., *Symp. Soc. Exp. Biol.*, **1**, Nucleic Acid, 66 (Camb. Univ. Press, 1947).
⁶ Wilkins, M. H. F., and Randall, J. T., *Biochim. et Biophys. Acta*, **10**, 192 (1953).

The above article by J. D. Watson and F. H. C. Crick is a historical landmark in modern biochemistry. (Reprinted in its entirety by special permission from *Nature*, April 25, 1953, p. 737.) It was followed some weeks later by a second article in which the replication process was more explicitly described.

Why Do We Publish Research Articles?

Always keep in mind that.... **your paper is your passport to your community!**

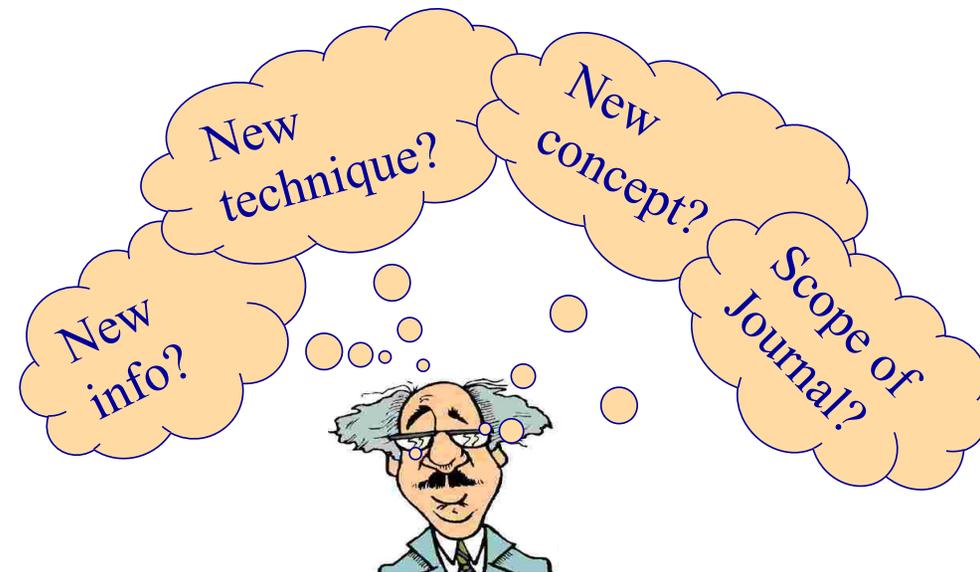


Your Personal Reason For Publishing



However, editors, reviewers, and the research community don't consider these reasons when assessing your work.

Editor's Reason For Publishing



Can this paper help other researchers in the field?

Scientific Writing

Types of Scientific Writing

- Reports
- Dissertations
- Journal Articles
- Books
- Proposal
- Patent

Contents of Scientific Writing

- Text
- Formulas
- Figures
- Tables
- References

The key to being a better writer is to write.
Habit is an invisible architecture of everyday life.
Daily writing is important as it becomes a habit.

Writing habit (Routine)

- Time
- Location
- Walking, driving, exercise
- Daily routine

Good writing practice

Just write it!
Keep writing.
Edit over and over.
Ask other's opinion.
Revise over and over.

EVERYBODY WRITES



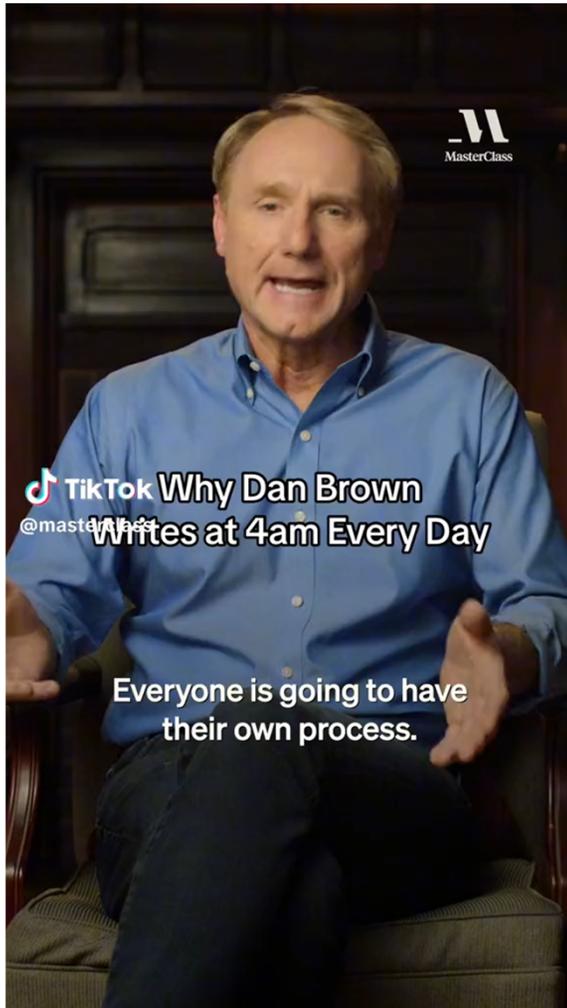
{ Your Go-To Guide to Creating
Ridiculously Good Content }

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WILEY

Everybody Writes: Your Go-To
Guide to Creating Ridiculously
Good Content. Ann Handley

Scientific Writing



The key to being a better writer is to write.
Habit is an invisible architecture of everyday life.
Daily writing is important as it becomes a habit.

Writing habit (Routine)

Time
Location
Walking, driving, exercise
Daily routine

Good writing practice

Just write it!
Keep writing.
Edit over and over.
Ask other's opinion.
Revise over and over.



Shakespeare in Love: "It Will Turn Out Well. --- It's a Mystery"



Type of Scientific Manuscripts

Original research articles

Review papers

Perspectives

Concept papers

Protocol papers

Letters to the Editor

Rapid/Short Communications

Self-evaluate your work:

Is it sufficient for a full article?

Are your results so thrilling that they need to be shown
as soon as possible?

Ask others for advice on manuscript type.

Usually, outsiders see things more clearly than you.

A Good Manuscript

Make every attempt to make the first submission a success.

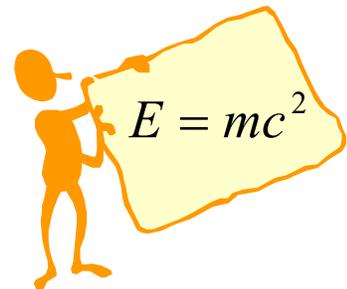
- **No one gets it right the first time!**

- **Write, and re-write**
- After writing a first version, take several days of rest. Come back with **a critical, fresh view**.
- Ask colleagues and supervisor to review your manuscript. **Ask them to be highly critical, and be open to their suggestions.**

Who is your audience?

- Do you want to reach specialists, multidisciplinary researchers, a general audience?
You will need to adjust **information** and **writing style** accordingly.
- Journals, even in similar subjects, reach readers with different background.
- Each journal has its own style; read other articles to see what gets accepted.
- Is readership worldwide or local?

Good **CONTENT** – useful and exciting &
Good **PRESENTATION** of the data – clear, logical



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AUTHOR INQUIRIES

The Writing Style Guide

Coghill 2006, The ACS Style Guide

The ACS Style Guide

Effective Communication of Scientific Information

Anne M. Coghill & Lorrin R. Garson, Editors. 2006

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The Writing Style Guide Examples

Coghill 2006, The ACS Style Guide

Usage and Style for Symbols

► Define all symbols for mathematical constants, variables, and unknown quantities the first time you use them in the text. If you use them in the abstract, define them there and then again at their first appearance in text. Do not define standard mathematical constants such as π , i , and e .

► Form the plurals of mathematical symbols by adding an apostrophe and “s” if you cannot use a word such as “values” or “levels”.

large r values *is better than* large r 's

► Do not use an equal sign as an abbreviation for the word “is” or the word “equals” in narrative text.

$PV = nRT$, where P is pressure (*not* where $P =$ pressure)

when the temperature is 50 °C (*not* when the temperature = 50 °C)

► Do not use a plus sign as an abbreviation for the word “and” in narrative text.

a mixture of A and B (*not* a mixture of A + B)

► Do not use an asterisk to indicate multiplication except in computer language expressions.

Box 12-1. Correct Forms for Alcohols

Correct forms

1-butanol, butyl alcohol
2-butanol, *sec*-butyl alcohol
2-methyl-1-propanol, isobutyl alcohol
2-methyl-2-propanol, *tert*-butyl alcohol
1-propanol, propyl alcohol
2-propanol, isopropyl alcohol

Incorrect forms

isobutanol

isopropanol
any combination of *sec*
or *tert* with the words
butanol or *propanol*

Polymers

Polymer names are often one or two words in parentheses following the prefix “poly”. “Poly” is a syllabic prefix, not a descriptor, and thus is set in roman type. Here is a short list of correctly formatted names of frequently cited polymers. (These names are not necessarily IUPAC or CA index preferences.)

| | |
|---------------------------------------|--|
| nylon-6 | poly(isobutyl methacrylate) |
| nylon-6,6 | polyisobutylene |
| polyacrylamide | polyisoprene |
| poly(acrylic acid) | poly(methacrylic acid) |
| polyacrylonitrile | poly(methyl acrylate) |
| polyamide | poly(methyl methacrylate) |
| poly(aryl sulfone) | poly(methylene) |
| polybutadiene | poly(<i>N,N'</i> -hexamethyleneadipamide) |
| 1,2-polybutadiene | poly(oxy-1,4-phenylene) |
| 1,4-polybutadiene | poly(oxyethylene) |
| poly(butyl acrylate) | poly(oxymethylene) |
| poly(butyl methacrylate) | poly(phenylene ether) |
| poly(<i>n</i> -butyl methacrylate) | poly(phenylene oxide) |
| poly(butylene terephthalate) | poly(phenylene sulfide) |
| polycarbonate | polypropylene |
| polychloroprene | poly(propylene glycol) |
| poly(<i>N,N</i> -dimethylacrylamide) | polystyrene |
| poly(dimethylsiloxane) | polysulfide |
| polyester | polysulfone |
| polyether | poly(tetrafluoroethylene) |
| poly(ether imide) | poly(tetramethylene oxide) |
| poly(ether ketone) | polythiazole |
| poly(ether sulfone) | poly(thiocarbonate) |
| poly(ethyl acrylate) | polyurethane |
| poly(ethyl methacrylate) | poly(vinyl acetate) |
| polyethylene | poly(vinyl alcohol) |
| poly(ethylene adipate) | poly(vinyl butyral) |
| poly(ethylene glycol) | poly(vinyl chloride) |
| poly(ethylene oxide) | poly(vinyl ether) |
| poly(ethylene terephthalate) | poly(vinyl trichloroacetate) |
| polyformaldehyde | poly(vinylidene chloride) |
| polyimidazole | poly(vinylpyrrolidone) |
| polyimide | povidone |

General Structure of a Research Article



**These are used for indexing and searching!
Make them informative, attractive, & effective.**

- Title..... Identify the main issue of the paper
- Abstract**..... Purpose, methods, key results, interpretation, and conclusion
- Keywords **Keywords determine whether your article is found or not!**

Main text

- Introduction..... Problem, existing solutions, limitations, and goal of the research (**Why?**)
 - Exp. Methods..... Details for others to repeat the work, and ethics committee approval (**How?**)
 - Results (Data)..... Main findings and highlight different and unexpected findings (**What?**)
 - Discussion..... Results in relation to the original question and interpretation (**Meaning?**)
-
- Conclusion..... Global and specific conclusions, uses and extensions, and future studies
 - Acknowledgement.... Funding, supports
 - References..... Cited research articles
 - Supplementary Data... Raw data, video clips, etc.

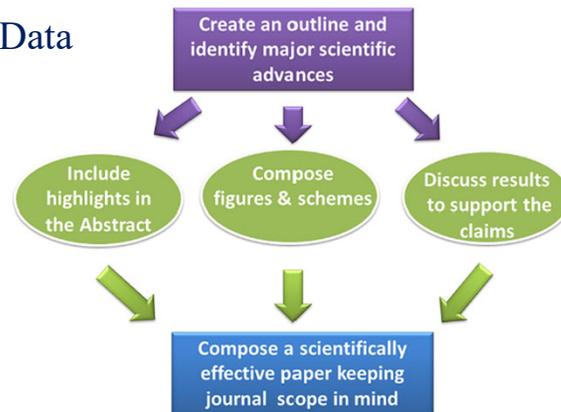
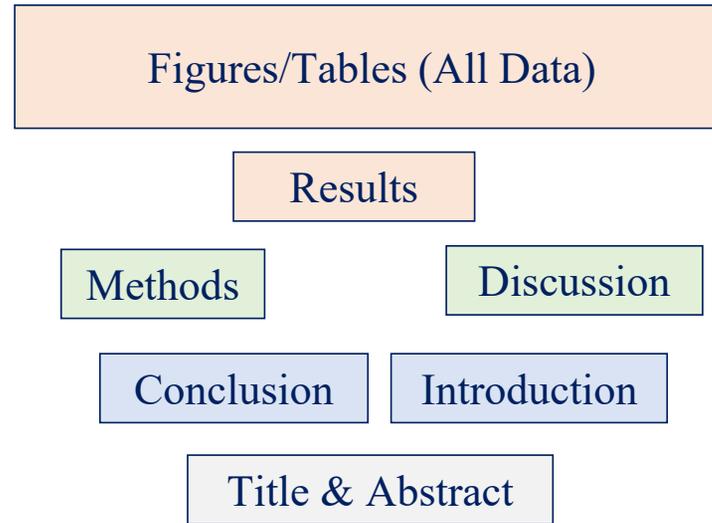
A Sequence of Writing a Research Article



Title
Abstract
 Keywords

Main text
 Introduction
 Exp. Methods
 Results (Data)
 Discussion

Conclusion
 Acknowledgement
 References
 Supplementary Data



State your case with confidence

Clarity is the sole obligation of the science writer, yet I find constantly that the **‘What’s new’** element is buried. Answering one central question — **What did you do?** — is the key to finding the structure of a piece. Every section of the manuscript needs to support that one fundamental idea.

Dallas Murphy. Nature 2018, The write stuff

Title & Key Words

A good title should contain the **fewest** possible words that **adequately** describe the contents of a paper.

Effective titles

- Identify the main issue of the paper.
- Begin with the subject of the paper.
- Are accurate, unambiguous, specific, and complete.
- Are as short as possible.
- With short, catchy titles are often better cited.
- Do not contain rarely-used abbreviations.
- Attract readers.

Keywords determine whether your article is found or not in an “electronic world!

Avoid to make them

- Too general (“drug delivery”, “mouse”, “tissue engineering”, etc.)
- Too narrow (so that nobody will ever search for it.)

Effective approach

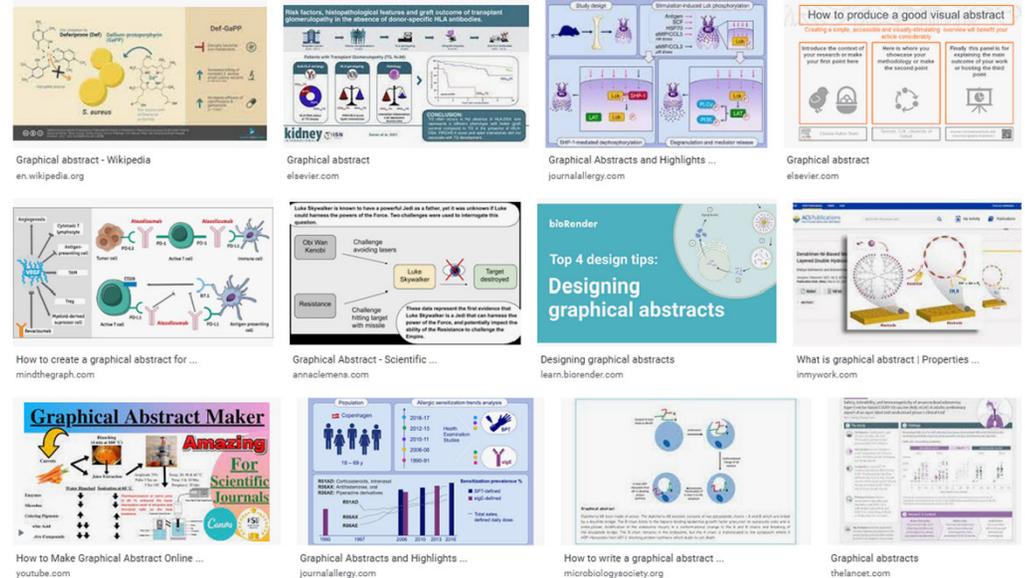
- Look at the keywords of articles relevant to your manuscript.
- Play with these keywords, and see whether they return relevant papers, neither too many nor too few.

Abstract

- Why:** Provides a short description of perspective and purpose of the paper.
(Do not overemphasize perspective by providing a literature review.)
- How:** Describes experimental approaches, if they are critical for the results.
- What :** Gives key results but minimizes experimental details.
(Abstract is what is readily seen in electronic searching.)
- Meaning:** Offers a short description of the interpretation/conclusion

Brief and certainly <250 words. Otherwise truncated by abstracting & indexing services

Graphical Abstract



Abstract of Abstract

Johnny Cash - A boy named Sue



Well, my daddy left home when I was three. And he didn't leave much to ma and me.
Just this old guitar and an empty bottle of booze. Now, I don't blame him 'cause he run and hid.
But the meanest thing that he ever did was before he left, he went and named me "Sue"

Well, he must've thought that it was quite a joke. And it got a lot of laughs from a lots of folks.
It seems I had to fight my whole life through. Some gal would giggle and I'd get red.
And some guy'd laugh then I'd bust his head. I tell ya, life ain't easy for a boy named "Sue."

Well, I grew up quick and I grew up mean. My fists got hard and my wits got keen.
Roamed from town to town to hide my shame. But I made me a vow to the moon and stars.
I'd search the honky-tonks and bars. And kill the man who gave me that awful name.

Well, it was Gatlinburg in mid-July. And I just hit town and my throat was dry.
I thought I'd stop and have myself a brew. At an old saloon on a street of mud.
There at a table, dealing stud. Sat the dirty, mangy dog that named me "Sue."

Well, I knew that snake was my own sweet dad. From a worn-out picture that my mother'd had.
And I knew that scar on his cheek and his evil eye. He was big and bent and gray and old.
And I looked at him and my blood ran cold. And I said, "My name is Sue! How do you do?
Now you're going to die!" Yeah, that's what I told him!

Well, I hit him hard right between the eyes. And he went down, but to my surprise.
He come up with a knife and cut off a piece of my ear. But I busted a chair right across his teeth.
And we crashed through the wall and into the street.
Kicking and a-gouging in the mud and the blood and the beer

I tell you, I've fought tougher men. But I really can't remember when.
He kicked like a mule and he bit like a crocodile. I heard him laugh and then I heard him cuss.
And he went for his gun and I pulled mine first. He stood there lookin' at me and I saw him smile.

And he said, "Son, this world is rough. And if a man's gonna make it, he's gotta be tough.
And I knew I wouldn't be there to help you along. So I give you that name and I said goodbye.
I knew you'd have to get tough or die. And it's that name that helped to make you strong." Yeah.

He said, "Now you just fought one hell of a fight. And I know you hate me, and you got the right.
To kill me now, and I wouldn't blame you if you do. But you ought to thank me, before I die.
For the gravel in your guts and the spit in your eye. Because I'm the son-of-a-bitch that named you Sue"

I got all choked up and I threw down my gun. And I called him my pa, and he called me his son.
And I came away with a different point of view. And I think about him, now and then.
Every time I try and every time I win. And if I ever have a son, I think I'm gonna name him.
Bill or George! Anything but Sue! I still hate that name!

Important Points to Remember

Before you write, put your work into **perspective** first.

Be brief, it is not a history lesson.

Avoid expressions self-praising terms.

Examples: “novel”, “first time”, “first ever”, & “paradigm shift”.

Avoid non-quantitative (qualitative) terms.

Examples: low/high, extremely, enormous, rapidly, dramatic, massive, considerably, exceedingly, major/minor, ...

Illustrations are critical.

Figures and tables are the most efficient way to present results.

Captions and legends must be detailed to make figures and tables self-explanatory.

Cite only relevant references.

Help the editor and the reviewer understand what you are writing about.

“One picture is worth a thousand words”

Sue Hanauer (1968)



<https://www.pinterest.fr/pin/861946816170444382/>

“A thousand words paints a picture...”



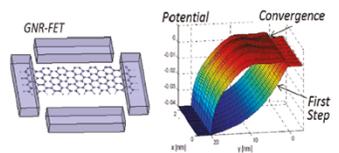
<https://www.deviantart.com/kurenko/art/Worth-a-thousand-words-2-53083005>

Importance of Graphical Abstracts

Love at first sight



2. A Multichannel Model for the Self-Consistent Analysis of Coherent Transport in Graphene Nanoribbons by Mencarelli et al.⁴



The vivid ToC image projects the main concepts of the paper immediately: models of graphene in a FET configuration, accompanied by detailed electrical studies of the device. The scheme of the modeled graphene is clear, so that experimentalists and theorists alike can relate to the proposed device architectures. The authors point out two items of interest: a first step and a convergence in the plot on the right that seem, even for the unacquainted, a good place to educate oneself with respect to the electrical properties of this remarkable material.

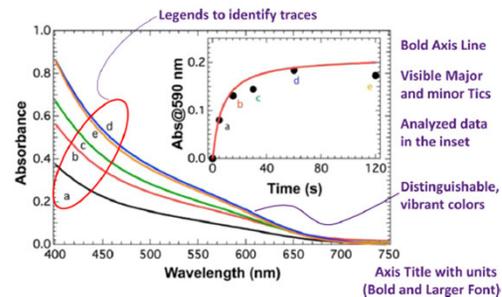


Figure 1. An example of graphical presentation of data. A few items in the figure are highlighted for clarity and accuracy of the presentation.

Summarize Your Work in 100 Milliseconds or Less... The Importance of the Table of Contents Image

The manuscript is finally complete—months and/or years of research packaged, trimmed, divided, molded, and painstakingly placed into the proper format, and then edited, edited, edited. The sometimes tumultuous back-and-forth of the manuscript between co-authors has led the final version—it is no longer a draft. The visual figures, the subject of precise care with an eye to detail, are beautiful, organized, and compelling. The cover letter is precise and succinct, and yet simultaneously descriptive, and the Methods section along with the Supporting Information are more than sufficient to allow those skilled in the art to reproduce every experiment. Sounds perfect, so press the "Submit" button.

Just a second! In about one-quarter of the papers submitted, the table of contents (ToC) image is missing. While a lack of a ToC image will certainly not prevent a worthy paper from going out for review, it does suggest, more broadly, that the ToC image may not be viewed as an important component of the manuscript, and perhaps even a nuisance.

We cannot stress enough how important the ToC image is, as it is typically the first glimpse a potential reader has of your published paper. Whether it be through a directed citation search at www.pubs.acs.org, or via the search feature on the ACS site, or through a Google/Google Scholar search that lands the potential reader on the abstract page of www.pubs.acs.org, the ToC image appears below the title and authors and is therefore part of the data almost instantaneously processed by the busy potential reader. A decision is made—to click or not to click! An equation combining neural synaptic speeds (direct relationship), number of coffees consumed (direct relationships), and mental overload (inverse relationship) probably leads to a time calculation of a few hundred milliseconds in which the decision is made: should the potential reader download the paper or move on with their search? As scientists and authors, we want our papers read, and we want to make a lasting impact on our fields of research. Every one of us at ACS Nano also wants the potential reader to click on your ACS Nano paper because we know that every single paper that has made it through our review process is indeed special and top quality.

So, perhaps it is best to consider what a ToC image must do, and then consider how this is best done. A good ToC image must, simultaneously:

- Resonate with the title (to provide synergistic support)
- Instantly provide a sense of what is to be learned
- Be clear and concise, while providing the information regarding (iii) above
- Be compelling—ensure that everything in the ToC image is comprehensible and lucid, and yet exciting. What made you, as the writer, excited about your own work?

It sounds easy, but really it is not. Your cover letter forced you to summarize all of your excitement into a few lines to convince the editors to move forward with your paper. The ToC image requires you to go even further, and to do so in one image. A common mistake is simply to cut and paste a figure from the paper to use as the ToC, but this approach typically is unsuccessful because it is too specific or detailed and, therefore, does not do justice to the education side of a paper—what will the reader learn? Another common mistake is to cram too much into the figure so that it lacks clarity and ends up as a jumble of items. A recent *Advanced Materials* article⁴ did a wonderful service to the scientific community by providing

The table of contents image is typically the first glimpse a potential reader has of your published paper.

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www.acsnano.org



Titles and Table of Contents Images: The Candy Store Analogy



Everyone is familiar with the scenario of the indecisive kid in the candy store—the vast array of choices can be overwhelming to anyone, since the final choice of what to buy is predicated upon many sources of information that are convoluted to become a train of thought, and ultimately a decision. Possible variables that influence the decision include the name of the candy (its title), one's past experience with candy (was it good/interesting?), one's learned preferences (I like chocolate/graphene, but I do not like items [oligonucleic acids], and a host of intangibles. It is similar for readers who may be shopping in a scientific "candy store," or journal, for potential papers—each reader must make a decision regarding which paper to click on, download, and read, all of which are actual separate and not entirely connected actions. The types of scientific candy stores frequented by readers may be quite varied, as some will skim tables of contents on journal web sites, and others will rely on social media or RSS feeds, search engine results, and/or a mix of any or all of these. So the question for all authors is this:

How do one maximize the chances that one's paper will be downloaded?

Both the title and the table of contents (ToC) image are important tools for authors to give potential interested readers insight into what a paper is about. As has been summarized in an earlier editorial, a reader may make a decision to click on a paper within 100 ms.⁴ A clear title and compelling ToC image will play a significant role during this short time, and we cannot emphasize enough the importance of these two parts of a paper. As scientists, we spend months or years working toward submission of a manuscript, and it would be a shame to present this new scientific insight to the world with an overly complicated title and/or a poorly executed ToC image. Scientists are humans, and so like dining at a high-end gourmet restaurant, the esthetics of presentation of the meal (or in our case, the paper) is an important part of the enjoyment and, ultimately, consumption of the meal (the scientific results). Time taken to develop an interesting and nicely presented ToC

image and title reflects pride in one's research, and since it is typically the first encounter of a potential reader with this particular piece of work, a good first impression is critical, the impact of which cannot be underestimated.

■ **TITLE**
A good title is one that is succinct, makes the focus obvious, and is free of acronyms and excessive jargon. The title may be difficult to write if one has not developed a clear emphasis for the paper and, thus, should serve as a red flag for authors that their manuscript requires more thought. A title that states that the material described within has promise for a laundry list of applications sounds unappealing, as does a title that places too much emphasis on the results being the highest, biggest, smallest, grandest, most novel, brightest, most efficient, best, etc. The latter "superlative" papers suggest that the work contained within is merely a series of incremental improvements, which may not be creative or interesting. As an author, you are telling a story, so be honest with your readers and portray the theme and subject matter of your story as lucidly as possible. Do not mislead, and hence frustrate, your readers; since your first readers are almost always the editors and reviewers, announce that the title does not accurately reflect the content of your paper could lead to negative consequences.

■ **TABLE OF CONTENTS (TOC) IMAGES**
The Chemistry of Materials Author Guidelines tries to provide the very basic premises of how to conceive of a good ToC image:
The ToC/abstract graphic should capture the reader's attention and, in conjunction with the manuscript title, should give the reader a quick visual impression of the essence of the paper without providing specific results... Some of the best images are simple, relatively free of text and technical characters, and make use of color for visual impact. It is best to stay away from complex structure schemes and small-sized details.
Do not simply cut and paste a figure from your manuscript to use as the ToC image, as they typically are ill-suited due to a high level of scientific detail, and they lack in the content to make them rapidly understood. One very useful article on how to design scientific figures, "A Brief Guide to Designing Effective Figures for the Scientific Paper," is a helpful place to look for pointers on graphical design, layout, and many "do not do this, and why" examples.⁵ While it may seem obvious, make sure that your font or other details are not too small to discern when shrunk down to the size they will appear on a screen or on the printed PDF page. Ensure that the ToC image resonates with your title so that it enhances your (potential) reader's wish to look further. This is a scientific candy store, with many other exciting papers within easy reach, so think about why authors will want to choose to spend time out of their busy day downloading and reading your paper.

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Graphical Excellence

It is the experience of every author that figures and illustrations in scientific papers are the gateway for effective communication of research findings to the scientific world. While the title and abstract of the paper draw the attention of any avid reader, the essence of the paper is captured by the figures and schemes. Well-drawn, scientifically correct figures make the first impression of the scientific findings. Yet, time and time again, we see poorly presented results, inaccuracy in plotted data, improperly defined axes, meaningless significant digits in axis scales, wrong or missing units, and undefined symbols or traces. Such inaccuracies can lead to *repet* recommendations from the editors and reviewers. We wonder why researchers who are passionate about communicating their findings, many times take little interest in effective presentation of their data.

The ease of computer software usage has contributed to some of the inattentiveness for presentation of data. Not too long ago, researchers plotted data on a graph sheet with a pencil. The origin was inserted first as (0, 0) and not with decimals, (e.g., (0.00, 0.00)) as you commonly see in many of the software-produced plots. (Note: Absolute zero has no decimals, but it is difficult to override the kernel in most plotting software.)

The researchers would then decide on the choice of scale, major ticks, units, and so forth. They inserted data points and checked the validity of any analytical solution included in the study. Straight line plots were explained with a supporting equation (e.g., kinetic plots). The manual checks at each step ensured accuracy of the data presentation. It was not a common practice to connect points on a plot; instead, a French curve or flexible curve was used to draw a trend line. Today, you select the data in a spreadsheet and let the computer figure out the plot. (Otherwise, how can you explain four or more significant digits for subtraction operations and associated rate constants when the excitation pulse has a pulse width of few nanoseconds or plots with no relationship between the X- and Y-axis as in relating an observed property with sample numbers or solvent name?)
The above discrepancies are not meant to imply that modern platforms of computer software are error-ridden. It is carelessness on the part of the researcher that contributes to the misrepresentation of the data. Analytical software programs are great tools for analyzing complex sets of data, and their contribution to modern science is undeniably important and significant. However, it is important to know the data collection procedure, limitations of the measurements, and the variation (error bars) in the distribution of values while processing the data with any available software. Figures that are produced with care and accuracy help to demonstrate the quality and reliability of research.

There are two aspects that need to be considered while drawing figures: (1) accuracy of data presentation and (2) aesthetics of the figure. According to Tufte, a figure or graphic is a well-designed representation of interesting data that consists of complex ideas communicated with clarity (no ambiguity or confusion), precision (truthful results with no distortions), and efficiency (minimal "chart junk").⁶ If you convey the greatest number of ideas in the shortest time with the least ink on the medium

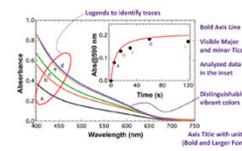


Figure 1. An example of graphical presentation of data. A few items in the figure are highlighted for clarity and accuracy of the presentation. Reproduced from ref 4.

space. A well-constructed graphic, with a complete description should stand alone, and the reader should be able to grasp the essence of the experiment as well as the analysis of the result.

We will now discuss important instructions that the authors can follow while preparing graphics for a scientific figure. A number of useful tips are summarized in Table 1, and we also note the examples given in Figure 1, which was taken from an earlier published paper. Although the focus of this Editorial is intended for preparing physical chemistry papers, readers from other disciplines can also find these tips useful.

Improving the Effectiveness of Data Presentation. Since ACS journals do not charge to reproduce colored figures, authors should make use of this feature to enhance the effectiveness of their figures. It is important to select colors that distinguish each data set and to use vibrant and bold colors in an appealing way. The choice of symbols and traces should be made wisely to represent multiple data sets. Avoid using curves with the same colors that are distinguished by dashes and dots as they lack distinguishability for closely spaced curves. It is also important to take into consideration the size of the figure. The "golden rectangle" (height/width, 1:1.6) is an appealing size for figures. Combining a set of related figures into a single panel is also an effective way to present multiple sets of results related to the same experiment.

Selecting Proper Axis and Units. Once the data have been collected and analyzed, the author should decide the best possible way to present the results so that the reader can visualize the theme and conclusions of the experiment. Decide whether an X–Y plot or bar diagram is appropriate for presenting the data. For an X–Y plot, there should be a direct causality or relationship. For example, sample names/numbers or different solvents if presented on the X-axis do not bring in causality. However, a sample or solvent property can show an important relationship with the Y-axis. Comparative data with a direct relationship between the X- and Y-axis should be presented as a bar diagram.

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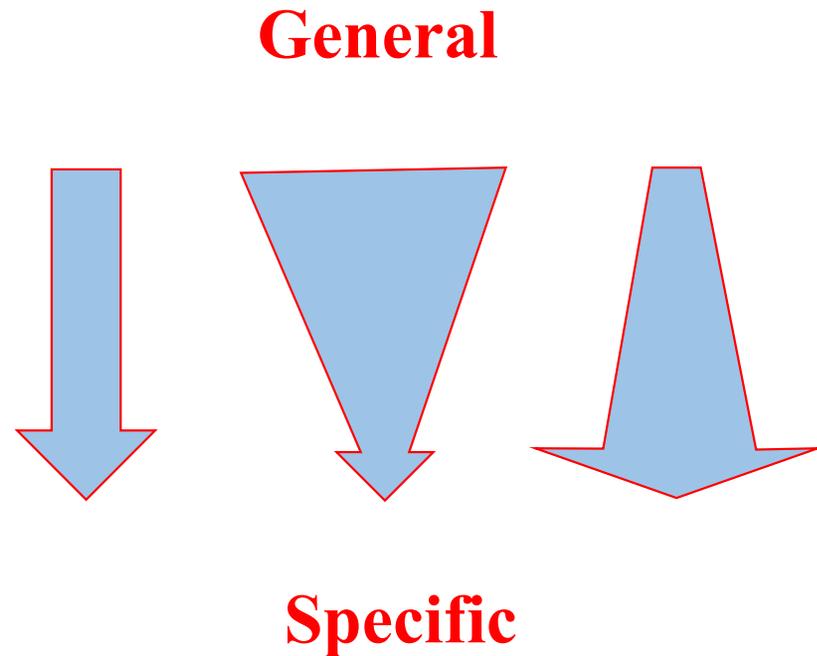
Buriak 2011, Summarize Your Work in 100 Milliseconds or Less... The Importance of the Table of Contents Image Buriak 2014, Titles and Table of Contents Images: The Candy Store Analogy Kamat 2014, Graphical Excellence

Introduction

The place to convince readers why your work is relevant.

Answer a series of questions:

- What is the problem?
- Are there any existing solutions?
- Which one is the best?
- What is its main limitation?
- What do you hope to achieve?



Experimental Methods

- **Include all important details for the reader to repeat the work.**

Details that were previously published can be omitted but a general summary of those experiments should be included.

- Give vendor names (and **physical addresses, or Uniform Resource Locator**) of **equipment** etc. used.

- All **chemicals** must be identified.

Do not use proprietary, unidentifiable compounds without description.

- Present **proper control** experiments.

- Avoid adding comments and discussion.

- Write in the past tense.

Most journals prefer the passive voice.

- Consider use of Supplementary Materials.

Documents, spreadsheets, audio, video,

Reviewers will criticize incomplete or incorrect descriptions, and may even recommend rejection.

Ethics Committee approval

- Experiments on **humans** or **animals** must follow applicable ethics standards, e.g., most recent version of the Helsinki Declaration or relevant (local, national, international) animal experimentation guidelines .
- **Approval** of the local ethics committee is required, and should be specified in the manuscript.
- Editors can make their own decisions as to whether the experiments were done in an ethically acceptable manner.
- Sometimes local ethics approvals are way below internationally accepted standard.

Experimental Methods

Reproducibility

While citations are important, it is about how many people you, in essence, have taught and now do what you do.

Many published results are not reproducible by others.

Why?

Experimental section usually does not describe the details that others can follow.



Editorial
pubs.acs.org/cm

Your Research Results Look Compelling, but Are They Reliable?

As we have described in an earlier issue of *Chemistry of Materials*, an experimental section that accurately captures the necessary details of your work to allow future researchers to reproduce your work is essential to the longevity of your paper.¹ If others can reproduce what you do, then your work will have a greater impact within your research area, well into the future. Irreproducible results lead to frustration, wasted resources (time, funds, materials), and questions from your peers regarding the quality of your work.

Your published work represents many months or years of time, thought, and effort. It is critical to convince future readers that the results you are presenting are reproducible, and that by following your experimental details, similar data can be obtained by a skilled worker in a safe manner. A future reader may decide that reproducing or building upon your work is too much of a risk, and hence this person may discard it—no one wants to waste time struggling to replicate published work. The ability to reproduce results is always important but becomes blatantly obvious when reporting device performance and the key material characteristics that make your paper exciting and unique. We have observed, throughout the scientific literature, a proliferation of device performance data lacking clear indication of reproducibility and statistics; if one experimental parameter is being changed within a device, can the reader truly ascertain that device 1 is better than device 2? We have also noticed important materials characterization central to the thesis of the paper presented without statistical data, such as a histogram to represent size distribution of the resulting nano/microparticle sizes, shapes, or other characteristics; is, for example, nanoparticle synthesis 1 truly producing a more monodisperse/smaller/better product than nanoparticle synthesis 2? Figure 1 shows a schematic representation of two parameters being compared—merely reporting the average values, or the best values, could be misleading if the differences are statistically insignificant. You do not want to leave the reader wondering if your reported device or materials results are, in fact, the very best of a series of ill-performing devices (also referred to as cherry picking), or if the spread of results is very large, or if only one device or sample was even made.² A lack of reported information, both with regards to data and experimental conditions, can only mean that any or all of these scenarios are possible and, hence, present a risk.

At *Chemistry of Materials*, in early 2014, we added some simple guidelines regarding device and materials reporting to our Information to Authors web page.³ These guidelines are stated below, with additional explanation. In no way can we hope to cover every single scenario regarding a new material or device; instead we try to outline the spirit of what you, as authors, can do to convince your readers that your results are reproducible. Since authors will typically already have statistics and comments about materials/device reproducibility in hand at the time of writing their manuscript, we do not believe that requiring the reporting of such additional data will be an impediment to publishing. On the contrary, inclusion of this information will encourage future readers to take your work

In no way can we hope to cover every single scenario regarding a new material or device; instead we try to outline the spirit of what you, as authors, can do to convince your readers that your results are reproducible.

seriously and feel confident that they can use your results as the foundation for their own research programs.

As stated in our Information to Authors, authors are asked to include the following when writing their manuscript:

(i) The number of devices examined and the range of results. This can be conveyed in bar graphs (histograms) to represent data for a statistically meaningful number of samples or could be reported as a specific number of samples with an accompanying specified standard deviation. The journal will not accept a single result that appears to be the best obtained. It is important to emphasize typical results and the degree of variation so that reviewers and future readers can assess reproducibility, and hence the validity, of the work.⁴

For instance, in the following example Wong and co-workers crystallized specific indene-C₇₀ bisadducts and incorporated them into organic photovoltaic devices (OPVs).⁴ As can be seen in Figure 2, the performance of the devices is provided with very clear statistics: the average performance metrics of 10 devices are shown, with standard deviations and an appropriate level of precision for each datum. Similar statistics should be provided for all other devices (for example, batteries, catalysts, thermoelectrics, etc.). In the case when materials are very rare or difficult to obtain, a paper reports only a small number of devices; in circumstances such as these, authors should simply state the limitations and reasons and allow the readers to arrive at their own conclusions.

In the case of materials reporting, we would like to encourage similar statistical treatments. In a recent paper by Cossari and co-workers, InP nanoparticles were prepared via two different routes, one using P(SiMe₃)₃ and another using a mixture of P(SiPh₃)₃ and P(SiMe₃)₃.⁵ As shown in Figure 3, the authors measured over 300 nanoparticles to produce a histogram to represent the size distribution. The authors can claim, with little ambiguity, that the first method (Figure 3a) produces smaller, less disperse nanoparticles since the average size in Figure 3a is 2.6 ± 0.6 nm, whereas the second route (Figure 3b) yields an average size of 3.4 ± 1.0 nm. The representation of data in this paper reassures future readers as to the reproducibility of this work.

(ii) Sufficient experimental data to reproduce the results and enable valid comparisons with other work. Manuscripts that report devices must provide additional important characteristics beyond those above to enable comparison with

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Editorial
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The Experimental Section: The Key to Longevity of Your Research

One of the greatest compliments anyone can give your published work is to reproduce it and build upon it. Your discovery starts to take on a life of its own, which is one of the strongest indicators that your work is meaningful, broadly speaking, to the scientific community. Seeing that others have learned from your own scientific research effort, and accompanying sweat, tears, and sheer hard work, is incredibly satisfying. While citations are important, it is about how many

While citations are important, it is about how many people you, in essence, have taught and now do what you do.

people you, in essence, have taught and now do what you do. For others to “do what you do”, an excellent experimental section is an essential component of your published paper. Science can only progress if you, as an author, are as open and inclusive with respect to details as possible, to enable future readers to learn from you, and build upon your work.

The scientific endeavor involves the discovery and creation of new ideas. Many of these do not stand the test of time and are abandoned, and those with merit are adopted and built upon. This effort is difficult and painstakingly slow and, unfortunately, is made even slower when experimental sections in many papers in a field are missing crucial details that enable successful replication, or worse, are critically flawed in a manner that is not apparent from the description of the experimental details. Only after wasting time trying to repeat the work does it become obvious that it is not reproducible. Irreproducible papers can cause enormous and undocumented harm because of the time wasted in the lab, or *in silico*, in the case of theoretical work. Those most affected tend to be younger scientists, the graduate students and postdoctoral associates working at the bench; the long-term impacts of their ensuing frustration can go beyond “simply” impeding their progress toward a degree or a job, as it could lead to their disillusionment with science altogether. There are only two reasons we can see that result in irreproducible papers, and neither is particularly flattering—one is sheer carelessness, and the other is a misguided attempt at obtaining or maintaining a competitive advantage. The latter, intentionally withholding critical details, can only result in very short-term gains (i.e., your peers cannot replicate your results, thus slowing their progress), but very profound long-term losses—your work has no impact within the scientific community, and your future papers are viewed with a skeptical eye, or simply ignored.

Experimental sections are, therefore, key to the longevity and continued impact of your research. So, how does one approach writing this critical section? Since your research is novel and original, you, the authors of the manuscript, are the only ones in the world who, at present, know how to carry out your experiments. Papers should never sweep important, and sometimes subtle, details under the rug. In new and emerging

fields especially, the experimental section can be daunting to write as there is often no standard nomenclature and the procedures are not well-established, making it necessary to provide a lot more detail than required for well-established fields. We have a few suggestions to help ensure future reproducibility:

(i) Provide as much detail as is feasible. If a particular parameter is tricky or absolutely critical for successfully completing an experiment, state it and describe how you controlled it or attempted to control it. Include details about what should be observed during the procedure—is there a color change or some observable characteristic that you look for to indicate that things are progressing in the right direction? What is the typical yield of each step? Provide statistics to indicate how much variability should be expected when carrying out the work. These details are important—they can catalyze the adoption of your methods by providing a specific goal for those willing to take the next step and make your methods even better. Reproducibility can often depend on an unusual or atypical feature, for instance, the use of a specific type of vessel, a reagent from a particular commercial source, or other parameter—if so, let your reader know. Put yourself in the shoes of an experienced colleague or graduate student “skilled in the art” and ask yourself the following: Would they be able to replicate your results after a couple of attempts?

(ii) Use the Supporting Information (SI) section for extra details, movies, and photos. You are free to include additional

Use the Supporting Information (SI) section for extra details, movies, and photos.

written details, photographs of experimental apparatus, and movies to demonstrate procedures. The oft-used adage of “pictures speak a thousand words” is certainly true, and you can almost hear the exclamation of “oh, now I get it” each time a movie is downloaded and watched. A movie may be a simpler and more direct way to make a point than a long and drawn out textual description of an apparatus, in some cases. Sometimes, the experimental details that you, the author, consider to be obvious may not be so evident for others—movies and photos help with the sharing of this more subtle information with readers.

As practicing materials chemists and engineers, we know that, when writing a paper, the experimental section is often seen as a tedious stage through which an author must suffer on the road to publication. It is true that the experimental section may lack the up-front glory, but these details enable the research community to build upon your results, leading to the longevity of your hard work. Papers with long-term impact are those that serve to inspire new work and become the foundation for future experiments and research by others well into the future. The

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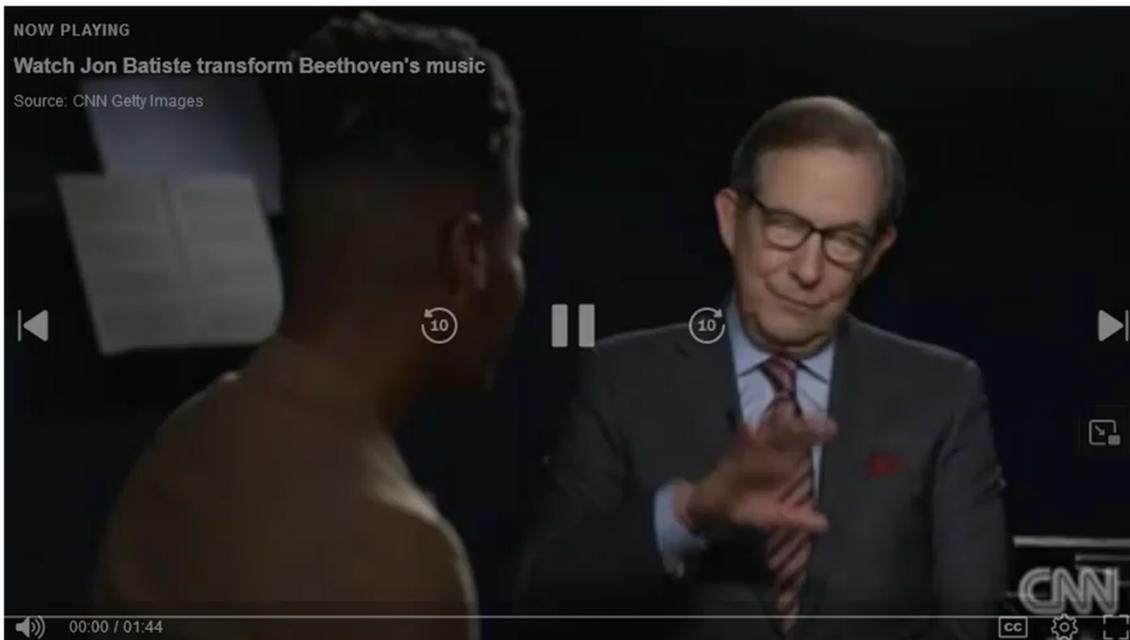
1765

dx.doi.org/10.1021/cm500321c1 Chem. Mater. 2014, 26, 1765–1766

Buriak 2014, The Experimental Section
Buriak 2014, Your Research Results Look Compelling, but Are They Reliable

Data Interpretation

Musician and singer Jon Batiste joins CNN's Chris Wallace to demonstrate how music can cross genres.



<https://www.cnn.com/videos/entertainment/2023/10/12/jon-batiste-piano-music-wallace-wtew-cprog-vpx.cnn>

Greek Philosophers

In ancient Greece, philosophers contemplated and theorized about many different ideas such as human nature, ethics, and moral dilemmas.

Pre-Socratic philosophers mostly investigated **natural phenomena**. They believed that humans originated from a single substance, which could be water, air, or an unlimited substance called “apeiron.” One well-known philosopher from this group was Pythagoras, the mathematician who created the Pythagorean Theorem.

The Socratic philosophers in ancient Greece were Socrates, Plato, and Aristotle. These are some of the most well-known of all Greek philosophers. Socrates (470/469–399 B.C.E.) is remembered for his teaching methods and for **asking thought-provoking questions**. Instead of lecturing his students, he asked them **difficult questions in order to challenge their underlying assumptions** - a method still used in modern-day law schools. Because Socrates wrote little about his life or work, much of what we know comes from his student Plato.

Plato (428/427–348/347 B.C.E.) studied **ethics, virtue, justice, and other ideas relating to human behavior**. Following in Socrates’ footsteps, he became a teacher and inspired the work of the next great Greek philosopher, Aristotle. Aristotle (384–322 B.C.E.), while also interested in ethics, studied different sciences like **physics, biology, and astronomy**. He is often credited with developing the study of logic, as well as the foundation for modern-day zoology.



Ph.D.: Doctor of Philosophy
Philosophy: Love of wisdom
Breaking the barrier of different disciplines

<https://education.nationalgeographic.org/resource/greek-philosophers/>

Data Interpretation

Bob Dylan - Blowing in the Wind



<https://www.google.com/search?q=Bob+Dylan:+Blowin%60+In+The+Wind&source=lmns&tbn=vid&bih=905&biw=1933&client=firefox-b-1-d&hl=en-US&sa=X&ved=2ahUKEwjRrYqc2dmDaxV6zckDHTytBV0Q0pQJKAF6BAgBEAQ#fpstate=ive&vld=cid:88c36b07,vid:vWwgrjjIMXA,st:0>

<https://www.youtube.com/watch?v=Ld6fAO4idaI>

Data Interpretation

Dolly Parton: I will always love you.



<https://www.youtube.com/watch?v=pW2TgGy5gjY>

Whitney Houston



Movie. The Bodyguard
<https://www.youtube.com/watch?v=3JWTaaS7LdU>

Data Interpretation

If I can dream (1968)



But as long as a man
Has the strength to dream
He can redeem his soul and fly

Dreamers (2022)



Look who we are, we are the dreamers. We make it happen 'cause we believe it.
Look who we are, we are the dreamers. We make it happen 'cause we can see it.
Here's to the ones that keep the passion. Respect, oh, yeah.
Here's to the ones that can imagine. Respect, oh, yeah.

Data Interpretation

The readers can interpret the contents differently from what the authors intended.

JANUARY 18, 2022 / BOOKS

5 CLASSICS THAT HAVE BEEN MISINTERPRETED BY MODERN AUDIENCES



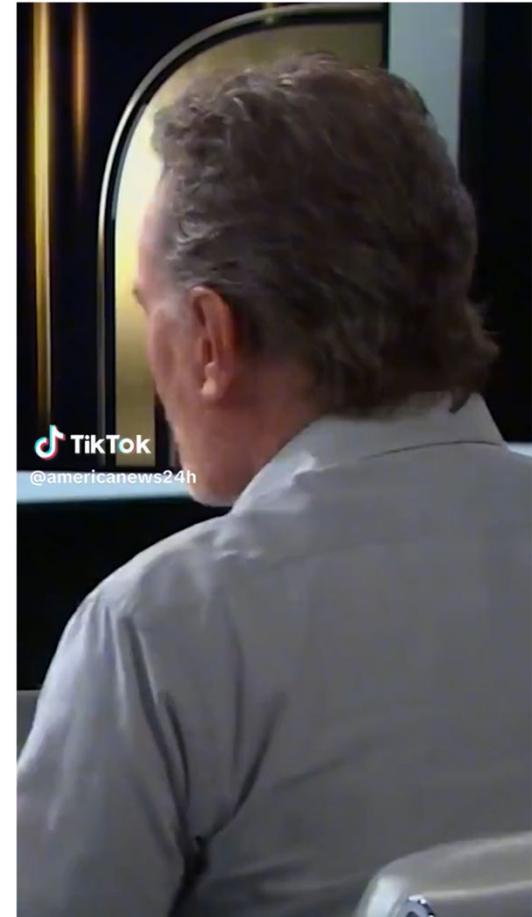
The Great Gatsby by F. Scott Fitzgerald

What people think it's about: The 1920s were so fun because everyone had money and went to parties and was glamorous.

What it's actually about: The main takeaway from this book is that the American Dream is absolutely bogus thanks to the concept of Old Money and New Money. Gatsby is New Money because he was born into a poor family and got his fortune through “good old-fashioned hard work and determination” while Daisy, Tom, and Jordan are Old Money because they were born into rich families and never had to work a day in their lives. **Even though they're all rich, they're not the same.** The lifestyle these people (Gatsby included) are portrayed as being empty and shallow and the book really beats it into the reader that **no amount of money or notoriety can ever give someone what they truly want.**

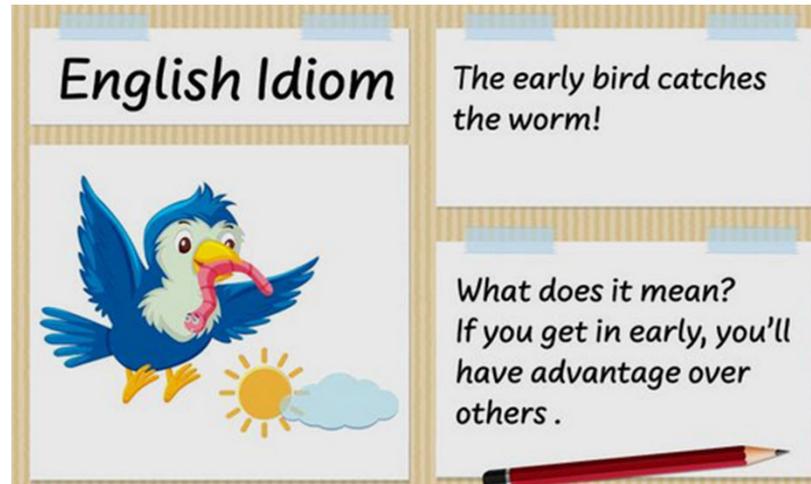
In Gatsby's case, what he really wants is Daisy, but his money and possessions can't give him Daisy back because they're just not the same. Her white supremacist brute of a husband is Old Money and that gives her a social standing. There's a lot to be said about social class here and how the American Dream has always been a broken concept due to class differences and people who are born rich looking down on even “self-made” millionaires. Basically, all the characters in this book suck and shouldn't be looked up to as role models for success or beauty or anything. I hate this book if you couldn't tell.

<https://monstrumology.com/5-misread-classics/>



Bryan Cranston

Data Interpretation: Interpretation is the freedom you can control.



The early bird gets the worm

A saying that means someone will have an advantage if they do something immediately, or before other people do it.

<https://www.alamy.com/stock-photo/the-early-bird-catches-the-worm.html?sortBy=relevant>
<https://dictionary.cambridge.org/us/dictionary/english/early-bird-catches-the-worm>



Discussion

Check List

- **Relation of the results to the original question** or objectives outlined in the Introduction section.
- **Interpretation** for each of the results presented.
- Consistency of the results with what other investigators have reported.
If different, explain why.
- **Limitations of the experimental methods and the results.**
Example: Targeted drug delivery in mice - limitation to the extrapolation to human patients.
- The discussion should logically lead to the conclusion.

Do Not

- Make statements that go beyond what the results can support.
- Suddenly introduce new terms or ideas.

Conclusions

Optional

- Present global and specific conclusions.
- Indicate uses and extensions if appropriate.
- Suggest future experiments and indicate whether they are underway.
- Do not summarize the paper.
It is for Abstract
- Avoid judgments about impact.
Others will decide this.

The Significance of Your Research



Abstract: Describing the Meaning of the Finding

Whitney Houston - One Moment In Time



One Moment in Time (Whitney Houston)

Each day I live, I want to be. A day to give the best of me.
I'm only one, but not alone. My finest day is yet unknown.
I broke my heart, fought every gain to taste the sweet.
I face the pain, I rise and fall. Yet through it all.
This much remains.

I want one moment in time. When I'm more than I thought I could be.
When all of my dreams are a heartbeat away.
And the answers are all up to me.

Give me one moment in time. When I'm racing with destiny.
Then in that one moment of time. I will feel. I will feel eternity.

I've lived to be the very best. I want it all. No time for less.
I've laid the plans. Now lay the chance. Here in my hands.

Give me one moment in time. When I'm more than I thought I could be.
When all of my dreams are a heartbeat away.
And the answers are all up to me.

Give me one moment in time. When I'm racing with destiny.
Then in that one moment of time. I will feel. I will feel eternity.

You're a winner for a lifetime.
If you seize that one moment in time. Make it shine.

Give me one moment in time, when I'm more than I thought I could be.
When all of my dreams are a heartbeat away.
And the answers are all up to me.

Give me one moment in time, when I'm racing with destiny.
Then in that one moment of time.
I will be. I will be. I will be free. I will be. I will be free.

Cover Letter

Your chance to speak to the Editor directly.

View it as a job application letter.

WHY did you submit the manuscript to THIS journal?

Mention special requirements.

Mention and explain conflicts of interest, if applicable.

Suggest suitable reviewers.

The editors have not traveled the long journey described above with the submitting authors and are likely hearing about the idea for the first time. In a perfect world, the authors and editors could discuss the manuscript over coffee to be sure the novelty and significance of the work are appreciated. It is likely that the authors could be more persuasive in person than in the formal text of the manuscript. Sadly, such meetings are seldom possible. However, one last chance at such an in-

it is by far the most vital. The cover letter provides the chance for authors to persuade the editors of the significance of their work in a less formal manner than what is written in the manuscript itself.

While most authors take advantage of this opportunity, there are many cases where the opportunity is squandered, even though it could be the difference between a manuscript sent for external review and one rejected without further consideration.

Hafner 2010, The Art of the Cover Letter

The Art of the Cover Letter

I have now served as an Associate Editor at *ACS Nano* for three months. As promised, doing so has provided unique insights into scientific publishing. Interestingly, the biggest surprise has not been something that authors do, but something they frequently neglect to do: constructing a well-written cover letter, including a statement justifying the importance of their work.

Consider the incredible effort that goes into a manuscript. First, an original idea must be generated by the small miracle of human inspiration, backed by years of research and study. To acquire resources to pursue that idea, it must be further refined, put into scientific and social contexts, and explained to other researchers in the form of a grant proposal, often many times over. Once funding and other resources have been secured, the real work can begin. A few courageous graduate students or postdocs must squander a part of their precious youth toiling in fluorescently lit laboratories, repeatedly executing experiments to see if, when, and how the idea works, to see what can be learned from it, or to see how it might be useful. The results of this effort will be analyzed, scrutinized, rejected, and repeated for months on end. Once a cohesive story can be assembled, the text is written, citations are added, and figures are prepared. The manuscript is now ready for submission. A journal is chosen, reviewers are suggested, and the upload button is pressed. The humble idea has become a work of science, yet its fate now rests with the editors and reviewers, who must evaluate its significance.

The editors have not traveled the long journey described above with the submitting authors and are likely hearing about the idea for the first time. In a perfect world, the authors and editors could discuss the manuscript over coffee to be sure the novelty and significance of the work are appreciated. It is likely that the authors could be more persuasive in person than in the formal text of

ings are seldom possible. However, one last chance at such an intimate step missing from the sequence of events above: the cover of information to be included in the cover letter is "a statement for *ACS Nano*". While this is just one of several requested elements, the cover letter provides the chance for authors to persuade the editors of the significance of their work in a less formal manner than what is written in the manuscript itself. In the absence of this opportunity, there are many cases where the opportunity could be the difference between a manuscript sent for external review and one rejected without further consideration.

When you prepare cover letters or are overly modest when you write your cover letter, your submission to be delayed by just one more day. Spend time to carefully prepare it with your coauthors for their input. As active researchers and often on the other side of the publishing process ourselves, the other *ACS Nano* editors and I realize that not every submitted result has the capability to cure cancer or to replace silicon in the semiconductor industry; however, a carefully crafted and straightforward description of the impact of one's work can go a

great deal. This is especially important in a field like nanotechnology where researchers having diverse and interdisciplinary backgrounds. Your reflection reveals new insights that could strengthen the

cover letter. I suggest to appease my fellow *ACS Nano* editors, please, I encourage you to include these in our published papers to our editors and reviewers(s) to the sources and topics of the basic discoveries presented are built.

In a perfect world, the authors and editors could discuss the manuscript over coffee to be sure the novelty and significance of the work are appreciated.



Jason H. Hafner
Associate Editor

www.acsnano.org

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10.1021/nn100907a

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Triage Rejection and Review

1. Outside the scope of the journal
2. Lack of generality requiring other specialty journals
3. Minor variation of published work
4. Marginal improvement over existing methodology
5. Lack of necessary in vivo data for certain formulations (e.g., claiming drug targeting without in vivo data)
6. Presentation of only preliminary data
7. Promotion of a specific product

Prescreening ensures that only those manuscripts that we believe have potential to be published in our pages reach the referees.

Buriak 2010, Rejecting without Review The Whys, the Hows

Rejecting without Review: The Whys, the Hows

With every issue of *ACS Nano*, I revel in the diversity and quality of publications that represent the excitement of nanoscience; this is exactly where I want to be scientifically, at the crossroads of seemingly all research disciplines. Each issue always contains surprises, intrigue, and eye-opening vistas that are connected only by a length scale and a desire to build upon the properties of materials that are neither molecules, nor bulk. Behind every table of contents, of course, is a submission and editorial process that must screen hundreds of manuscripts each month, assist in constructively improving them, and ultimately publish those that shine through the review process. Owing to the very simple ratios of the number of submissions, the number of papers we can publish in any given (monthly) issue, and availability of reviewers, a large fraction of papers submitted to *ACS Nano* must be rejected without review. We receive far more submissions than we could ever publish, and thus it is a necessity. To be on the receiving end of a reject-without-review letter, however, is far less pleasant than the simple explanation about ratios and numbers would suggest. It seems like nasty business when it comes down to the heart of the matter because the basic premise of peer review—a fair and careful analysis of one's work—appears to be bypassed. I would argue, however, that the integrity and constructiveness of the peer review system is kept intact by this process, because prescreening ensures that only those manuscripts that we believe have potential to be published in our pages reach the referees; overloading an already busy audience of reviewers would lead to less time spent carefully and properly analyzing the papers they receive. This would lead to greater overall dissatisfaction, longer review times, highly annoyed authors and reviewers, and ultimately, lower quality publications. No one wants that. Rejecting without review also has positive aspects, including lessening of the chances for a manuscript to dwell unproductively in an unsuccessful cycle of peer review. It also has a negative feature of which we are fully cognizant: Many interesting papers will inevitably be overlooked, but I will attempt to address this problem, at least in part.

Prescreening ensures that only those manuscripts that we believe have potential to be published in our pages reach the referees.

At *ACS Nano* each paper is carefully read by *at least* two pairs of eyes, which is a combination of associate editors and our editor-in-chief. While in no way can I summarize the thought process for each person involved, I will try to give a sense of what makes a successful submission:

(i) The most important aspect, the (nano)science: We are looking for that almost indescribable "wow" factor—a subject or theme that sheds light on and gives insight into a perplexing problem or fundamental issue, for example, a new way of looking at a material (such as a new set of properties or mechanistic understanding) that may be the result of an interdisciplinary collaboration drawing expertise from a variety of areas, or an intriguing new application based on nanomaterials. The nanomaterials and their properties must be the star of the show. If the nanoscience is not front and center, then the article may not be of sufficiently broad interest to *ACS Nano* readers. If we believe that your manuscript is appropriate in scope for another ACS journal, we will make the recommendation. I do not make such a recommendation frivolously.

www.acsnano.org

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10.1021/nn1022318

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Manuscript Revision

In Response

Prepare a detailed Response Letter

Copy-paste each reviewer comment, and type your response below it.

State specifically which changes you made to the manuscript.

Include page/line numbers.

No general statements like “Comment accepted, and Discussion changed accordingly.”

Provide a scientific response to comments to accept,

..... or a convincing, solid and polite rebuttal when you feel the reviewer was wrong.

Write in such a manner, that your response can be forwarded to the reviewer without prior editing.

Do not do yourself a disfavor, but cherish your work.

You spent weeks and months in the lab or the library to do the research

It took you weeks to write the manuscript.

Reviewer 1

This manuscript provides important information about the self-assembly and self-replication of nanoscale rabbits. I have a number of concerns, however, related to the characterization of their fur.

1) The authors state that the fur appears brown, but the UV-Vis spectra suggest that it is usually white. Please explain.

We thank the referee for noticing this oversight. The referee is correct, in that the nanorabbits are white in the winter, and brown in the summer. We did not label the effects of the seasons on the UV-Vis spectra of the nanorabbits, and thus we have added these labels to the revised manuscript on page 6. This clarification does not change the conclusions of the work because the color of the fur has no effect on their dual-auricle morphology.

Referees are the heart of the peer review process. They are experts in their fields who provide independent evaluations of a manuscript, and they are anonymous to the authors. In their written reviews, referees offer comments on the technical content of a manuscript, opinions about its significance, novelty, and potential impact, and a recommendation as to whether or not the manuscript should be considered for publication.^{1,2} At *ACS Nano*, we greatly value our referees—their expertise, their input, their time, and their dedication. They are our authors, our readers, and our editorial advisors, and they are an integral part of our journal's extended family. What then does one do, as an author on the receiving end of an anonymous peer review, when one does not agree with the comments of the referees?

As authors, we have all been there. Reviews that are returned to us sometimes offer conflicting opinions, or there are inaccurate or inappropriate comments, or the content of the reviews indicates that the reviewers “just didn't get it”. As editors, we do our best

to arrive at a decision on a manuscript based on the aggregate of available feedback rather than on singular or anomalous comments, but we cannot change the comments of the reviewers, so their feedback reaches the authors unfiltered. How should authors respond to such reviews?

As part of a revised manuscript, authors are expected to address each and every referee comment explicitly. This reply is fairly simple when an author agrees with a comment and has made the suggested change to the manuscript. But what about those other comments with which we disagree? What is appropriate? There are a number of questions that an author should ask before getting upset with a reviewer who “doesn't get it”:

(i) **Were we, the authors, clear when making the critical point that the reviewer did not understand?** This point requires a good hard look at one's own paper. We notice that much of the time, a reviewer's “misunderstanding” actually points to a lack of clarity in the manuscript that arises from inexact language or overly convoluted arguments. Before getting angry with the reviewer, please consider the origins of the misunderstanding. It is typically best to clarify the manuscript to prevent future readers from having the same confusion (*vide infra*).

(ii) **Could the reviewer actually be correct, but in a way that we, the authors, had not considered?** Again, we suggest taking a deep breath and giving the reviewer the benefit of the doubt. Was there another aspect that had not been considered? Discuss the possibility with co-authors and others to work through it. Like the point above, it is better that these new perspectives be considered and incorporated now than to have future readers arrive at the same conclusions as the reviewer.

(iii) **Is the reviewer wrong?** After having *patiently* gone through (i) and (ii), it can certainly be the case that the reviewer is wrong. One possible reason is the type of problem mentioned in part (i) (above), so we suggest the following. In a few lines, in professional and polite language, state that you believe that there is a misunderstanding, and clarify the manuscript. Briefly but succinctly write what you believe to be the situation, and assist the reviewer (and the editors) in understanding your point. Once you have completed this effort, have a look back at your manuscript, and think about how the reviewer could have arrived at their conclusions. Is there something you can change or add in order to prevent future readers from coming to the same conclusions as the reviewer?

Authors have the freedom to choose any appropriate format for the letter that details their responses to the reviewers' comments. However, we believe that a straightforward and clear

What then does one do, as an author on the receiving end of anonymous peer review, when one does not agree with the comments of the referees?

Published online May 22, 2012
10.1021/nr3019046

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Manuscript Revision

Reply to Reviewer # 1's comments

Point 1.1: *The work claims recurrently cell uptake of TPL whereas it is unclear if the term "uptake" is used here to refer to "accumulation" or "intracellular uptake". If the term is used to refer to "accumulation", it would be helpful for this to be clearly defined in the text.*

We agree with the reviewer's point. As the reviewer commented, flow cytometry and fluorescent microscopy techniques used in this study does not allow the distinction of surface bound and internalized fraction of liposomes. Thus, to clarify the meaning, we corrected the word "uptake" with "accumulation" in the revised manuscript **as follows**.

Abstract section

After incubating with TPL for 9 h, cellular accumulation efficiency into A375 human melanoma cells, which express integrin $\alpha\beta3$ at high density, was high ($98.5\% \pm 0.5\%$ of cells), whereas that in KB cells, which express integrin at a very low density, was much lower ($35.1\% \pm 4.5\%$). (revised manuscript page 2, lines 7- 10).

Materials and method section

2.6. Accumulation in tumor cells

Cellular accumulation of liposomes containing rhodamine-DHPE was observed using fluorescent microscopy and flow cytometry. (revised manuscript page 8, lines 1- 3).

Result section

3.3. Enhanced cellular accumulation of TPL

Consistent with their relative surface expression levels of integrin $\alpha\beta3$, KB

Highlight all changes in the text

Previous work in mice with genital HSV-2 infection has demonstrated that RNA interference (RNAi) - using targeted short interfering RNA (siRNA) molecules - can down-regulate proteins involved in HSV-2 infection and propagation [12, 13]. Specific proteins down-regulated include UL29.2 (a viral DNA binding protein affecting virus replication) and nectin-1 (a host cell receptor protein integral to initial virus binding and subsequent spread) [12, 13]. However, siRNA molecules are difficult to deliver intracellularly, and their effects can be short in duration. In previous studies, delivering siRNA against nectin-1, UL29.2, or both was more effective when siRNA was complexed with a transfection reagent such as Oligofectamine™ (OLF, lipoplexes), or conjugated to cholesterol [12, 13]. Yet even in the best cases, these studies extended survival against a lethal dose of HSV-2 from 9 days (untreated mice) to 14 days (with optimal lipoplex or cholesterol-conjugated treatment). Further, many vectors that promote intracellular delivery of siRNA - particularly those that are based on cationic lipids - are toxic to the sensitive mucosal epithelium of the female reproductive tract, and have been found to induce inflammation at high concentration [13, 18]. **In this work we synthesized, characterized, and delivered intravaginally formulations of siRNA (against virus and host targets), encapsulated in poly(lactic co-glycolic acid) (PLGA) NPs to inhibit HSV-2 infection. To our knowledge, this is the first study that uses PLGA NPs [18], which we have previously shown to be safe for intravaginal administration, for delivery of siRNAs directed against HSV-2 host and viral targets and the first to evaluate survival after treatment in an HSV-2 murine model.**

We previously demonstrated that intravaginal administration of PLGA NPs loaded with siRNA against EGFP provide RNAi throughout the mouse reproductive tract [18]. Here, we test the hypothesis that vaginal delivery of siRNA-containing NPs, specifically targeting genes necessary for HSV-2 infection and progression, extends the survival of mice administered a lethal dose of HSV-2 beyond that seen with other siRNA delivery vehicles.

Ethics Issues in Publishing

Scientific misconduct

Falsification of results

Publication misconduct

Plagiarism

Different forms / severities

The paper must be original to the authors

Duplicate publication

Duplicate submission

Appropriate acknowledgement of prior research and researchers

Appropriate identification of all co-authors

Conflict of interest

These are just not worth it!

Recycling Is Not Always Good: The Dangers of Self-Plagiarism

Plagiarism is an act of academic fraud that implies "taking over the ideas, methods, or written words of another, without acknowledgment and with the intention that they be taken as the work of the deceiver."¹ If one "borrows" one's own ideas from one's own publication(s) without attribution, is the deception still academic fraud? Yes, it is, because it is an intentional attempt to deceive a reader by implying that new information is being presented. Intentional deception is fraud, one of the two definitions of fraud in the Oxford English Dictionary is:

*"a person or thing intended to deceive others, typically by unjustifiably claiming or being credited with accomplishments or qualities"*²

As a result, recycling old data as new material (the accomplishment or quality), when it is not so, is tantamount to attempting to deceive one's audience.³

There are a number of serious problems that arise from self-plagiarism that can affect both the scientific community as a whole and individual researchers.

Thankfully, much thoughtful consideration has been given to defining, describing, recognizing, and avoiding self-plagiarism.^{4,5} A number of sources are given here, but an excellent place to start to explore the concept is with a detailed piece by Miguel Roig on the Office of Research Integrity's Web site.⁶ According to this helpful and scientifically oriented summary of questionable practices in writing, there are a number of serious problems that arise from self-plagiarism that can affect both the scientific community as a whole and individual researchers. The motivation for self-plagiarism is simple and relates back to the overused saying "publish or perish."^{7,8} The conflict of interest inherent in a highly competitive system that "counts" papers when promotions and grant proposals are being evaluated can lead to dangerous temptation. Self-plagiarism is problematic for a number of reasons as it:

- i) overworks an already overloaded peer-review and editorial system. When one considers the time taken to carry out careful, thorough, and thoughtful reviews, the handling of the manuscript by one or more journals, and the reading of the manuscript by future readers, recycled data in a self-plagiarized paper can be seen to dilute the quality of science across the board. Time wasted on a self-plagiarized paper is, simply, time wasted, and in research, no one has the luxury of excess time. This aspect bothers us a great deal. As a side note, to date, the majority of cases of self-plagiarism have been caught by referees, but we are adding new tools in our editorial offices to check submissions prior to wasting referees' time.
- ii) generates a poor reputation for one's self and one's group. When encountering a case of self-plagiarism, one cannot help but feel slighted, angry, and frustrated. We wonder, "Did this person really think, in this day and age with all electronic access and tools, that no one would notice?" and, "if they recycle data/text, how can I trust anything this group publishes?" The negative impact on past, current, and future students, colleagues, and one's institution cannot be underestimated.
- iii) may result in copyright infringement. Without explicit permission from the publisher for reuse of material, republication of text/figures could be an infringement of copyright. It is better to be forthright and to ask the editor beforehand to avoid problems later. Previously published data can be reused with permission if (and only if) properly quoted and cited.

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VOL. 6 ■ NO. 1 ■ 1-4 ■ 2012

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Publication ethics – How it can end

"I deeply regret the inconvenience and agony caused to you by my mistake and request and beg for your pardon for the same. As such I am facing lot many difficulties in my personal life and request you not to initiate any further action against me.

I would like to request you that all the correspondence regarding my publications may please be sent to me directly so that I can reply them immediately. To avoid any further controversies, **I have decided not to publish any of my work in future."**

A "pharma" author
December 2, 2008

Retraction

doi:10.1016/j.sigpro.2005.07.019  Cite or Link Using DOI
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RETRACTED: Matching pursuit-based approach for ultrasonic flaw detection

N. Ruiz-Reyes^a,  , P. Vera-Candeas^a,  , J. Curpián-Alonso^a,  , J.C. Cuevas-Martínez^a,   and F. López-Ferreras^b,  

^aElectronics and Telecommunication Engineering Department, University of Jaén, Linares, Jaén, Spain

^bSignal Theory and Communications Department, University of Alcalá, Alcalá, Madrid, Spain

Available online 24 August 2005.

This article has been retracted at the request of the Editor-in-Chief and Publisher. Please see <http://www.elsevier.com/locate/withdrawalpolicy>.

Reason: This article is virtually identical to the previously published article: “New matching pursuit-based algorithm for SNR improvement in ultrasonic NDT” , *Independent Nondestructive Testing and Evaluation International*, volume 38 (2005) 453 – 458 authored by N. Ruiz-Reyes, P. Vera-Candeas, J. Curpián-Alonso, R. Mata-Campos and J.C. Cuevas-Martínez.

 Corresponding author. Tel.: +34 953648554; fax: +34 953648508.

Signal Processing
Volume 86, Issue 5, May 2006, Pages 962-970

The article of which the authors committed plagiarism: It won't be removed from the journals. Everybody who downloads it will see the reason of retraction...

the echoes issuing from the flaws to be detected. Therefore, it cannot be cancelled by classical time averaging or matched band-pass filtering techniques.

Many signal processing techniques have been utilized for signal-to-noise ratio (SNR) improvement in ultrasonic NDT of highly scattering materials. The most popular one is the split spectrum processing (SSP) [1–3], because it makes possible real-time ultrasonic test for industrial applications, providing quite good results. Alternatively to SSP, wavelet transform (WT) based denoising/detection methods have been proposed during recent years [4–8], yielding usually to higher improvements of SNR at the expense of an increase in complexity. Adaptive time-frequency analysis by basis pursuit (BP) [9,10] is a recent technique for decomposing a signal into an optimal superposition of elements in an over-complete waveform dictionary. This technique and some other related techniques have been successfully applied to denoising ultrasonic signals contaminated with grain noise in highly scattering materials [11,12], as an alternative to the WT technique, the computational cost of the BP algorithm being the main drawback.

In this paper, we propose a novel matching pursuit-based signal processing method for improving SNR in ultrasonic NDT of highly scattering materials, such as steel and composites. Matching pursuit is used instead of BP to reduce the complexity. Despite its iterative nature, the method is fast enough to be real-time implemented. The performance of the proposed method has been evaluated using both computer simulation and experimental results, even when the input SNR (SNR_{in}) is lower than 0dB (the level of echoes that the microstructures is above the level of the echoes).

2. Matching pursuit

Matching pursuit was introduced by Mallat and Zhang [13]. Let us suppose an approximation of the ultrasonic backscattered signals $x[n]$ as a linear expansion in terms of functions $g_i[n]$ chosen from an over-complete dictionary. Let H be a Hilbert

space. We define the over-complete dictionary as a family $D = \{g_i; i = 0, 1, \dots, L\}$ of vectors in H , such as $\|g_i\| = 1$.

The problem of choosing functions $g_i[n]$ that best approximate the analysed signal $x[n]$ is computationally very complex. Matching pursuit is an iterative algorithm that offers sub-optimal solutions for decomposing signals in terms of expansion functions chosen from a dictionary, where l^2 norm is used as the approximation metric because of its mathematical convenience. When a well-designed dictionary is used in matching pursuit, the non-linear nature of the algorithm leads to compact adaptive signal models.

In each step of the iterative procedure, vector $g_i[n]$ which gives the largest inner product with the analysed signal is chosen. The contribution of this vector is then subtracted from the signal and the process is repeated on the residual. At the m th iteration the residue is

$$r^m[n] = \begin{cases} x[n], & m = 0, \\ x^{m-1}[n] + \alpha_{k(m)} g_{k(m)}[n], & m \neq 0, \end{cases} \quad (1)$$

where $\alpha_{k(m)}$ is the weight associated to optimum atom $g_{k(m)}[n]$ at the m th iteration.

The weight α_k^m associated to each atom $g_k[n] \in D$ at the m th iteration is introduced to compute all the inner products with the residual $r^m[n]$:

$$\alpha_k^m = \frac{\langle r^m[n], g_k[n] \rangle}{\langle g_k[n], g_k[n] \rangle} = \frac{\langle r^m[n], g_k[n] \rangle}{\langle g_k[n], g_k[n] \rangle} = \langle r^m[n], g_k[n] \rangle. \quad (2)$$

The optimum atom $g_{k(m)}[n]$ (and its weight $\alpha_{k(m)}$) at the m th iteration are obtained as follows:

$$g_{k(m)}[n] = \underset{g_k[n] \in D}{\operatorname{argmin}} \|\alpha_k^m\|^2 \\ = \underset{g_k[n] \in D}{\operatorname{argmax}} |\alpha_k^m|^2 = \underset{g_k[n] \in D}{\operatorname{argmax}} |\langle r^m[n], g_k[n] \rangle|. \quad (3)$$

The computation of correlations $\langle r^m[n], g_k[n] \rangle$ for all vectors $g_k[n]$ at each iteration implies a high computational effort, which can be substantially reduced using an updating procedure derived from Eq. (1). The correlation updating procedure [13] is performed as follows:

$$\langle r^{m+1}[n], g_k[n] \rangle = \langle r^m[n], g_k[n] \rangle \\ - \alpha_{k(m)} \langle g_{k(m)}[n], g_k[n] \rangle. \quad (4)$$



Research Proposals

National Institute of Health (NIH)

Types of Grant Programs (RO1, R03, R13, R15, R21, R34, R41/R42, R43/R44, R56, U01, K99/R00, P01, P20, P30, P50, R24, R25, X01)

NIH Research Project Grant Program (R01)

- Used to support a discrete, specified, circumscribed research project
- NIH's most commonly used grant program
- No specific dollar limit unless specified in FOA
- Advance permission required for \$500K or more (direct costs) in any year
- Generally awarded for 3 -5 years

NIH Exploratory/Developmental Research Grant Award (R21)

- Encourages new, exploratory and developmental research projects by providing support for the early stages of project development. Sometimes used for pilot and feasibility studies.
- Limited to up to two years of funding
- Combined budget for direct costs for the two year project period usually may not exceed \$275,000.
- No preliminary data is generally required

Small Business Technology Transfer (STTR) (R41/R42)

- Intended to stimulate scientific and technological innovation through cooperative research/research and development (R/R&D) carried out between small business concerns (SBCs) and research institutions (RIs)

https://grants.nih.gov/grants/funding/funding_program.htm



Understanding Types of Grants and Funding

The NIDCD funds research through a variety of award mechanisms.

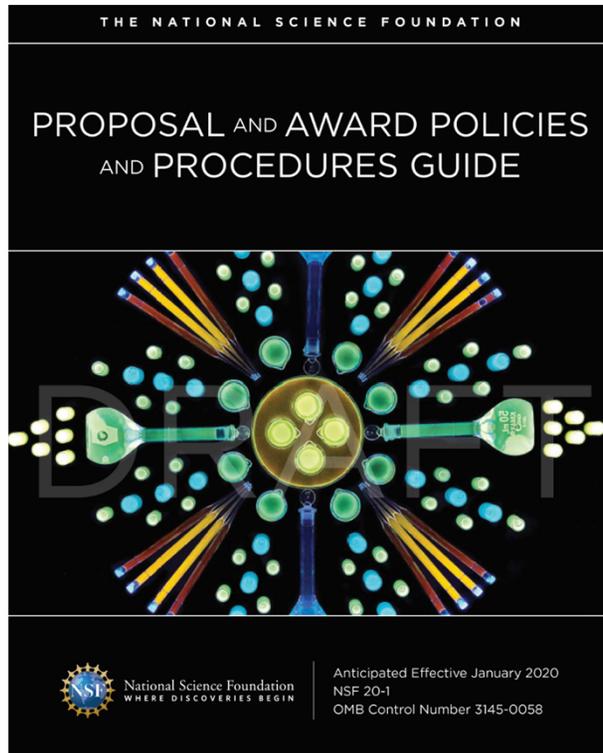
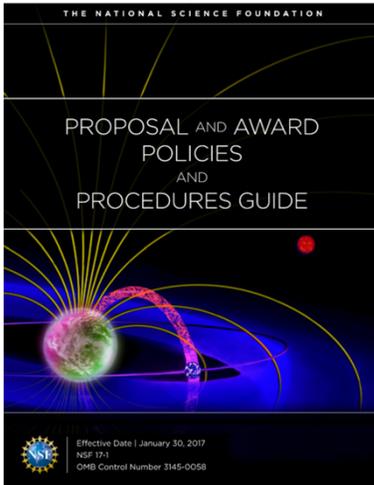
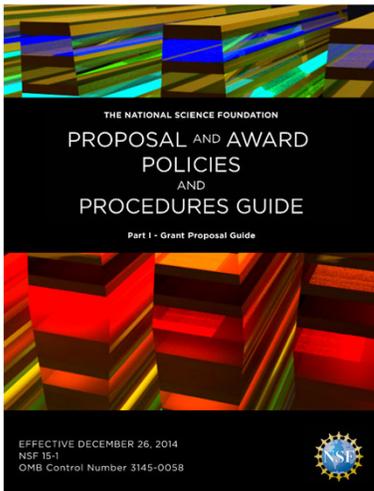
- Research grants (R series)
These grants may be awarded to individuals at universities, medical and other health professional schools, colleges, hospitals, research institutes, for-profit organizations, and government institutions.
- Research training and career development (NRSA, K series, and more)
These include individual fellowships, institutional awards, career development awards, and other opportunities.
- Small business grants (SBIR/STTR)
- Clinical research center grants (P50)
- Conference grants
- Administrative supplements
- Funding for drug development
- Loan repayment programs (NIH)

<https://www.nidcd.nih.gov/funding/types>

National Science Foundation



Chapter II - Proposal Preparation Instructions





National Science Foundation
WHERE DISCOVERIES BEGIN

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Proposal & Award Policies & Procedures Guide

NSF 20-1 June 1, 2020
Chapter II - Proposal Preparation Instructions

Each proposing organization that is new to NSF or has not had an active NSF assistance award within the previous five years should be prepared to submit basic organization and management information and certifications, when requested, to the applicable award-making division within the Office of Budget, Finance & Award Management (BFA). The requisite information is described in the [NSF Prospective New Awardees Guide](#). The information contained in this Guide will assist the organization in preparing documents which NSF requires to conduct administrative and financial reviews of the organization. This Guide also serves as a means of highlighting the accountability requirements associated with Federal awards.

Proposers should be aware of core strategies that are essential to the fulfillment of NSF's mission, as articulated in [Building the Future: Investing in Discovery and Innovation - NSF Strategic Plan for Fiscal Years \(FY\) 2018 - 2022](#). These strategies are integrated in the program planning and implementation process, of which proposal review is one part. NSF's mission is particularly well-implemented through the integration of research and education and broadening participation in NSF programs, projects, and activities.

One of the strategic objectives in support of NSF's mission is to foster integration of research and education through the programs, projects, and activities it supports at NSF grantee organizations. These organizations recruit, train, and prepare a diverse science, technology, engineering, and mathematics (STEM) workforce to advance the frontiers of science and participate in the U.S. technology-based economy. NSF's contribution to the national innovation ecosystem is to provide cutting-edge research under the guidance of the Nation's most creative scientists and engineers. NSF also supports development of a strong STEM workforce by investing in building the knowledge that informs improvements in STEM teaching and learning.

NSF will not tolerate research misconduct in proposing or performing research funded by NSF, reviewing research proposals submitted to NSF, or in reporting research results funded by NSF. For additional information, see [Chapters I.D.3, IX.B, and XII.C](#).

NSF's mission calls for the broadening of opportunities and expanding participation of groups, organizations, and geographic regions that are underrepresented in STEM disciplines, which is essential to the health and vitality of science and engineering. NSF is committed to this principle of diversity and deems it central to the programs, projects, and activities it considers and supports.

A. CONFORMANCE WITH INSTRUCTIONS FOR PROPOSAL PREPARATION

It is important that all proposals conform to the proposal preparation instructions contained in Part I of the PAPPG or the NSF [Grants.gov Application Guide](#). Conformance is required and will be strictly enforced unless an authorization to deviate from standard proposal preparation requirements has been approved. NSF will not accept or will return without review proposals that are not consistent with these instructions. See [Chapter IV.B](#) for additional information. NSF authorization to deviate from these instructions must be received prior to proposal submission. Deviations may be authorized in one of two ways:

- through specification of different requirements in an NSF program solicitation; or
- by the written approval of the cognizant NSF Assistant Director/Office Head or designee. These approvals to deviate from NSF proposal preparation instructions may cover a particular program or programs or, in rare instances, an individual deviation for a particular proposal.

Proposers may deviate from these instructions only to the extent authorized. Proposals must include an authorization to deviate from standard NSF proposal preparation instructions in one of the following ways, as appropriate: (a) by identifying the solicitation number that authorized the deviation in the appropriate block on the Cover Sheet; or (b) for individual deviations, by identifying the name, date and title of the NSF official authorizing the deviation.

B. FORMAT OF THE PROPOSAL

Prior to submission, it is strongly recommended that proposers conduct an administrative review to ensure that proposals comply with the guidelines established in Part I of the PAPPG or the NSF [Grants.gov Application Guide](#). The Proposal Preparation Checklist ([Exhibit II-1](#)) may be used to assist in this review. The checklist is not intended to be an all-inclusive repetition of the required proposal contents and associated proposal preparation guidelines. It is, however, meant to highlight certain critical items so they will not be overlooked when the proposal is prepared.

During completion of the proposal Cover Sheet (See [Chapter II.C.2.a](#)), the PI will be prompted to select the applicable response that describes the nature and type of proposal being developed:

Significant Changes and Clarifications

PAPPG - Introduction

A. About the NSF

B. Foreword

C. Acronym List

D. Definitions

E. NSF Organizations

Table of Contents

Part I: Proposal Preparation and Submission Guidelines

I. Pre-Submission Information

II. Proposal Preparation Instructions

III. NSF Proposal Processing and Review

IV. Non-Award Decisions and Transactions

V. Renewal Proposals

Part II: Award, Administration and Monitoring of Grants and Cooperative Agreements

VI. NSF Awards

VII. Grant Administration

VIII. Financial Requirements and Payments

IX. Grantee Standards

X. Allowability of Costs

XI. Other Post Award Requirements and Considerations

XII. Grant Administration Disputes and Misconduct

Subject Index

Privacy Act and Public Burden Statements

Proposal Page Limits

| Section of Application | Activity Codes | Page Limits * |
|---|--|-------------------------|
| Project Summary/Abstract | For all Activity Codes | 30 lines of text |
| Project Narrative | For all Activity Codes excluding C06,UC6 and G20. | three sentences |
| Introduction to Resubmission and Revision Applications | For all Activity Codes (including each applicable component of a multi-component application) | 1 |
| Specific Aims | For all Activity Codes that use an application form with the Specific Aims section (including each component of a multi-component application) | 1 |
| Research Strategy | For Activity Code DP1 | 5 |
| | For Activity Codes R03 , R13 , U13 , R13 , U13 , R16, R21 , R35 , R36 , R41 , R43 , SC2 , SC3 , X01¹ , X02¹ , R50 , UT1 | 6 |
| | For Activity Code DP2 | 10 |
| | For Activity Codes DP3 , DP5 , G08 , G11 , G13 , RC2 , RC4 , RF1 , R01 , R15 , R18 , R21 / R33 , R24 , R28 , R33 , R34 , R42 , R44 , R61 , R61 / R33 , RL1 , SB1 , SC1 , SI2 , UB1 , UC2 , UH2 , UH3 , UG1 , UC4 , UF1 , UG3 / UH3 , UH2 / UH3 , U01 , U18 , U24 , U2C , U34 , U42 , U44 , UT2 , X01¹ , X02¹ | 12 |
| | For all other Activity Codes | Follow FOA instructions |
| Commercialization Plan | For Activity Codes R42 , R44 , SB1 , UT2 , U44 , UB1 (Attachment 7 on SBIR/STTR Information form) | 12 |
| Biographical Sketch | For all Activity Codes (including DP1 and DP2 which previously had special page limits) | 5 |

<https://grants.nih.gov/grants/how-to-apply-application-guide/format-and-write/page-limits.htm>

Goals of Shortened Page Limits

Reduces burden / maximize reviewer time

Focuses on the essentials of the science

Emphasizes impact

Avoids information overload

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ABOUT GRANTS

- Grants Process Overview
- Get Started +
- How to Apply +
- Application Referral and Review +
- Pre-Award and Post-Award Processes +
- Forms Library
- Information For +

Page Limits

Follow the page limits specified below for the attachments in your grant application, unless otherwise specified in the funding opportunity announcement (FOA) or related NIH Guide notice. FOA instructions always supersede general application guide instructions and NIH Guide notice information supersedes both the FOA and the application guide. If no page limit is listed in the table below, in Section IV of the FOA under Page Limitations, or in a related notice, you can assume the attachment does not have a limit.

When preparing an administrative supplement request, follow the appropriate page limits for the activity code of parent award.

Standard page limits are organized by Activity Code

- Fellowship (F) Applications
- Individual Career Development Award (K, excluding K12) Applications
- Institutional Training (T), International Training (D43, D71, U2R), Institutional Career Awards (K12, KL2), and Research Education (R25, UE5, R38, DP7) Applications
- S10, R01, U01, R03, R21, and all other applications

<https://grants.nih.gov/grants/how-to-apply-application-guide/format-and-write/page-limits.htm>

The Main Contents of a Proposal

Specific Aims

Research Strategy

Impact addresses: Probability of whether the research will exert a sustained, powerful influence on the research field.

Significance addresses: Does the project address an important problem or a critical barrier to progress in the field?

If the aims are achieved, how will scientific knowledge, technical capability, and/or clinical practice be improved?

Investigator

Environment

Reviewers Benefit from Shorter Applications

• Old Practice

- Too much focus on how to “do” the research.
- Significant mentoring on how to revise.
- Long, detailed application/too much to read.

• New Focus

- Impact: Is research worth doing?
- Clear signal via criteria whether to resubmit.
- Streamlined applications (easier to validate, less to read).

Approach

- Are the overall strategy, methodology, and analyses well-reasoned and appropriate to accomplish **the specific aims** of the project?
- Are potential problems, **alternative strategies**, and benchmarks for success presented?
- If the project is in the early stages of development, will the strategy establish **feasibility** and will particularly risky aspects be managed?

If the Project Involves Clinical Research:

Are plans justified for:

- protection of human subjects
- inclusion of minorities, both sexes/genders, and children

Investigators

- **Personal Statement:**
 - Why their experience and qualifications make them particularly well-suited for their roles in the project
- **Publications:**
 - Recommended: no more than 15---up to five of the *best*; up to five of the *most relevant* to the proposed research; up to five of the *most recent*
- If *Early Stage Investigators or New Investigators*, do they have appropriate experience and training?
- If *Established*, have they demonstrated ongoing record of accomplishments that have advanced their field(s)?



Innovation

- Does application challenge/seek to shift **current research or clinical practice paradigms** by utilizing novel theoretical concepts, approaches or methodologies, instrumentation, or interventions?
- Concepts, approaches or methodologies, instrumentation, or interventions **novel to one field of research** or novel in a broad sense?
- Refinement, improvement, or new application of theoretical concepts, approaches or methodologies, instrumentation, or interventions proposed?
- *Not all applications need to be innovative !*



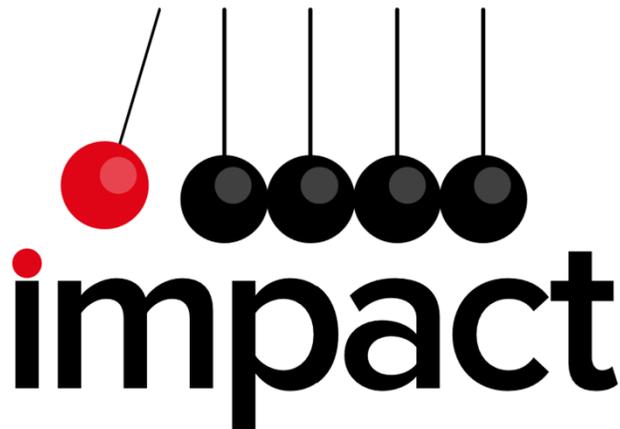
What is the Difference between Impact and Significance ?

Impact addresses:

- Probability of whether the research will exert a sustained, powerful influence on the research field.

Significance addresses:

- Does the project address an important problem or a critical barrier to progress in the field?
- If the aims are achieved, how will scientific knowledge, technical capability, and/or clinical practice be improved?



3

SIGNIFICANCE SECTION

Use these exact words in your proposal!

- ⊙ Explain **importance of the problem** or **critical barrier to progress** in the field that the proposed project addresses
- ⊙ Explain how proposed project will **improve scientific knowledge, technical capability, and/or clinical practice** in one or more broad fields (this is innovation)
- ⊙ Describe **how** the concepts, methods, technologies, treatments, services, or preventative interventions that drive this **field will be changed** if the proposed aims are achieved

Patents



US011000479B2

United States Patent Yoon et al.

(10) Patent No.: US 11,000,479 B2
(45) Date of Patent: May 11, 2021

(54) INJECTABLE LONG-ACTING NALTREXONE MICROPARTICLE COMPOSITIONS

(71) Applicants: **Chong Kun Dang Pharmaceutical Corp.**, Seoul (KR); **Purdue Research Foundation**, West Lafayette, IN (US)

(72) Inventors: **Gwangheum Yoon**, West Lafayette, IN (US); **Bong Kwan Soh**, West Lafayette, IN (US); **Andrew David Otte**, West Lafayette, IN (US); **Kinam Park**, West Lafayette, IN (US)

(73) Assignees: **Chong Kun Dang Pharmaceutical Corp.**, Seoul (KR); **Purdue Research Foundation**, West Lafayette, IN (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: 16/653,707

(22) Filed: Oct. 15, 2019

(65) **Prior Publication Data**
US 2020/0113835 A1 Apr. 16, 2020

Related U.S. Application Data

(60) Provisional application No. 62/745,805, filed on Oct. 15, 2018.

(51) **Int. Cl.**
A61K 9/16 (2006.01)
A61K 9/00 (2006.01)
A61K 31/485 (2006.01)

(52) **U.S. Cl.**
CPC **A61K 9/1647** (2013.01); **A61K 9/0019** (2013.01); **A61K 9/1611** (2013.01);
(Continued)

(58) **Field of Classification Search**
CPC .. A61K 9/1647; A61K 9/0019; A61K 9/1694; A61K 9/1652; A61K 9/1623;
(Continued)

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(Continued)

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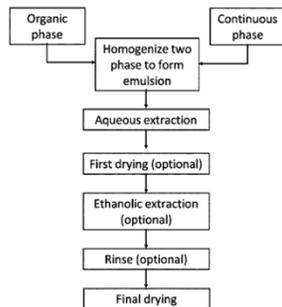
Dinarvand et al. Preparation of Biodegradable Microspheres and Matrix Devices Containing Naltrexone, AAPS PharmSciTech, 4(3), Article 34, pp. 1-10 (Year 2003).
(Continued)

Primary Examiner — Carlos A Azpuru
(74) *Attorney, Agent, or Firm* — Fish & Richardson P.C.

(57) ABSTRACT

The present disclosure relates to naltrexone sustained release microparticle delivery systems for the treatment of diseases ameliorated by naltrexone. The injectable microparticle delivery system includes naltrexone encapsulated in biodegradable microparticles administered in a pharmaceutically acceptable vehicle.

17 Claims, 5 Drawing Sheets



Intrinsic evidence & Extrinsic evidence

What is claimed is

19

US 11,000,479 B2

20

TABLE 10

| Formulation summary for formulations characterized in vivo | | | | | | | |
|--|---|--|------------------------------|--------------------|----------------------|--------|--|
| Formulation (F) | PLGA Concentration in DCM or EA (% w/w) | Naltrexone Concentration in BA (% w/w) | Organic Phase Solvent System | Dose Level (mg/kg) | Drug Loading (% w/w) | EE (%) | |
| F12-1 | 20.0 | 38.6 | DCM/BA | 76 | 28.1 | 80.7 | |
| F12-2 | 20.0 | 32.1 | DCM/BA | 76 | 21.7 | 58.6 | |
| F12-3 | 20.0 | 38.6 | DCM/BA | 50 | 34.2 | 92.4 | |
| F12-4 | 15.0 | 24.0 | EA/BA | 50 | 28.5 | 77.0 | |
| F12-5 | 20.0 | 39.6 | DCM/BA | 50 | 36.1 | 80.2 | |
| F12-6 | 20.0 | 44.0 | DCM/BA | 50 | 37.8 | 84.0 | |
| F12-7 | 20.0 | 30.0 | DCM/BA | 50 | 27.8 | 79.9 | |

Drug Loading (% w/w) is based on the microparticle weight.

Test Procedures

In Vitro Release of Naltrexone from Test Formulations

The medium, 20 mL of pH 7.4 phosphate buffered saline with 0.05% Tween 20 (Sigma Aldrich, St. Louis, Mo.) and 0.0625% (w/v) sodium ascorbate (Sigma Aldrich, St. Louis, Mo.) and approximately 5 mg of test article were placed in a stoppered 50 mL Erlenmeyer flask and placed in a 37° C. water bath at 100 RPM. Samples were taken at various time points and replaced with fresh release medium. Naltrexone content in buffer was measured via High Performance Liquid Chromatography (HPLC).

Reversed Phase HPLC for the Quantitation of Naltrexone

The HPLC had the following conditions: Mobile Phase: 65:35 methanol:potassium phosphate buffer, pH 6.6; flow rate: 1.0 ml/min; autosampler temperature: room temperature; column temperature: 30° C.; detection: 210 nm (UV); total run time: 7 min; injection volume: 10 µL; column: Zorbax SB-C18 150x4.6 mm, 5 µm; approximate retention time of naltrexone: 4.8 min.

In Vivo Pharmacokinetic Studies

All rat preclinical studies were conducted in Sprague-Dawley rats. Three to five rats per test formulation were injected subcutaneously in the scruff behind the neck or in the scapular region with a dosage of naltrexone ranging from 50 mg/kg to 100 mg/kg in 1 ml of an aqueous-based vehicle, composed of 0.9% sodium chloride, 0.02% Tween 20, and 0.5% sodium carboxymethylcellulose.

During the course of the study, the animals were observed for overt toxicity and any existing test site abnormalities, including redness, swelling, bleeding, discharge, and bruising at the injection site. In addition, body weights were taken and recorded at administration and at the conclusion of the study.

At selected time points, rats were anesthetized and bled (approximately 250 µL) via the tail or submandibular vein. Blood was collected in labeled potassium ethylenediaminetetraacetic acid tubes. The blood was centrifuged for 10 min at 4,000 rpm at 4° C. The plasma fraction was transferred to labeled 1 mL plastic tubes and stored at -80° C. prior to analysis.

What is claimed is:

1. An injectable microparticle formulation comprising a microparticle including naltrexone and poly(lactide-co-glycolide) with a lactide:glycolide ratio of about 85:15, wherein sustained release of naltrexone is longer than 4 weeks and up to 100 days.

2. The microparticle formulation according to claim 1, wherein sustained release of naltrexone is about 8 weeks to about 12 weeks.

3. The microparticle formulation according to claim 1, wherein the naltrexone is in the form of free base, salt, solvate, cocrystal or combinations thereof.

4. The microparticle formulation according to claim 1, wherein the naltrexone is about 20-40% (w/w) of the microparticle.

5. The microparticle formulation according to claim 1, wherein the poly(lactide-co-glycolide) has a number average molecular weight of 50,000 to 150,000 Daltons.

6. The microparticle formulation according to claim 1, wherein the microparticle is administered in a biocompatible vehicle, including an aqueous-based vehicle, an oil-based vehicle or combination thereof.

7. The microparticle formulation according to claim 6, wherein the aqueous based vehicle comprises a tonicity agent such as sodium chloride, a viscosity enhancing agent such as sodium carboxymethylcellulose, a wetting agent such as polysorbate, or combinations thereof.

8. The microparticle formulation according to claim 6, wherein the oil-based vehicle comprises peanut oil, sesame oil, cottonseed oil, or combinations thereof.

9. The microparticle formulation according to claim 1, wherein the microparticles have particle size in the range of 25 to 125 µm.

10. A method for treating or preventing diseases related to opioid abuse or overdoses, alcohol dependence or pain comprising administering an effective amount of the injectable microparticle formulation according to claim 1 to a subject in need of such a treatment or prevention.

11. A method for preparing the injectable microparticle formulation according to claim 1, the method comprising:

(a) mixing a first phase comprising polyvinyl alcohol and a first solvent, and a second phase comprising a biodegradable polymer, naltrexone and a second solvent to prepare a mixture; and

(b) performing an extraction process on the mixture with water or an aqueous solution to obtain microparticles.

12. The method according to claim 11, wherein the first solvent comprises at least one selected from the group consisting of water, dichloromethane, benzyl alcohol, and ethyl acetate.

13. The method according to claim 11, wherein the second solvent comprises at least one selected from the group consisting of dichloromethane, benzyl alcohol, and ethyl acetate.

14. The method according to claim 11, the aqueous solution comprises at least one selected from the group consisting of polyvinyl alcohol, dichloromethane, benzyl alcohol, and ethyl acetate.

Scientific Paper vs. Patent

Patent is not about something NEW.

Patent is about something **UNEXPECTED AND UNPREDICTED.**

Prior art: **Teaching or Teaching away**
Doctrine of Equivalence

The most important part: Claims

Non-infringement & Invalidity

The Person of Ordinary Skill in the Art

Patent Validity and Ground of Invalidity

Patentability

Novelty
Inventive step
Detailed description
Narrow enough claim

Challenging a Patent:

Each word of a claim is important
Examples: “on” vs “in”.
“Consist of” vs “Comprise”

Plaintiff vs. Defendant

Ground of Invalidity

Anticipation
Obviousness
Lack of Written Description
Lack of Enablement

Nanoparticle vs. Picoparticle

Patent Rules Vary in Different Countries

Australian Court Upholds Patents on Human Genes

The Federal Court of Australia rejected an appeal of a ruling that allows companies to patent isolated human genes.
By Molly Sharlach | September 8, 2014

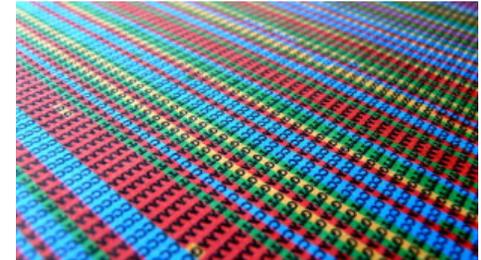
The Federal Court of Australia has upheld an earlier decision in favor of Myriad Genetics, a US-based genetic testing company that holds a patent on naturally occurring mutations in the BRCA1 gene, which can predict a woman's risk for certain types of breast or ovarian cancer. On September 5, the court denied an appeal by the plaintiffs in the lawsuit, the patient advocacy group Cancer Voices Australia and Yvonne D'Arcy, a breast cancer survivor.

In its original February 2013 ruling, **the court argued that the process of isolating a human gene creates an “artificial state of affairs” that may be protected by a patent.** In last week's decision, a different set of judges maintained that the actual isolated DNA is materially distinct from the DNA in the human body: “The chemical and physical makeup of the isolated nucleic acid renders it not only artificial but also different from its natural counterpart.”

In contrast, the US Supreme Court, in a case that also involved Myriad Genetics and the BRCA1 and BRCA2 genes, invalidated patents on the isolation of human genes in June 2013, but held that synthetic genes, including complementary DNA (cDNA), may be patented.

The US decision could lower the cost of genetic testing by increasing competition, a potential benefit to public health. Matthew Rimmer of the Australian National University in Canberra, an intellectual property law expert, told New Scientist that he was disappointed by the Australian judges' failure to consider such implications. “Particularly with controversial patents in the life sciences, there is a need for judges to grapple with the wisdom of the patent system,” he said.

The plaintiffs are considering another appeal, which would bring the case to the nation's top court, the Australian High Court.



Patent Rules Differ from the Nobel Committee

CRISPR Patent Ruling

The US Patent and Trademark Office yesterday (February 28) ruled that the Broad Institute of MIT and Harvard will retain its intellectual property over the use of CRISPR-Cas9 gene editing in eukaryotes. While the University of California, the University of Vienna, and Emmanuel Charpentier (collectively known as the CVC group in legal filings) maintain their original patent over the use of CRISPR-Cas9 to edit genes in vitro and in prokaryotes and some other intellectual property pertaining to the technology, the ruling in this latest proceeding effectively invalidates filings that specifically covered use in eukaryotes, potentially forcing companies that have licensed the technology from the CVC group to negotiate new deals with the Broad or other stakeholders. The ruling is the latest twist in the battle for ownership of a technique being explored commercially for everything from crop improvement to treating genetic diseases.

She adds that even once these ongoing disputes on the foundational CRISPR patents are settled, which she estimates will take years, there will be other aspects of the technology to consider, including approaches to reduce off-target effects, improve efficiency of cleavage, and develop safe scaffolds for use in humans. “The key patent rights for CRISPR-Cas technology for human therapeutics may not [have been] granted yet.”

Charpentier, now at the Max Planck Institute for Infection Biology, and UC Berkeley’s Jennifer Doudna shared the 2020 Nobel Prize in Chemistry for adapting CRISPR to gene editing, and that innovation remains uncontested, notes Cook-Deegan. “**What the Nobel committee decided was a whole different thing than the specific invention of CRISPR in eukaryotes.**”



Jef Akst

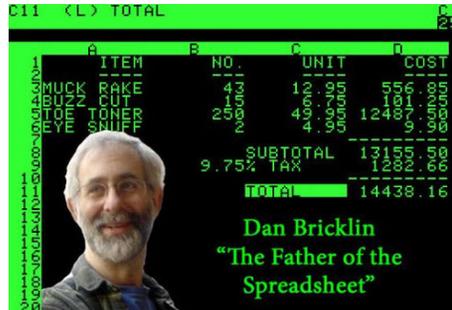
https://www.the-scientist.com/news-opinion/crispr-patent-ruling-favors-broad-institute-69753?utm_campaign=TS_DAILY_NEWSLETTER_2022&utm_medium=email&_hsmi=205544706&_hsenc=p2ANqtz--WhDDGBkJ0RWA3H-rUWWKL0zVfrVX7YL-CtpdLhIYct105I2SvGHKkPBop6fOg6-E1TPxXBX3b5xOGelJnEssDC38hxA&utm_content=205544706&utm_source=hs_email

Patent or Not?

Computer scientists who revolutionized the world



Ken Thompson and Dennis Ritchie. Unix



Tim Berners-Lee.
WWW



Linus Torvalds.
Linux

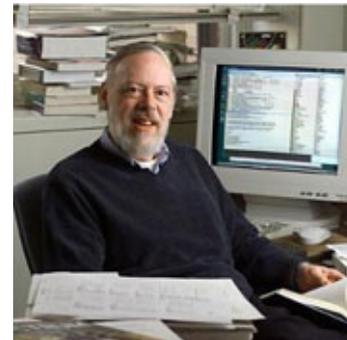
Diverse Ideas!

“Most good programmers do programming not because they expect to get paid or get adulation by the public, but because **it is fun to program**” (Linus Torvalds)



ATTENTION

Both Died in the same year and same month
But Steve was considered as a hero and Dennis was ignored by the world.
Only a handful of Programmers who really know the value of Dennis even know his death



“UNIX is simple.
It just takes a genius to understand its **simplicity.**”
Dennis Ritchie (Creator of Steve Jobs, Linus Torvalds, Bill Gates)

Without Steve there is no iPhone, iPad, Mac, and Apple Computers. But is that a big deal? I mean I am in computer science field and I have't used an apple product in my life and I'm Good enough.

But think!!!

Without Dennis there is no C. If there is No C, then there is no C++ that means No Unix, Windows, Linux, No Crysis warhead and other cool games, No Photoshop, No Firefox, No VLC, No FL Studio, No playstation, No XBOX and the list continues.
90% of the applications in the world are written in C and C++.

Professionals Steal

Professionals Make Better Decisions

**Early Apple
(75-81)**



**Macintosh
(81-85)**

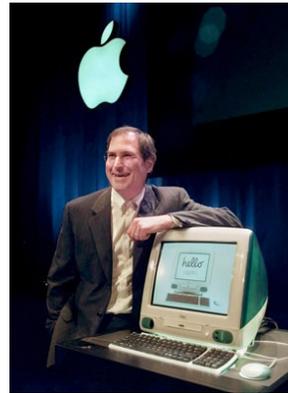
Macintosh 1984



**NeXT
(85-95)**



**Comeback
(1995-97)**

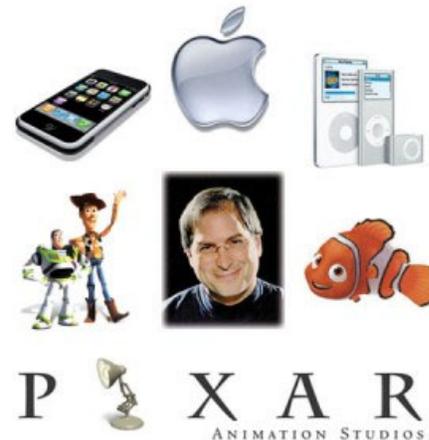


**iMac
(98-01)**



**iPod
(01-06)**

**Pixar
(03-06)**



**iPhone, iPad
(06-11)**



Xerox Alto 1972



IBM PC 1981

**Steve Jobs:
~500 U.S. patents,
>1100 patents globally**

<https://medium.com/predict/moores-law-is-alive-and-well-adc010ea7a63>

Information Technology Silicon Sagas

The Man Who Could Have Been Bill Gates

A new book says Gates got the rewards due Gary Kildall. What's the real story?

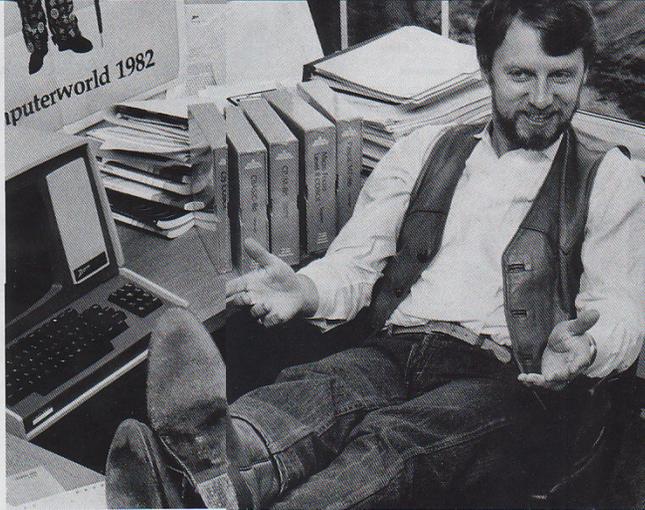
THE SAGA OF THE COMPUTING industry is rich with outside characters and surprising plot turns, but there's one story that has risen over time to mythic proportions. It's the tale of how software pioneer Gary Kildall missed out on the opportunity to supply IBM with the operating system for its first PC—essentially handing the chance of a lifetime, and control of tech's future, to rival Bill Gates and Microsoft Corp. In the process, he may have missed out on becoming the world's richest man.

The legend goes like this: One fateful day in the summer of 1980, three buttoned-down IBMers called on a band of hippie programmers at Digital Research Inc. located in Pacific Grove, Calif. They hoped to discuss licensing DRI's industry-leading operating system, CP/M. Instead, DRI founder Gary Kildall blew off IBM to gallivant around in his airplane, and the frustrated IBMers turned to Gates for their operating system. This anecdote has been told so often that techies need only be reminded of "the day Gary Kildall went flying" to recall the rest. While he's revered for his

technical innovations, many believe Kildall made one of the biggest mistakes in the history of commerce.

But what if that's not what happened? What if IBM and Microsoft deprived Kildall not only of untold riches but also of the credit for a seminal role in the PC revolution? That's the thesis of a chapter about Kildall in *They Made America*, a serious coffee-table history book by renowned author and former newspaper editor Harold Evans. The book, published by Little Brown on Oct. 12, profiles 70 American innovators and is the inspiration for an upcoming PBS series. And while other tech authors have debunked the galvanizing story before, Evans bases his Kildall chapter on a 226-page, never-published memoir written by Kildall just before his death in 1994. Early on, Kildall seemed to represent the best hopes of the nascent computer industry. But by the time he died at age 52, after falling in a tavern, he had become embittered and struggled with alcohol.

They Made America is certain to elicit cries of protest. That's because it attacks the reputations of some of the key players of the early PC era—Gates, IBM, and Tim Paterson, the Seattle programmer



who wrote an operating system, QDOS, based partly on CP/M that became Microsoft's DOS. Evans asserts that Paterson copied parts of CP/M and that IBM tricked Kildall. Because Gates rather than the more innovative Kildall prevailed, according to the book, the world's PC users endured "more than a decade of crashes with incalculable economic cost in lost data and lost opportunities." David G. Lefter, one of Evans' two collaborators, says: "We're trying to set the record straight. Gates didn't invent the PC operating system, and any history that says he did is wrong."

How Kildall Lost Out

On a few fateful days in the early 1980s, PC software pioneer Gary Kildall missed the opportunity to supply the operating system for IBM's first PC—opening the door to rival Bill Gates of Microsoft. Here's how it happened.

AUG. 21, 1980 IBMers visit Bill Gates at Microsoft and lay out their plans for a PC. They discover that he can't supply an operating system. He refers them to Gary Kildall and Digital Research Inc., which has an

operating system called CP/M. **AUG. 22, 1980** IBMers meet at Digital Research in Pacific Grove, Calif., with Dorothy McEwen, Kildall's wife and DRI's business manager. IBMers say that they were un-

able to come to a nondisclosure agreement with McEwen, and they didn't meet Kildall. But Kildall, in his memoirs, says he met with IBMers and reached an oral agreement to license CP/M to them.

AUG. 28, 1980 Gates signs a consulting contract with IBM, agreeing to develop software for the PC. Later he pays \$50,000 for an operating system, QDOS, that was similar to CP/M. Microsoft improves

QDOS, renames it DOS, and licenses it to IBM. **JULY 21, 1981** Kildall confronts IBMers with his claim that DOS infringes on his copyright for CP/M. He agrees not to sue in exchange for IBM's promise to

sell CP/M in addition to the PC. **AUG. 12, 1981** IBM announces its PC, offering CP/M for \$240 and DOS for just \$40. DOS far outsells CP/M and becomes the de facto standard operating software for the PC.

There's no doubt that Kildall was one of the pioneers of the industry. He invented the first operating system for microcomputers in the early 1970s, making it possible for hobbyists and companies to build the first personal computers. Legacies aside, Microsoft's original DOS was based in part on Kildall's CP/M. His insight was that by creating an operating system separate from the hardware, applications could run on computers that were made by different manufacturers. "What really drove Gary was inventing things," says friend and former DRI executive Tom Rolander in an interview with *BusinessWeek*.

Still, Evans' book falls short of clarifying exactly how Kildall lost out to Gates. He relies primarily on Kildall's memoir, his family, and his friends. Evans says he requested an interview with Gates, which he says Microsoft denied. He didn't make contact with IBM or Paterson, but tapped previously published accounts for that side of the story. IBM would not talk to *BusinessWeek* for this article, but former IBMers take issue with Kildall's version of events. Microsoft calls the book "one-

TWO VERSIONS Kildall said he had a deal with IBM. But one IBMer says no

sided and inaccurate," and says the company is proud of the "foundational role" it played in the industry. Paterson denies he stole Kildall's intellectual property. He says he's stunned that the authors failed to get in touch with him. "You'd think they might have asked, 'I'm not hard to find,'" he says.

HAZY MEMORIES

WHAT'S HARD TO FIND is the truth. A dozen interviews with *BusinessWeek* with people on all sides paint a blurry picture of those crucial days in the summer of 1980. While Kildall claims in his memoir that he met with IBM that first day and reached a handshake agreement, DRI's own lawyer at the time, Gerry Davis, says there was no deal. One of the IBMers who visited DRI that day insists he didn't talk to Kildall, but another, Jack Sams, now retired, says it's possible he was introduced to Kildall, although he doesn't remember it. Sams says faulty memories and self-serving accounts make it nearly impossible to tell exactly what happened during those chaotic weeks. "Back in those days, there was a lot of misinformation that was deliberate," he says, pointing out that IBM originally claimed it had made the PC all by itself. "We spun it, Kildall spun it, and Microsoft spun it."

The story begins unambiguously. A group of IBMers, working on a secret project to build a personal computer, flew to Seattle in August, 1980, to see if Gates could supply them with an operating system. He couldn't—and referred them to Kildall. When they showed up at DRI's offices the next day, Kildall's then-wife, Dorothy McEwen, the company's business manager, refused to sign their nondisclosure agreement. She is now ill with brain cancer and can't remember the events, according to daughter Kristin Kildall. But Rolander, who flew with Kildall on a business trip that morning, tells *BusinessWeek* they returned in the afternoon and Kildall did meet with IBM.

If Kildall struck a handshake deal that day, it didn't stick. Sams says he did get together with Kildall in Pacific Grove a short time later, but they couldn't reach an agreement. At around the same time, he saw Gates again. He and Gates both

Information Technology Silicon Sagas



GATES IN 1985 His DOS was similar to Kildall's CP/M system

the University of Washington in 1992 invited Kildall to attend the 25th anniversary of its computer science program. He was one of its earliest and most distinguished graduates, earning a PhD, yet they had picked as keynote speaker Gates, a Harvard dropout. Kildall says it was this dig that prompted him to write his memoir. "Well, it seems to me that he did have an education to get there. It happened to be mine, not his," Kildall wrote.

Kildall's resentment is understandable, but even his friends agree that he was partly to blame. For all his technical brilliance, he was a poor businessman. One big mistake was not moving ahead fast enough with a more advanced version of CP/M. He was slow to deliver a 16-bit operating system. It was that delay that created an opening for Paterson to design a 16-bit alternative, and because DRI didn't have its own version ready in the summer of 1980 IBM decided to deal with Gates, says Sams. Once IBM agreed to market his software, Kildall demanded a relatively high royalty—contributing to its being priced so high, say former DRI execs.

World history have taken a different path if Kildall triumphed in those early days? "I'm convinced," says John Wharton, a tech consultant and Kildall pal. He believes the industry would have been more collegial and innovative if Kildall rather than Gates sat at the crossroads of computing. But others say Kildall didn't have what it took to lead an industry. "Bill succeeded because he was a tenacious businessman," says lawyer Davis. "Gary was not tenacious."

As for Kildall's family, they're grateful his story is finally being told. "The truth is different for everybody," says daughter Kristin. "I think everybody believes they're presenting the truth. Obviously, they're different. I don't know why. I'm just glad my truth is out there." History may typically be written by the victors. But in this case, Gary Kildall has secured—and deserves—more than just a footnote.

By Steve Hamm in New York and Jay Greene in Seattle

knew of the operating system Paterson had built at Seattle Computer Co. As Sams recounts, "Gates said: 'Do you want to get [QDOS], or do you want me to?' I said: 'By all means, you get it.'" Gates bought Paterson's program, called QDOS, for \$50,000, renamed it DOS, improved it, and licensed it to IBM for a low per-copy royalty fee.

THE SHOUTING

IT WASN'T UNTIL nearly a year later that Kildall discovered that Gates, a longtime friend, had plucked the plum software deal out of his grasp. IBM sent test versions of its PC out shortly before it was announced in August, 1981, and a consultant working for DRI noticed the operating system was remarkably similar to CP/M. The consultant, Andy Johnson-Laird, remembers that Kildall looked at the screen and was stunned. "There were some shallow changes, but it was essentially the same program," says Johnson-Laird in an interview with *BusinessWeek*.

Kildall was furious. He and DRI's vice-president for marketing, John Katsaros, met with Gates in a Seattle restaurant to hash things out. "It was one of those meetings where everybody was nice to each other, then everyone shouted at each other, then everyone shouted at each other," recalls Katsaros in a *BusinessWeek* inter-

view. Nothing was resolved. Kildall also confronted IBM. But his problem was that software copyright had just become law three years earlier, and it wasn't clear what constituted infringement. Davis, the DRI lawyer, believes that based on the number of similarities DRI's forensic consultants found between the original DOS and CP/M, "in today's world, you could take it to court and get an infringement." But not in 1981. So rather than sue, Kildall agreed to license CP/M to Big Blue. He was floored when the PC was released and IBM charged \$240 per copy for CP/M and just \$40 for DOS. Kildall's conclusion, according to his memoir: "I believe the entire scenario was contrived by IBM to garner the existing standard at almost no cost."

Within a couple of years, the IBM PC was the undisputed champ, and Microsoft was the leading operating system provider and on its way toward PC industry domination. CP/M gradually faded into irrelevance. Kildall ultimately sold his company to Novell Inc. in 1991 for \$120 million. He went on to create some pioneering multimedia technology, but never again was an industry player. Friends say that, for years, he cringed when people brought up the "flying when IBM visited" story.

The last straw was when



IBM and Microsoft came out on top, and Kildall's OS faded away

BusinessWeek online For a Q&A with author Harold Evans, go to www.businessweek.com/magazine/extra.htm