Phys-466
Topics in Biophysics and Physical Biology

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Course goals

- Learn about breakthroughs in biophysics
- Access scientific insights through diverse resources
- Integrate context and history to synthesize knowledge
- Gain confidence in navigating despite incomplete knowledge

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Course structure

- One lecture and one exercise session per week. Tu, 10:15-12:00 (SM). Th, 14:15-15:00 (GT or WS)
- Weekly readings: PBOC or an article (~1-2 hours)
- Lectures will introduce and develop topics
- Exercises: reading journal articles, filling in worksheets

Resources:
- Moodle
- Lecture slides (TAKE NOTES)
- Physical Biology of the Cell by Rob Phillips, Jane Kondev and Julie Theriot.
- Selected journal articles, video, audio

Course credit
In-course participation: Worksheets, discussions. **(10 pts)**

Oral presentation: Choose one paper authored by a Prize recipient (Delbruck, APS, IUPAP), and present your analysis of it using the tools developed during the course. **(20 pts)**

Written essay: Choose one paper authored by a Prize recipient (Delbruck, APS, IUPAP), and present your analysis of it using the tools developed during the course (expository or argumentative). **(20 pts)**

The oral presentation and the written essay must be on different scientists, but within the same topic.

Total **50 pts**

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Course content

Topics (lectures)**:**
1. **Introduction** (1)
2. **Structure** (2-5)
3. **Single molecule mechanics** (6-9)
4. **Collective/emergent properties** (10-12)
5. **Student presentations** (13-14)

Course structure:
1. **Introduction to topic**
2. **Awardees (1-2 per week)**
   - **History, first-person, second-person accounts (C)**
   - **Article, analysis of scientific work (E)**
3. **Discussion of topic, outlook**

Why is the course designed this way?
Explore the way science is done and who scientists are
Access resources beyond textbooks, to gain insights and experience

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Lecture 1 outline

Today's goal: Overview, introductions

- Scientific texts
- Scientific revolutions
- Biomolecules, central dogma

PBOC Chapter 1.1, 1.2

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Scientific texts

Attributes	Primary literature	Journalistic versions	Textbooks
Authors	Scientists	Journalists	Educators
Audience	Scientists	General public	Students
Genre	Argumentative	Various (expository, narrative, argumentative)	Expository
Content	Evidence to support conclusions	Facts with minimum evidence	Facts
Structure	Canonical	Non-canonical	Non-canonical, reflects knowledge structure of discipline
Presentation of science	Uncertain	Various degrees of certainty	Certain

Many science curricula do not take into account the practical reasoning required in scientific knowledge production.

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Your essay

Include a "thesis statement," a central idea (1-2 sentences) which motivates the essay.

Expository writing:
Presents information in a logical manner without expressing an opinion, neutral.
Gives overview, balanced and objective.

Argumentative writing:
Establishes a position / opinion on a topic.
Presents evidence to support the thesis, but also describes alternative opinion(s).

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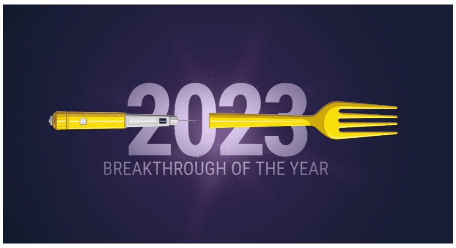
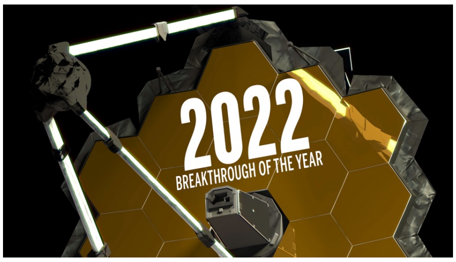
Breakthrough research

What characterizes breakthrough research?



Glucagon-like peptide-1 receptor agonists



James Webb Space Telescope

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What is a scientific revolution?

Copernicus/Kepler, Newton, Lavoisier, Darwin, Einstein

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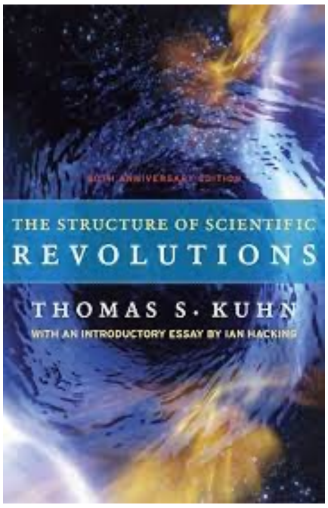
The structure of scientific revolutions



1962

Biography:

- Theoretical physicist, graduate student
- Teaching physical science for non-scientists, observed an inconsistency in the way the practice of science was described
- Became a historian of science

Aim of textbooks:

- Persuasive and pedagogic
- Like a tourism brochure's attempt to capture a national culture
- Describes a steady accumulation of individual discoveries and inventions
- A different concept of science emerges from the historical record of research activity

Thomas S. Kuhn

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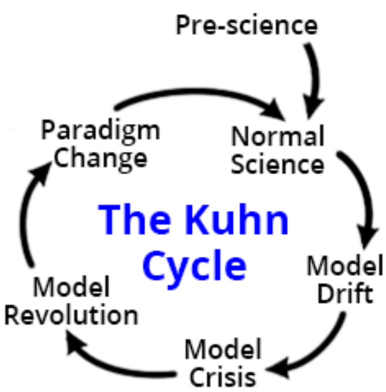
The structure of scientific revolutions



Pre-science refers to a period before a scientific consensus has been reached

- Disorganized and diverse activity
- Constant debate over fundamentals
- As many theories as there are theorists
- No commonly accepted observational basis

Normal science is research firmly based upon past scientific achievements (shared paradigm)

Measurements may repeatedly discover inconsistencies, resulting in **model drift**

When the profession can no longer avoid anomalies, **model crisis**

Extraordinary investigations lead to a new basis of understanding: **model revolution** and **paradigm change**

Thomas S. Kuhn

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The structure of scientific revolutions

Normal science:
Does not aim to produce major novelties, conceptual or phenomenal. If you look at any research journal, you will find three types of problems addressed:
(1) determination of significant facts
(2) matching of facts with theory
(3) articulation of theory

Contrast ”normal” science with “breakthrough” science

Thomas S. Kuhn

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The structure of scientific revolutions

Paradigm:
1. A scientific community’s reigning methods and theories

2. Exemplars or model problems, the worked examples on which students and young scientists cut their teeth

Thomas S. Kuhn

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The structure of scientific revolutions

IN RETROSPECT
The Structure of Scientific Revolutions

David Kaiser marks the 50th anniversary of an exemplary account of the cycles of scientific progress.

Nature, 12 April 2012

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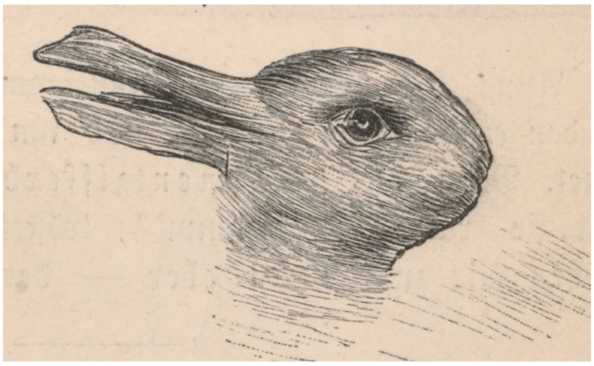
The structure of scientific revolutions



Incommensurability : Scientists have no way to compare concepts on either side of a scientific revolution.

For example, the idea of 'mass' in the Newtonian paradigm is not the same as in the Einsteinian one; each concept draws meaning from separate webs of ideas, practices and results.

If scientific concepts are bound up in specific ways of viewing the world, like a person who sees only one aspect of a Gestalt psychologist's duck–rabbit figure, then how is it possible to compare one concept to another?

Thomas S. Kuhn

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The structure of scientific revolutions

The most intriguing idea, however, is to use Kuhn's thinking to interpret his own achievement. In his quiet way, he brought about a conceptual revolution by triggering a shift in our understanding of science from a Whiggish paradigm (steady march toward the truth) to a Kuhnian one, and much of what is now done in the history and philosophy of science might be regarded as "normal" science within the new paradigm. But already the anomalies are beginning to accumulate. Kuhn, like Popper, thought that science was mainly about theory, but an increasing amount of cutting-edge scientific research is data- rather than theory-driven. And while physics was undoubtedly the Queen of the Sciences when *Structure…* was being written, that role has now passed to molecular genetics and biotechnology. Does Kuhn's analysis hold good for these new areas of science? And if not, isn't it time for a paradigm shift?

Thomas Kuhn: the man who changed the way the world looked at science
John Naughton, The Guardian, 19 August 2012

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An alternative view

The key thing about scientific knowledge is that science is cumulative: we now know more about the world, in a better way, than we did 100 years ago. That doesn't hold for artistic creation. So, for example, we can't prove that Keats was a better writer than Shakespeare. 'Better' doesn't really mean anything in that context. Science is progressive, in that it builds upon previous knowledge. What's interesting—and what scientists are aware of—is that that progress is incredibly nonlinear. You make mistakes all the time and the road not taken is often, in retrospect, the interesting one.

[There is] a parallel between the way that science develops and the way that each of us grew from a single cell into an adult human. It looks like it was inevitable that we ended up the way we are, but in reality there was nothing inevitable about it. There are a whole set of possibilities that could have produced completely different versions of us which don't exist. If you're trying to untangle the processes involved in organismal development, then you need to understand all those conditionalities. Otherwise, you end up with a very simple, inevitabilist view of what is going on.

Matthew Cobb, Professor of Zoology

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An alternative view

'Science' in fact covers a whole set of disciplines: scientific discoveries bleed into technological discoveries and, vice versa, technology allows us to discover things.

[Before the second half of the nineteenth century] the interpenetration of commercial interests and more focussed research were extremely important. We're at that stage again now: we're under great pressure to provide impact—preferably financial in terms of patents and new processes. For those of us who don't work in areas that lend themselves to such immediate exploitation, this can be a difficulty.

… parallel with developments in industry, where you start with very simple craft techniques that were gradually built up into largescale industry. You can see similar changes in various scientific disciplines: molecular biology is a very good example. It started off with very simple, relatively crude techniques carried out by a handful of individuals. Then there was a wave of 'industrialisation' with the creation of larger and larger research groups. Finally, we ended up with machines taking over a large part of what were extremely important human technical skills for much of the second half of the 20th century, many of which are now forgotten.

on John Pickstone's "***Ways of Knowing: A New History of Science, Technology, and Medicine"***

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What is biophysics?

Biophysics is the field that applies the theories and methods of physics to understand how biological systems work.

Biophysics has been critical to understanding the mechanics of how the molecules of life are made, how different parts of a cell move and function, and how complex systems in our bodies—the brain, circulation, immune system, and others— work. Biophysics is a vibrant scientific field where scientists from many fields including math, chemistry, physics, engineering, pharmacology, and materials sciences, use their skills to explore and develop new tools for understanding how biology—all life—works.

(Biophysical Society)

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What is physics of life?

Active matter includes living and non-living systems that have in common that they contain energy-consuming and force-generating microscopic constituents that drive emergent dynamic properties on larger scales. (Das et al., Soft Matter 2020)

Active matter, which ranges from molecular motors to groups of animals, exists at different length scales and timescales, and various computational models have been proposed to describe and predict its behaviour. The diversity of the methods and the challenges in modelling active matter primarily originate from the out-of-equilibrium character, lack of detailed balance and of time-reversal symmetry, multiscale nature, nonlinearity and multibody interactions. Models exist for both dry active matter and active matter in fluids, and can be agent-based or continuum-level descriptions. They can be generic, emphasizing universal features, or detailed, capturing specific features.
(Shaebani et al., Nat. Rev. Phys. 2020)

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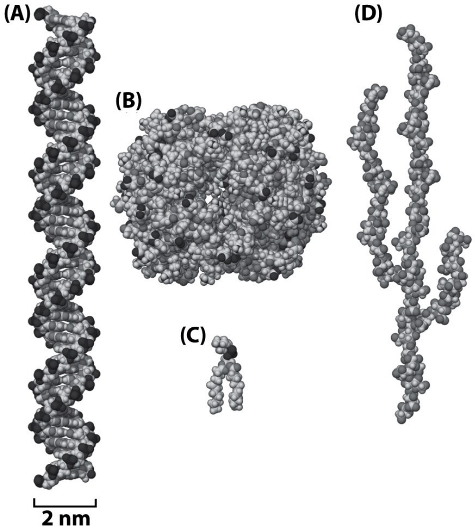
The stuff of life

What macromolecules are cells made of?



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The stuff of life

What macromolecules are cells made of?

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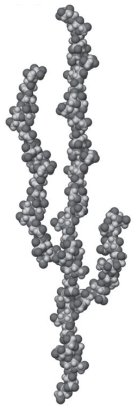

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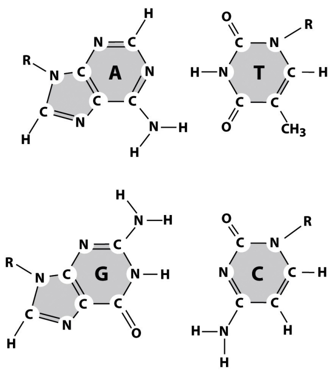

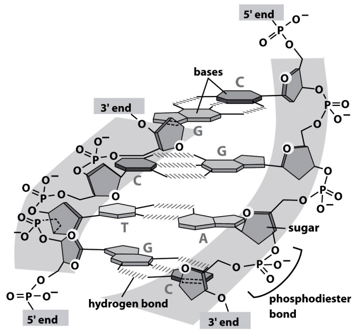

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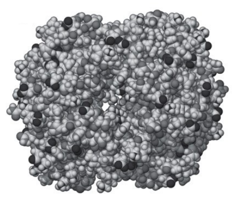

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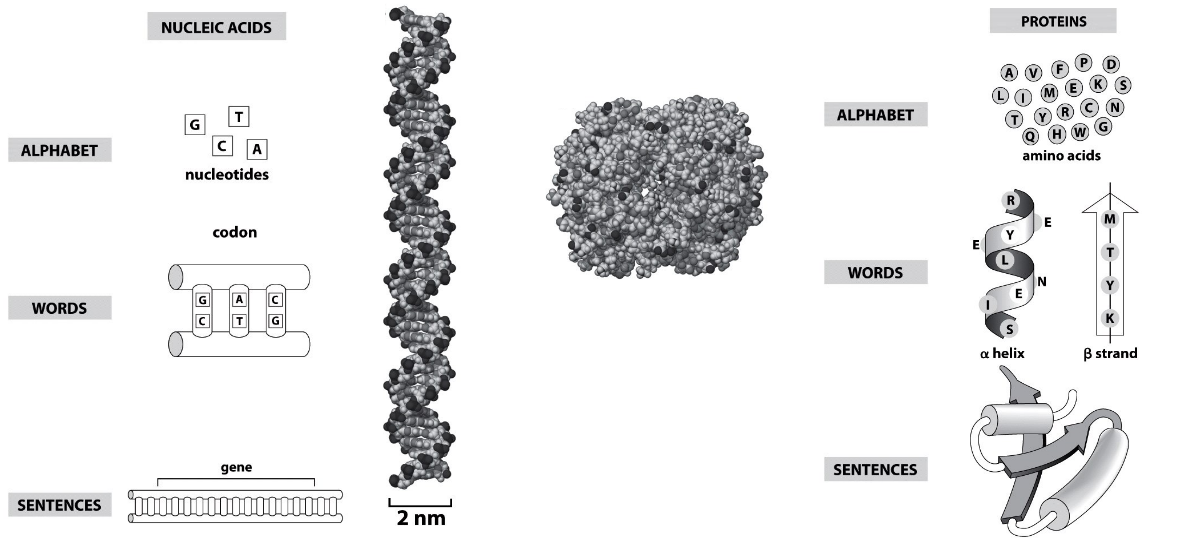
The stuff of life

Nucleic acids and proteins are polymer languages



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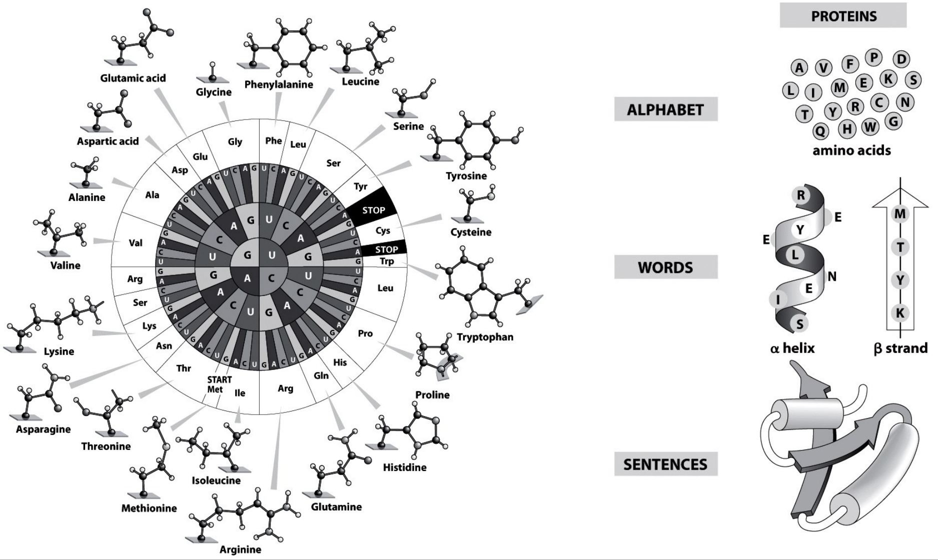

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The stuff of life

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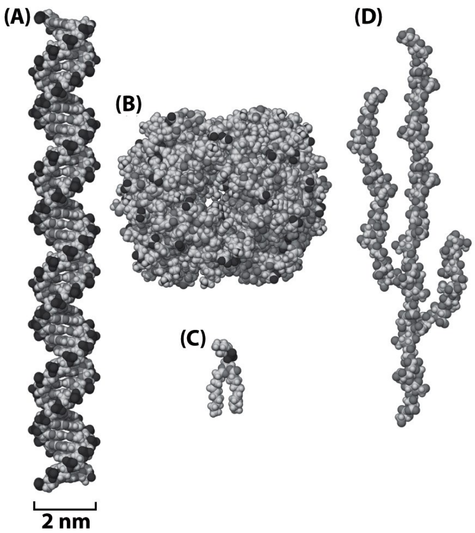

Advantages:
- Each class can be assembled by the cell from a small set of simpler subunits
- Combinatorial assembly gives rise to diversity
- Limited repertoire of chemical reactions needed
- Facilitates existence of food chain

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Lecture 2

- What is a structure?
- Proteins and random walks
- History of discoveries regarding protein structure

PBOC Chapter 8.1, 8.4

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