Activities and Classroom Demonstrations in Biological Physics

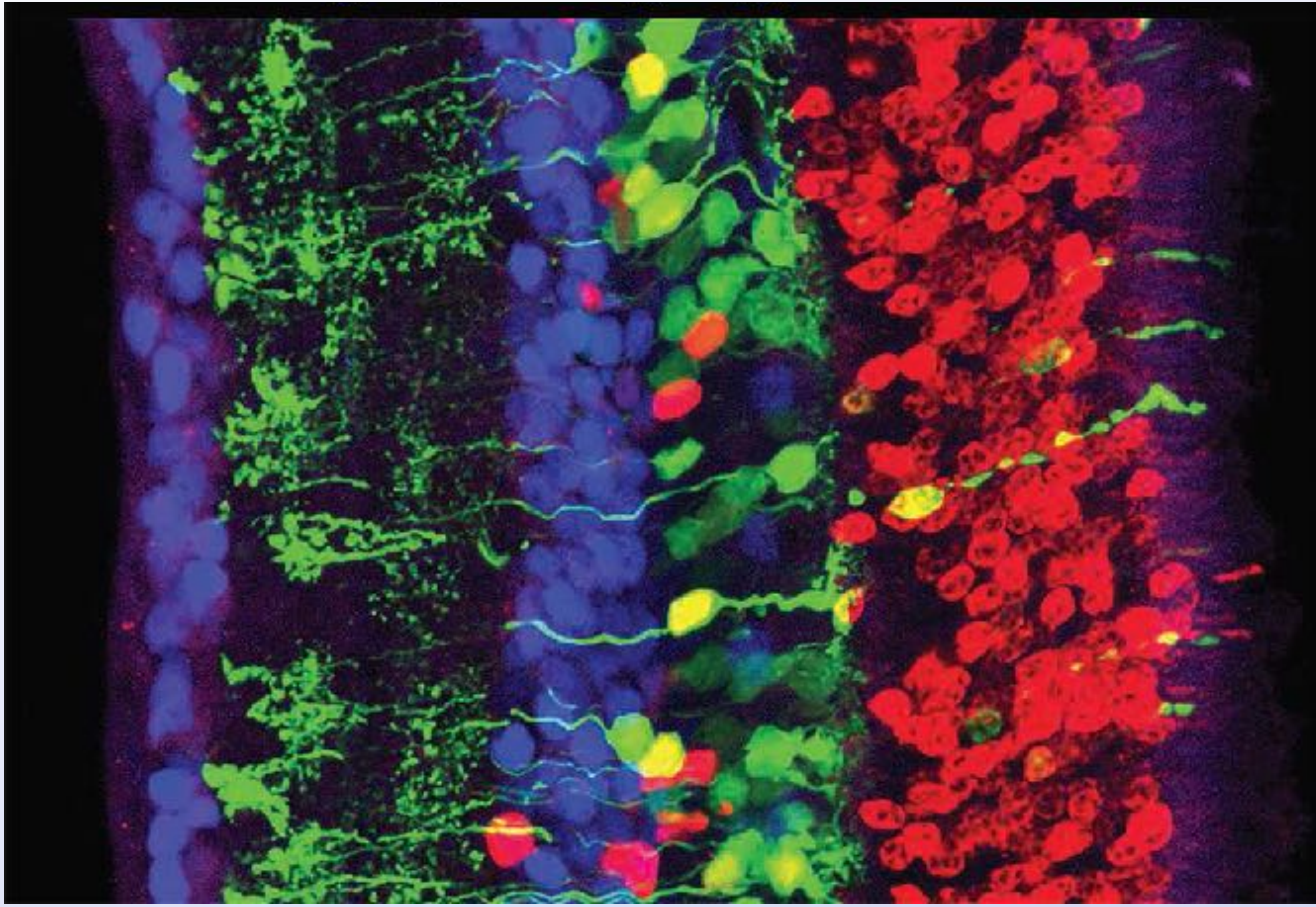

Image of mouse retina courtesy Sui Wang and Constance Cepko

Phil Nelson and Bill Berner
University of Pennsylvania

These slides will appear at
www.physics.upenn.edu/~pcn
Bill's amazing shows are also available from a link at that page.

Plan

1. Indoctrination
2. Skill set
3. Algorithmic thinking and data visualization
4. Some surprising phenomena: Materials
5. : Dynamics
6. : Optics
7. Student assessment
8. Outcomes

Phil Nelson

1: Is this your situation?

"I'm interested in biological physics.
and
So are many students in my university.
but
My department doesn't want to assign me to a new course, and they're not too sure this stuff is physics anyway."

One message today is:
There have recently been *revolutions* in single-molecule manipulation, in optical methods, and in synthetic biology.
and
Those revolutions are still *ongoing*.
and
You need a lot of *physics* to understand it.
and
I'm talking about *cool* physics, not traditional first-year material shoehorned into pseudo-relevance
and
It brings in *non-majors* who would otherwise not have taken another physics course.
so
Of course your department should let you offer it!

Phil Nelson

1. Challenge/opportunity

I love Physics–so do you–but if we want Physics to flourish, we need to recruit new physicists.

Our instruction must account for what skills and concepts are already in the students' heads before they arrive. Often, what's in their heads includes a lot of life science. Instead of moaning about how they lack certain mathematical skills, can we work with this ***strength?***

In fact, let me propose to turn standard thinking on its head: In addition to the usual:

- "Physics is so important for understanding biology etc." (which is of course true)

I've also observed that for many students,

- Life science is an ideal ***context*** in which to teach ***serious physics***.

For these students, the subject *comes alive only when developed with a scientific motivation that they find compelling*.

Interdisciplinary

Here are some things one hears, explicitly or not. Each may contain a grain of truth, but I'm not going to agree with any of them:

- "Any course that stays within the confines of one discipline is *ipso facto* boring and obsolete."
- "(Also my research is better than yours because it's interdisciplinary.)"
- "To be interdisciplinary, a course must be team-taught by members of two or more `disciplines.' And it must be attended by a similarly ecumenical group of students."

I do think an interdisciplinary course can be useful if a practitioner of one discipline shows students pursuing a different discipline how his methods have been *useful in solving problems of independent interest in the other field*.

One goal today is to give some details.

What physics-style courses can give to life-science students

- Frame topics around "**How could anything like that possibly happen?**" puzzles. It's crazy but you just saw it with your eyes.
- Stress that understanding is tested by falsifiable quantitative prediction. Shake the hypothesis till it yields up a testable prediction. Push it to a region of parameter space different from the observations that motivated it in the first place.
- Consciously teach the art of throwing out details. The theory should not be more elaborate than the data can support. Don't stop with a successful prediction – next seek an *alternative* model that succeeds equally well and see how to test it.
- Approximation/estimation is not bad. Appropriate approximation – which is not just sloppiness or laziness – is essential to understanding.

What physics-style courses can give to life-science students, II

- You can be handed a problem you've never seen before, even on a timed exam, reach into your toolkit, pull out the right tool without being told, and solve the problem.
- In fact your instructor is simulating that process when she stands at the blackboard and invents the subject right before your eyes -- sometimes even making mistakes, finding them and fixing them.
- Long chains of logic actually do lead to real conclusions, with the help of mathematical discipline. There's a nontrivial synthetic step, and suddenly there's *new knowledge* that wasn't there before -- or at least a testable hypothesis, which will turn into new knowledge when an experiment is done.
- This by the way is a miracle -- the **basic epistemological miracle of physical science**. It doesn't always work, but is has worked in the past.

2 Skills

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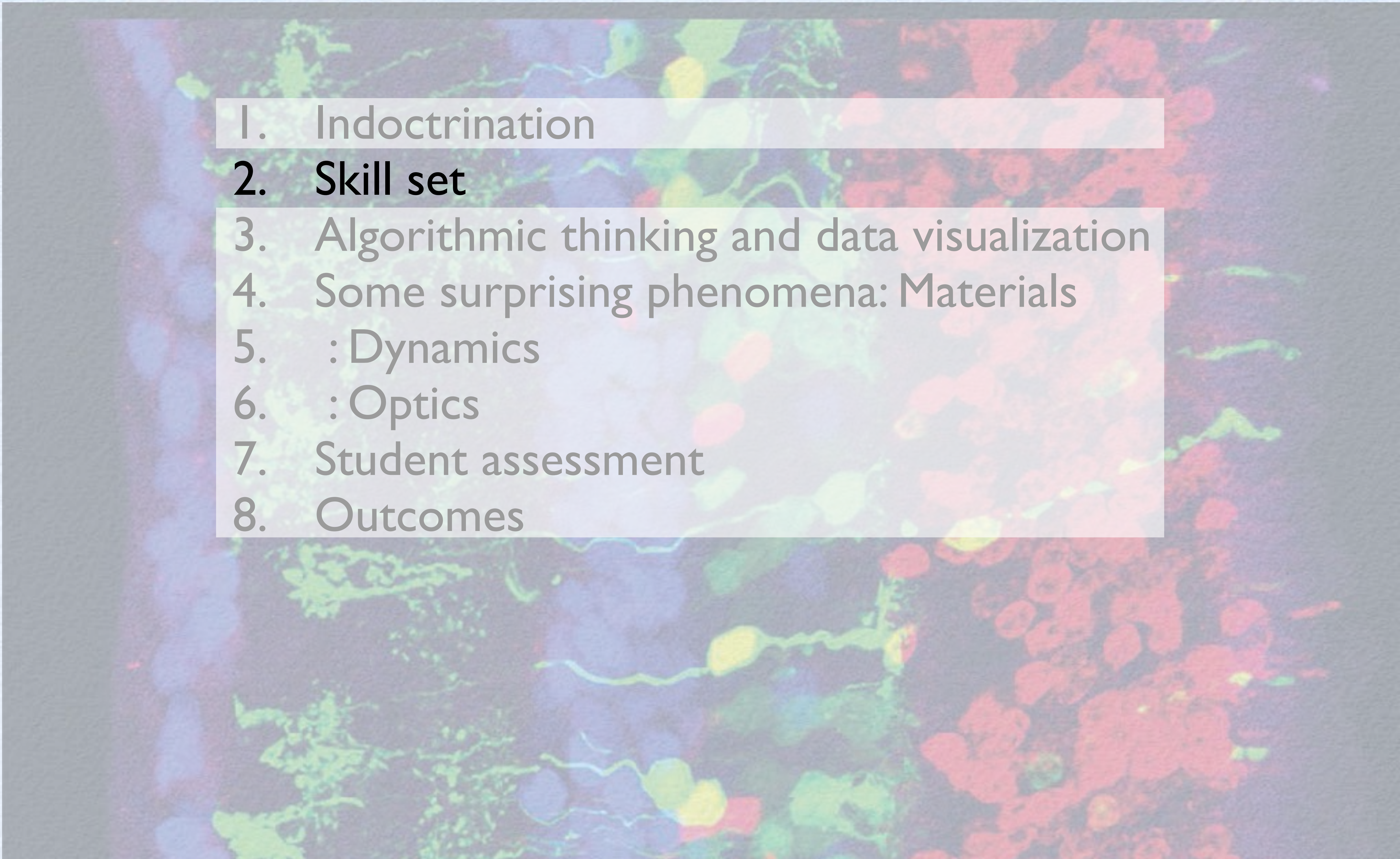

What do we really want our undergrads to get, as early as possible?

Science needs imagination: "Reason can answer questions, but imagination has to ask them." — Ralph W. Gerard

Imagination must be coupled to discipline: "Seek simplicity, and distrust it." — Alfred North Whitehead

Science involves modeling: "We all know that Art is not truth. Art is a lie that makes us realize the truth." — Pablo Picasso

Quantitative models are the most falsifiable: "A single number has more genuine and permanent value than an expansive library full of hypotheses." — Robert Mayer, 1814--1878

What kind of skills and frameworks?

- **A physical model is different from – more than – a mathematical model.** Don't let the applied mathematicians stake out biomodeling as their exclusive domain; the physical approach gives extra kinds of intuition and insight.

- **Randomness is inescapable in the physical world, and yet conclusions can nevertheless be drawn with the help of ideas from probability.** The Bayesian viewpoint now sweeping many branches of science is important to learn early and often.

- **The basics of computer programming, in any general-purpose platform, are now easy enough to cover in a small fraction of a semester.** Incorporating it into any class is probably more important than whatever else you were going to do with those two weeks.

Any science or engineering student benefits from explicit, repeated exposure to these ideas. *(And at my institution, at least some Physics majors are graduating without exposure to any of them.)*

From Official Guide for the MCAT ^{2015} Exam

The *Biological and Biochemical Foundations of Living Systems* and the *Chemical and Physical Foundations of Biological Systems* sections are designed to:

- target **basic research methods and statistics concepts** described by many baccalaureate faculty as important to success in introductory science courses; and
- require you to demonstrate your scientific inquiry and reasoning, research methods, and statistics skills as applied to the natural sciences.

Understanding the processes unique to living organisms, such as growing and reproducing, **maintaining a constant internal environment, acquiring materials and energy, sensing and responding to environmental changes, and adapting,** is important to the study of medicine.

Foundational Concept 2*B*. ***The structure, growth, physiology, and genetics of prokaryotes and viruses***

Foundational Concept 3: **Complex systems of tissues and organs sense the internal and external environments of multicellular organisms, and through integrated functioning, maintain a stable internal environment within an ever-changing external environment**

Foundational Concept 4: ***Complex living organisms transport materials, sense their environment, process signals, and respond to changes using processes understood in terms of physical principles.***

4D. How light interacts with matter

4E. Atoms, nuclear decay, electronic structure, and atomic chemical behavior

Skill 1: Knowledge of Scientific Concepts and Principles

- Recognizing correct scientific principles
- Identifying the relationships among closely-related concepts
- Identifying the **relationships between different representations of concepts (e.g., verbal, symbolic, graphic)**
- Identifying examples of observations that illustrate scientific principles
- **Using mathematical equations to solve problems**

Skill 2: Scientific Reasoning and Problem-solving

- Reasoning about scientific principles, theories, and models
- Analyzing and evaluating scientific explanations and predictions
- Evaluating arguments about causes and consequences
- Bringing together theory, observations, and evidence to draw conclusions
- Recognizing scientific findings that challenge or invalidate a scientific theory or model

Skill 3: Reasoning about the Design and Execution of Research

- Identifying the role of theory, past findings, and observations in scientific questioning
- **Identifying testable research questions and hypotheses**
- **Distinguishing between samples and populations and results that support generalizations about populations**
- Identifying independent and dependent variables
- Reasoning about the features of research studies that suggest associations between variables or causal relationships between them (e.g., temporality, random assignment)
- Identifying conclusions that are supported by research results
- Determining the implications of results for real-world situations

Phil Nelson

Skill 4: Data-based and Statistical Reasoning

- **Using, analyzing, and interpreting data in figures, graphs, and tables**
- **Evaluating whether representations make sense for particular scientific observations and data**
- **Using measures of central tendency (mean, median, and mode) and measures of dispersion (range, inter-quartile range, and standard deviation) to describe data**
- **Reasoning about random and systematic error**
- **Reasoning about statistical significance and uncertainty (i.e., interpreting statistical significance levels, interpreting a confidence interval)**
- **Using data to explain relationships between variables or make predictions**
- **Using data to answer research questions and draw conclusions**

General Mathematical Concepts and Techniques

- **Recognize and interpret linear, semilog, and log-log scales and calculate slopes from data found in figures, graphs, and tables**
- **Demonstrate a general understanding of significant digits and the use of reasonable numerical estimates in performing measurements and calculations**
- **Use metric units, including conversion of units within the metric system, conversions between metric and English units (conversion factors will be provided when needed); dimensional analysis (using units to balance equations)**
- **Demonstrate a general understanding (Algebra II-level) of exponentials and logarithms (natural and base ten), solving simultaneous equations**
- **Demonstrate a general understanding of the following trigonometric concepts: definitions of basic (sine, cosine, tangent) and inverse functions; sin and cos values of 0°, 90°, and 180°; relationships between the lengths of sides or right triangles containing angles of 30°, 45°, and 60°**
- **Demonstrate a general understanding of vector addition and subtraction.**

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3: Skills: Algorithmic thinking and data visualization

We hear a lot about the importance of training STEM students to work well in teams, and certainly that's true.

But there is another skill set that will be critical for our students' future, one that's much less talked about but that jumped out at me as I read *Average is Over* by Tyler Cowen: In many areas, even beyond STEM, the successful professionals are going to be the ones who can integrate with machines to ***do things that neither humans nor computers can do by themselves***. We may not want to hear this, but as artificial intelligence takes over more and more routine white-collar work there will be an ever-increasing premium on this skill set.

My message here is instead that writing code from scratch, in a general-purpose programming language, is a skill that

- Many of even our best students have not yet acquired;
- Is central to most kinds of current scientific research;
- Represents an entirely new mode of mental activity distinct from the other things we teach students to do;
- Enables an instructor to assign much more interesting and real-world problems;
- Gets many students excited and gives them a toolkit that they can and do carry over into all their subsequent classes and beyond.

BIO2010 report

RECOMMENDATION #1.3

The principles of physics are central to the understanding of biological processes, and are increasingly important in sophisticated measurements in biology. The committee recommends that life science majors master the key physics concepts listed below. Experience with these principles provides a simple context in which to learn the relationship between observations and mathematical description and modeling.

The typical calculus-based introductory physics course taught today was designed to serve the needs of physics, mathematics, and engineering students. It allocates a major block of time to electromagnetic theory and to many details of classical mechanics. In so doing, it does not provide the time needed for in-depth descriptions of the equally basic physics on which students can build an understanding of biology. By emphasizing exactly solvable problems, the course rarely illustrates the ways that physics can be applied to more recalcitrant problems. Illustrations involving modern biology are rarely given, and computer simulations are usually absent. Collective behaviors and systems far from equilibrium are not a traditional part of introductory physics.

http://books.nap.edu/

Phil Nelson

How to get there on time

- On Day 1 of the class, I tell the students where to get a ***free download*** of the Python language, and I distribute installation instructions. I tell them they need to come to class *on Day 2* with a laptop, with this system installed and running. I pass out and collect a questionnaire.
- The questionnaire asks students for their general experience level with any computer math system. I use the responses to make teams of two students each. I ***assign partners*** so that a student from the lower self-evaluation levels is paired with one from the higher. I send everybody an e-mail with their partner's contact, saying "even if you're an expert, you must come to support your partner."
- On Day 2 of class I say, "Figure out if you or your partner has more computer experience; then that person should be ***advising, not touching*** the computer." I talk a little, show some things on the big screen, then stop and let the students try some things in the First Computer Lab section of the book. I walk around troubleshooting, along with 1 or 2 grad students. After maybe 10 minutes, I interrupt them and talk a little more, repeating till the class ends.
- Then we have some regular classes, followed by a second computer lab structured the same way but with ***different assigned partners,*** covering some new skills.
- After that I say, "If you liked either of your assigned partners, keep working together, but from now on work with whomever you like."

This is all the explicit programming instruction I do. From then on, I spend a little class time introducing some new syntax needed for that week's homework, and lots of instruction goes on in office hours. ***There's still room for a lot of physics.***

Skills: What one does with data

- Students should be confronted with situations in which statistical variation is not just a nuisance to be minimized, but rather is telling us something quantitative and central to the hypotheses being confronted.
- Students should be exposed to statistical methods that they can actually understand and adapt for themselves, not just the incantations of authority figures or black-box buttons on canned software.
- Those methods should prepare students to evaluate others' work, and hence should include the Bayesian framework now sweeping through many fields.

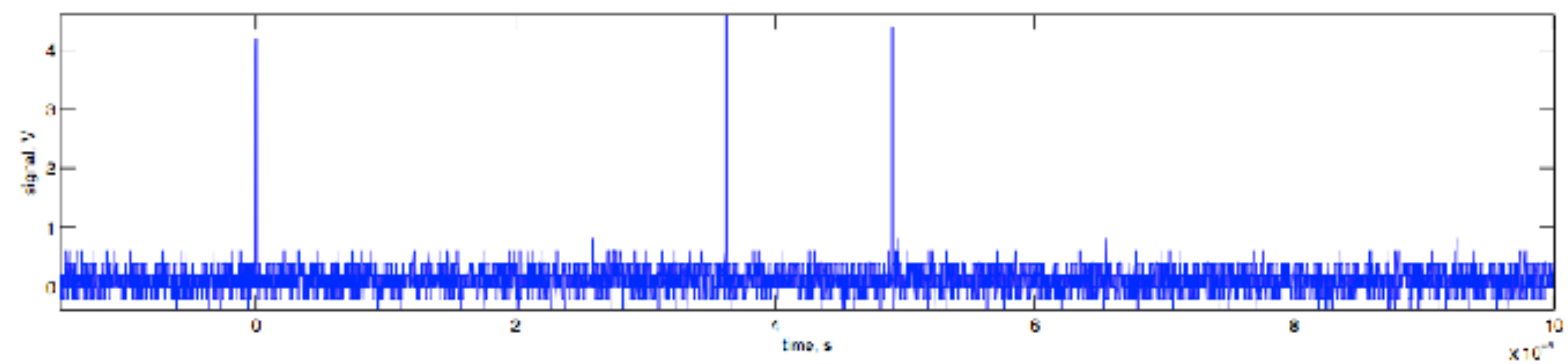
Biophysical problems are an interesting road into probability theory with high-profile, current applications that can motivate students.

(Do your life-science students really understand it when they take their department's biostatistics course?)

Example: What is a "fit?" Could jiggle till they look good... could hit the "fit" button on our canned software... or we could maximize the *likelihood*.

We can detect very dim light with a photomultiplier tube or avalanche photodiode. Either way, light causes discrete clicks in the detector. ***Dimmer light gives equally big clicks, just less frequent***:

Dim illumination:



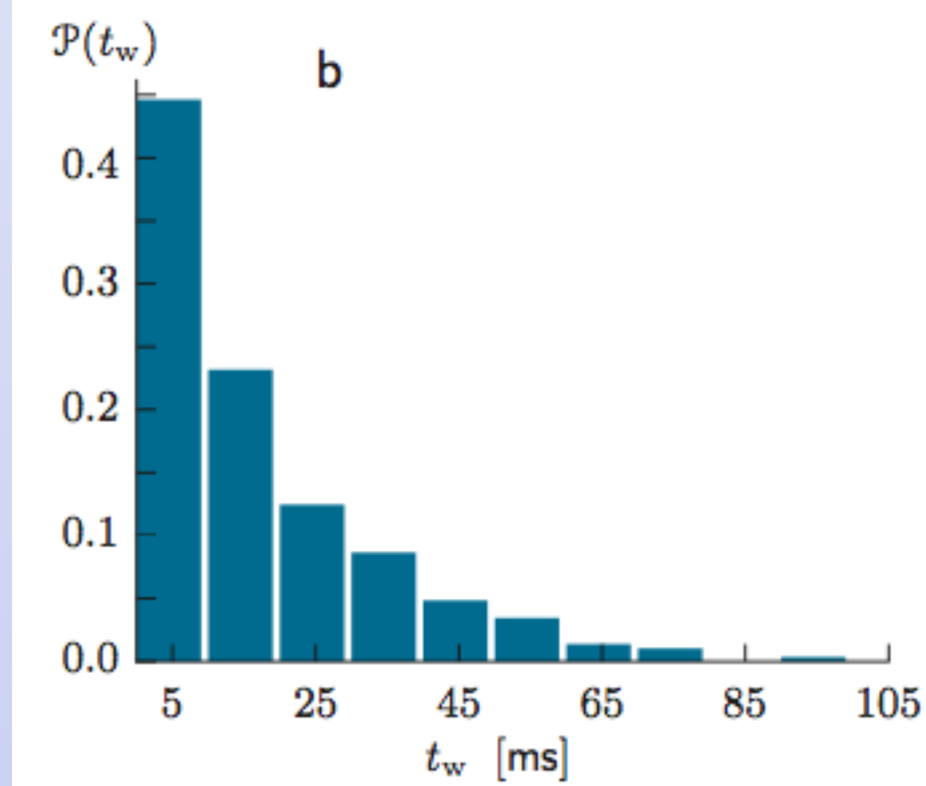
Slightly brighter (still very dim):

uniform blips audio clip

actual experimental data

simulated Poisson process

How can we learn anything from “just noise?” To get a handle on what’s going on, notice that the absolute times of individual clicks aren’t very significant, but the *intervals* between successive clicks are:



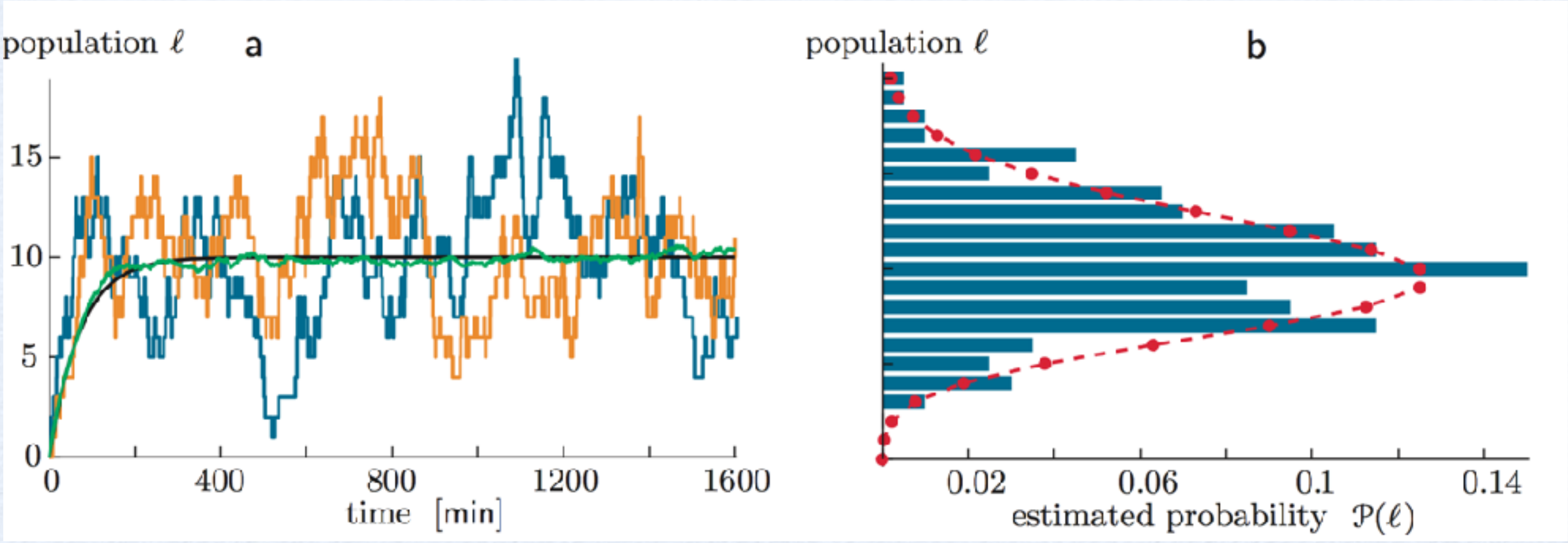
Hmm. That looks familiar. Could that stupid Geometric distribution have anything to do with the cosmic mystery of light? Which tormented Einstein all his life?

Experimental data courtesy J. F. Beausang.

3.2 From random quantities to random processes

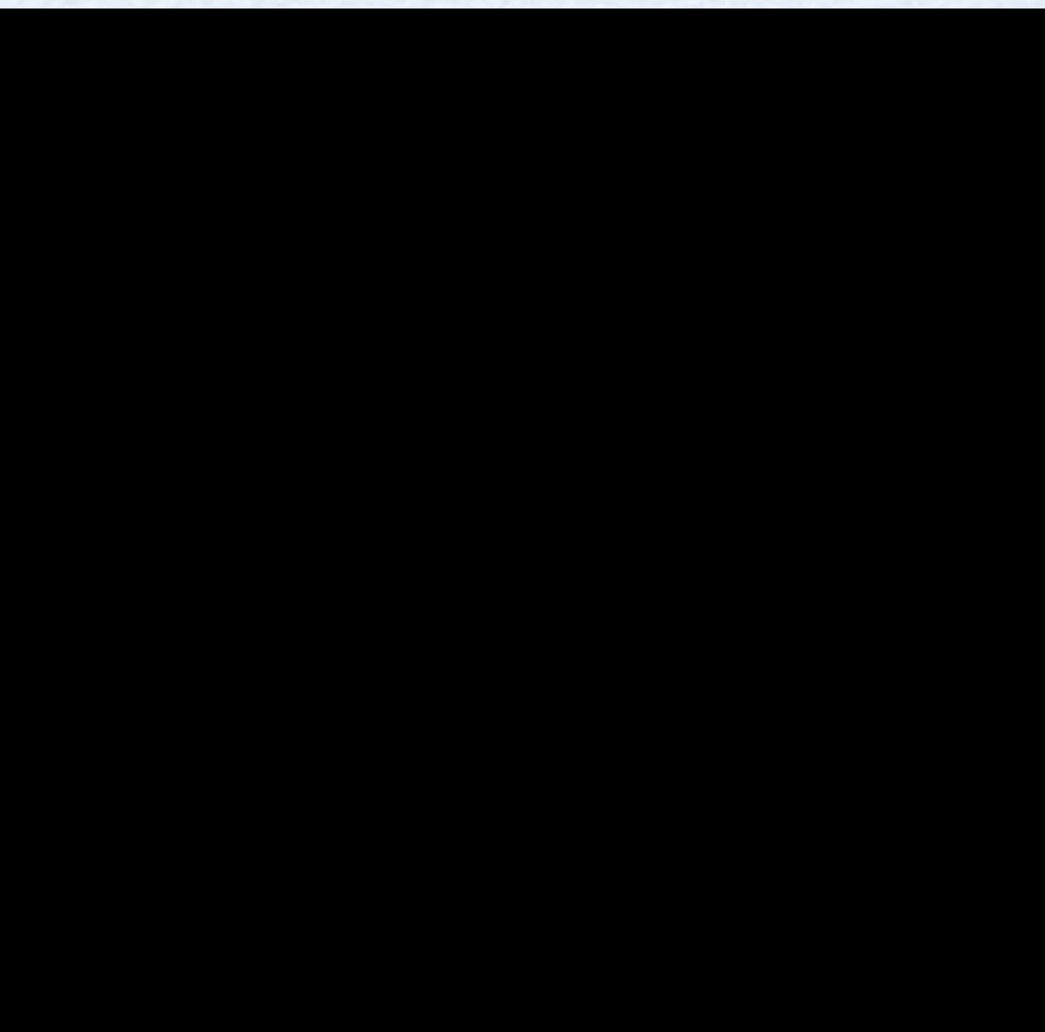
Simulations that they create for themselves can also foster critical attitudes about when continuous, deterministic approximations are useful.

Just a few lines of code suffice to simulate a birth-death process resembling transcription. For small molecule numbers, it doesn't look deterministic at all, but for larger numbers it does settle down. That's a key insight.

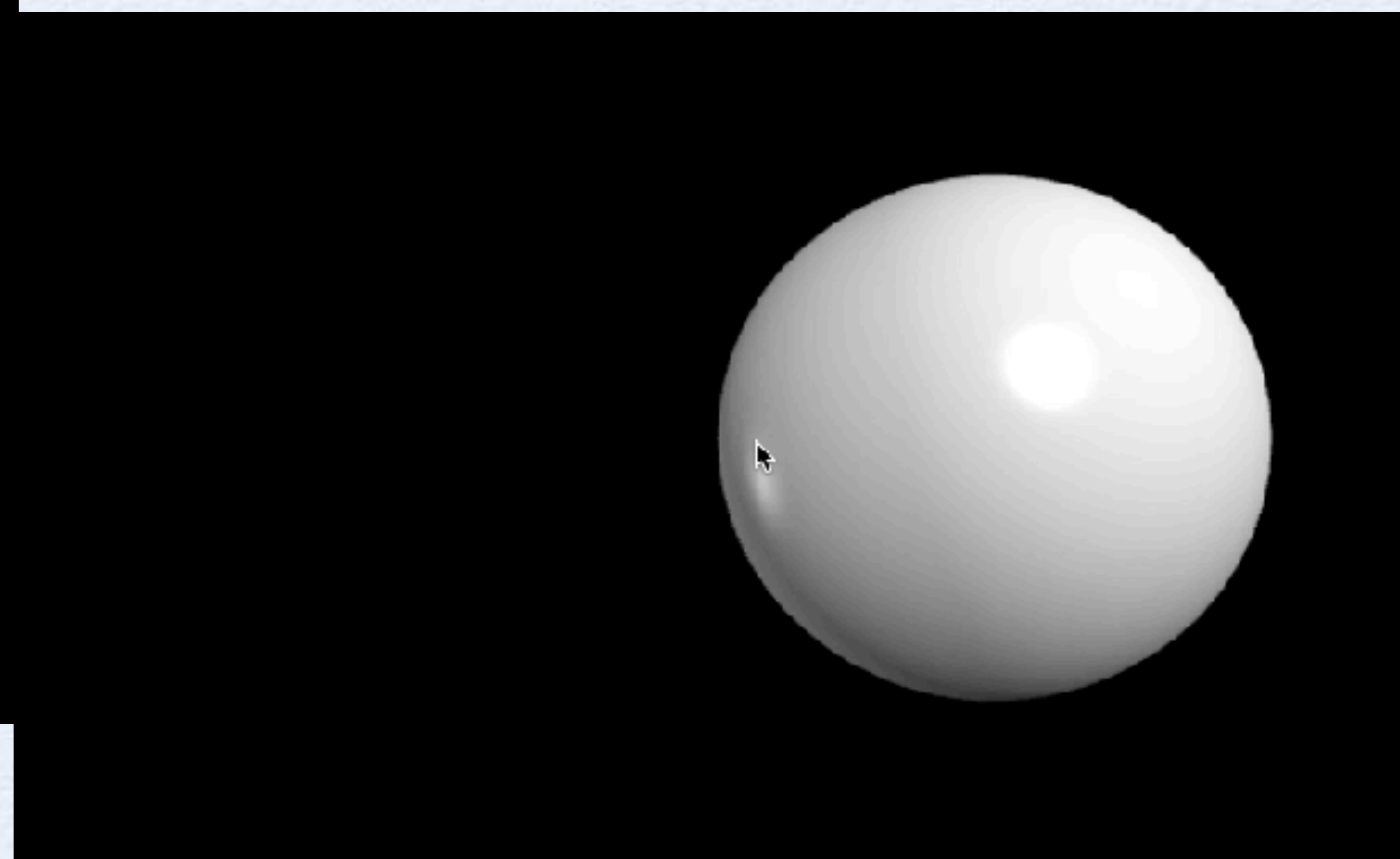


3.3 Animation

Physical processes unfold over time. Our minds grasp physical mechanisms largely via narrative. So it is not surprising that some of the most vivid physics demonstrations also play out over time. Simulations of physics that unfold over time are similarly powerful; interactive simulations are better; and simulations created by the student can be best of all.



See code `flipper.ipynb` in the handout.



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4. Demo-based modules

Demos are the heart and soul of physics instruction.
In what other discipline can we give students a *direct, unfiltered experience of Nature,* showing something weird, surprising (at least after you think a bit).
Here are a few not usually seen in high school or freshman classes, with thought-provoking tie-ins to the living world.

BIO2010 report

“ Many science and mathematics courses are taught as sets of facts, rather than by explaining how the material was discovered or developed over time. Covering the history of the field, demonstrating the process of discovery, or presenting other stories as examples of how scientists work—while clearly illustrating why the knowledge that has been gained is relevant to the lives and surroundings of the students—is an excellent way to engage undergraduates.

Much of today's biomedical research is at the interface between biology and the physical, mathematical, or information sciences. Most colleges and universities already require their biology majors to enroll in courses in mathematics and physical science. However, faculty often do not integrate these subjects into the biology courses they teach. This can result in students with a shortsighted view of the connections between all the scientific disciplines involved in the study of the biological world, and produce students who do not see the relevance of their other science courses to their chosen field of study. ”

http://books.nap.edu/

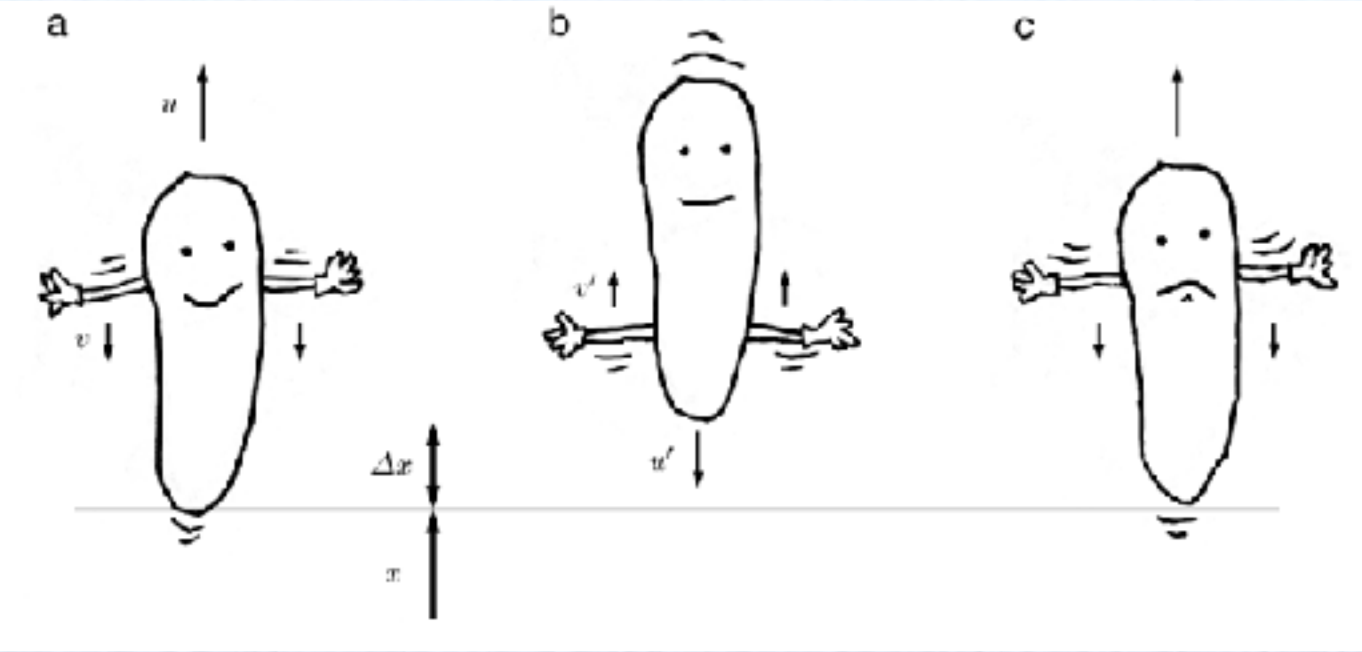
4.1 Fluids in the microworld

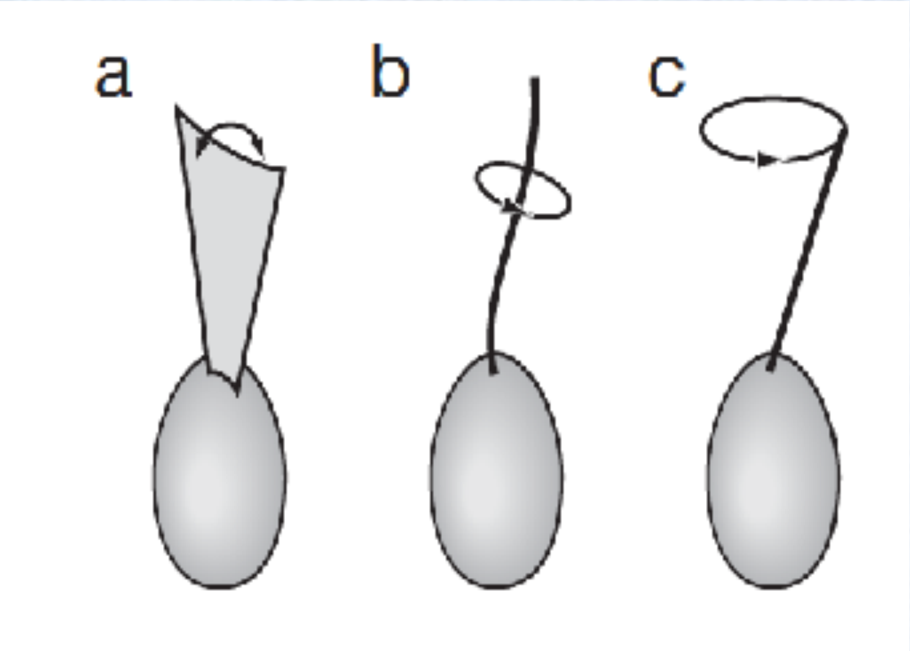
How could anything like that possibly happen?

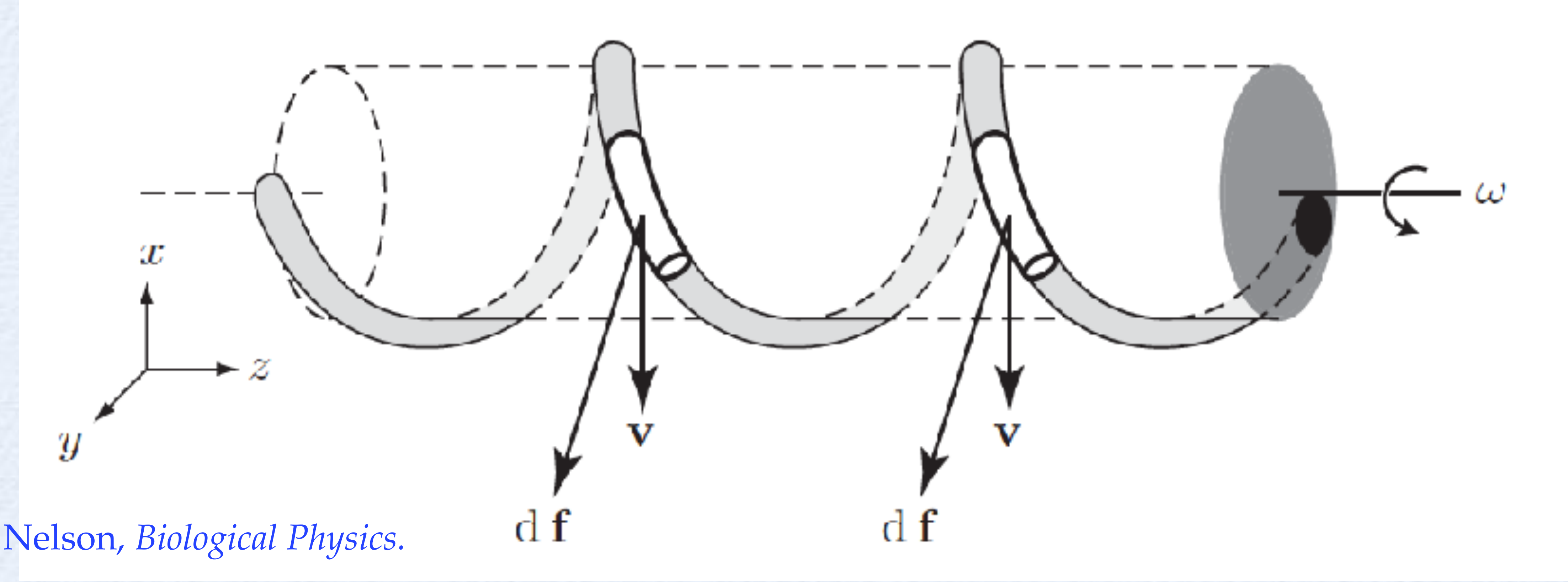
https://www.youtube.com/watch?v=PhsmOc7Hb8Q

Phil Nelson

4.1 Low Reynolds propulsion



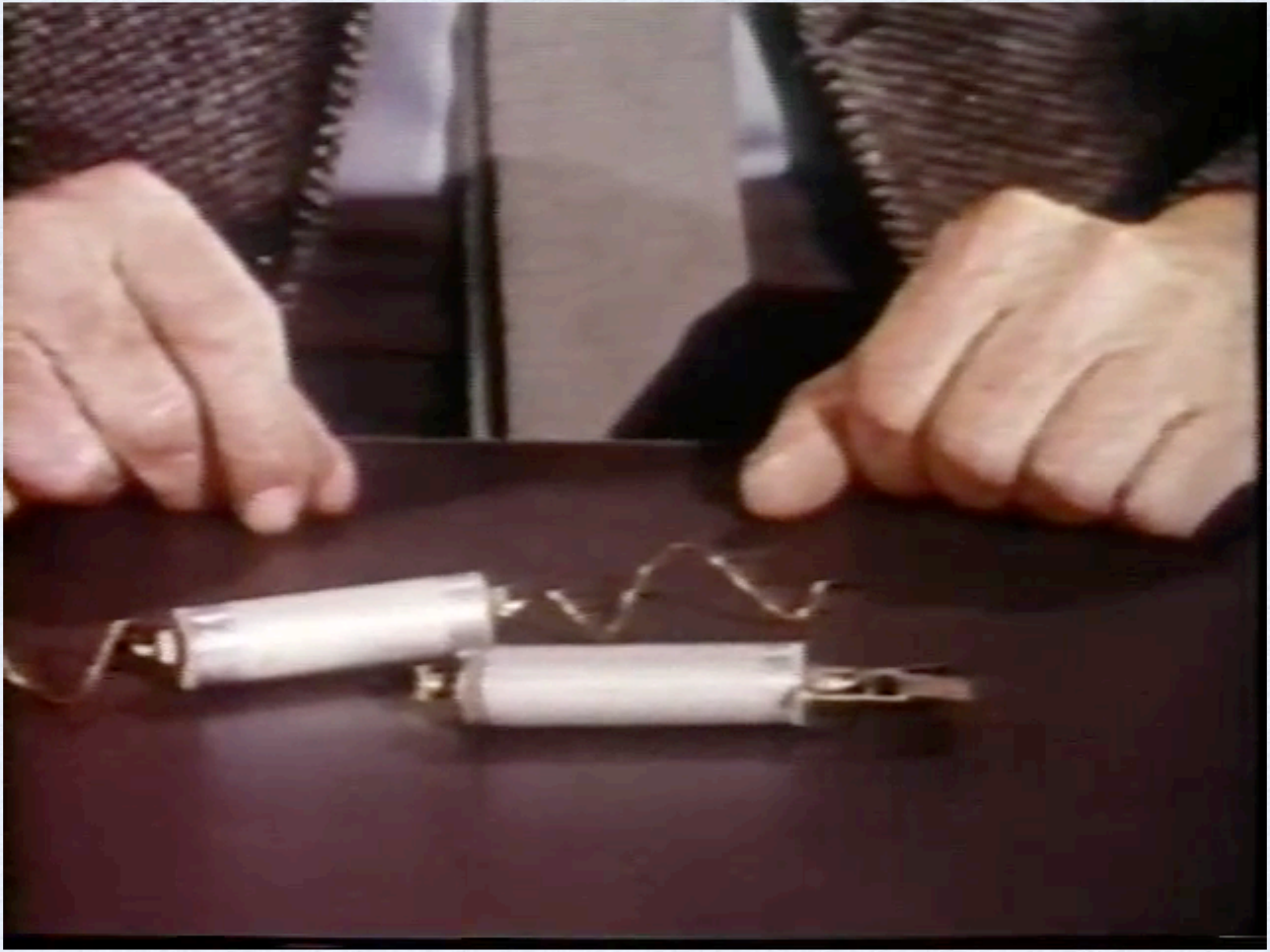




From Nelson, *Biological Physics.*

Phil Nelson

4.1 Low Reynolds propulsion



https://www.youtube.com/watch?v=PhsmOc7Hb8Q

Phil Nelson

4.2 Energy in the thermalworld

Time to mention the unmentionable.
I'm talking about *dissipation*.

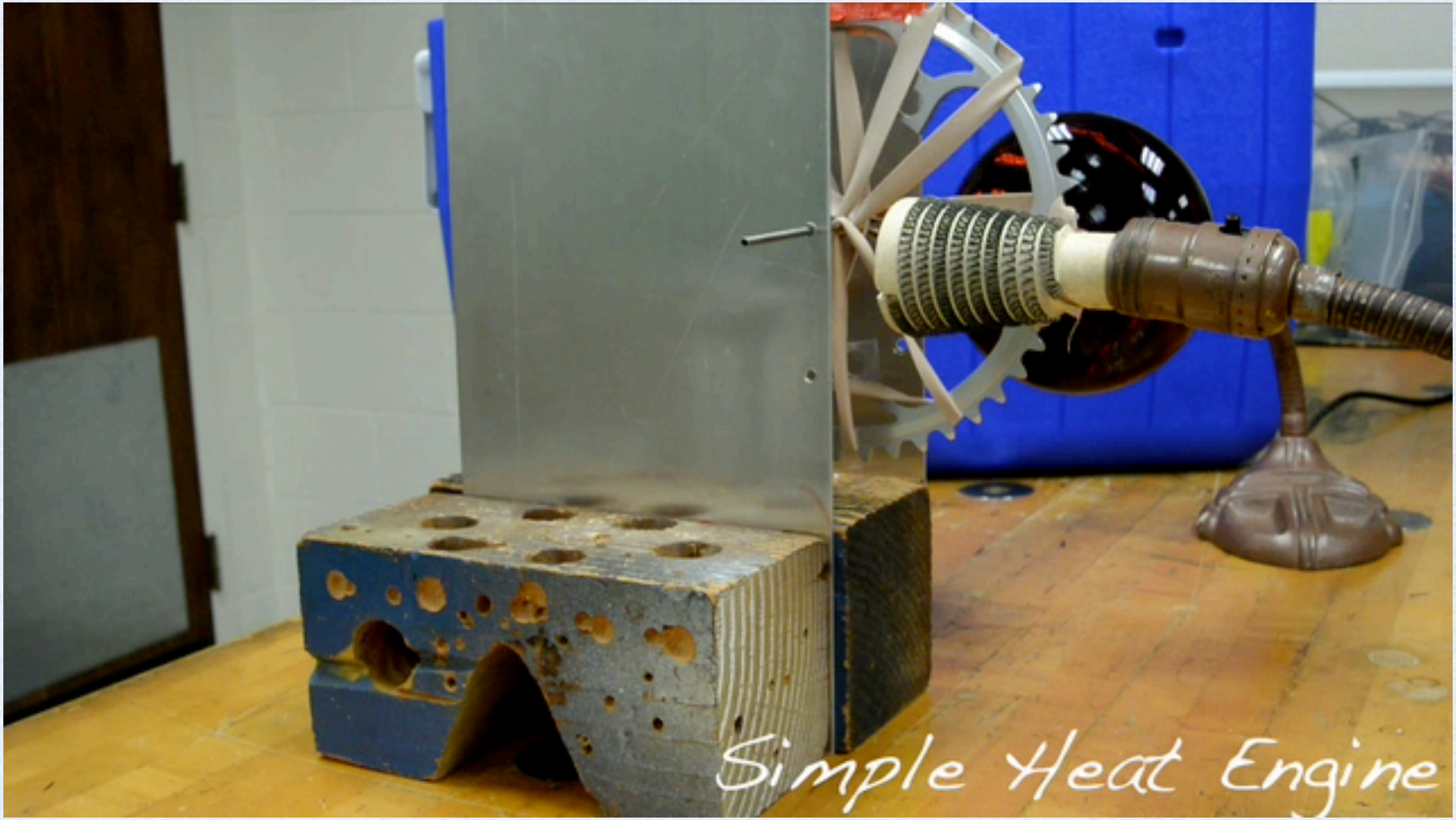
Phil Nelson

4.2.2 Polymer elasticity

Apart from water, our bodies are mostly made of polymers. Polymers have interesting properties.

A rubber sheet gets *colder* as it relaxes. You can even feel this with a wide rubber band on your lip or other sensitive area. But an IR camera makes a dramatic demo. **How could anything like that possibly happen?**

4.2.2 Polymer elasticity



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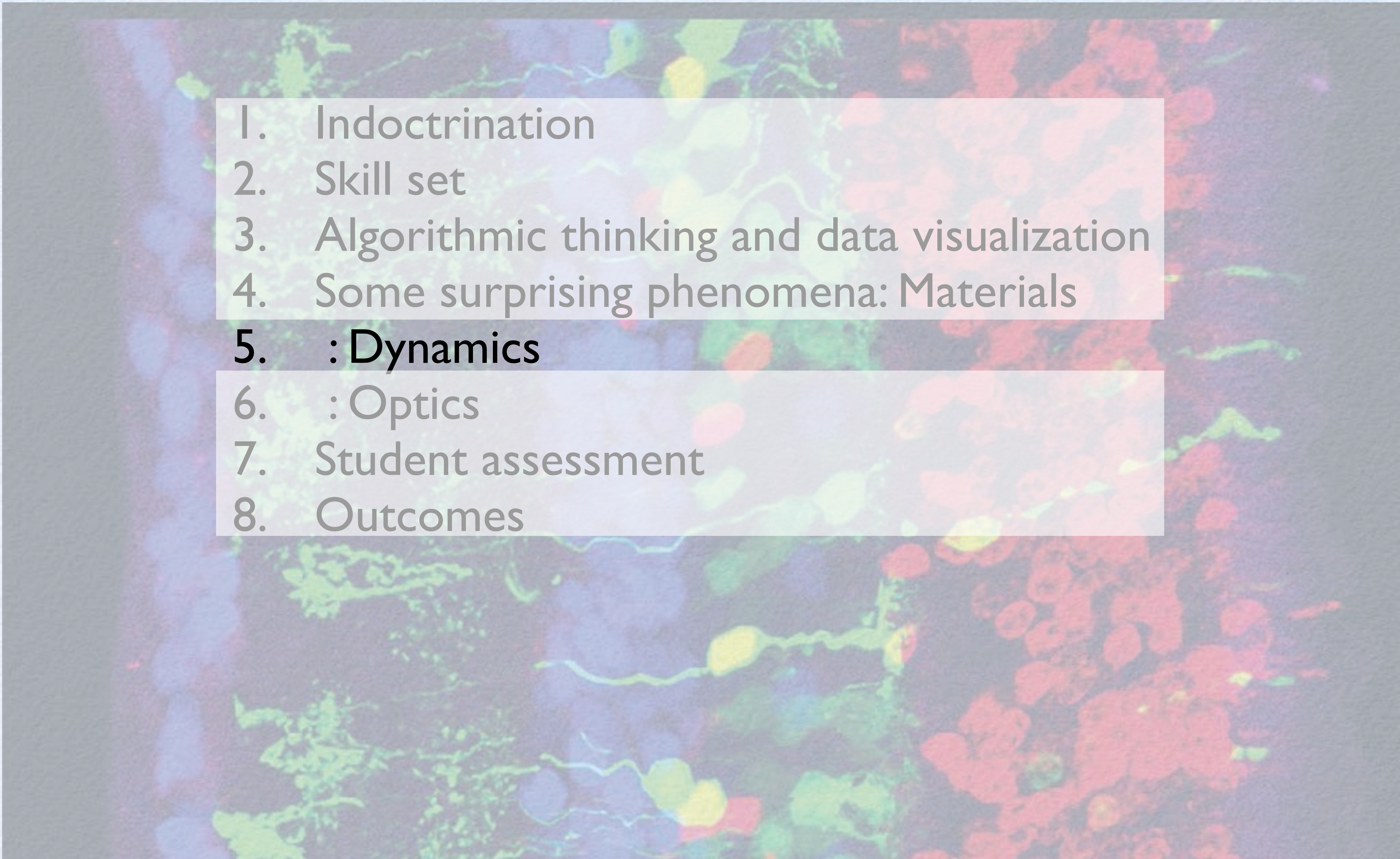

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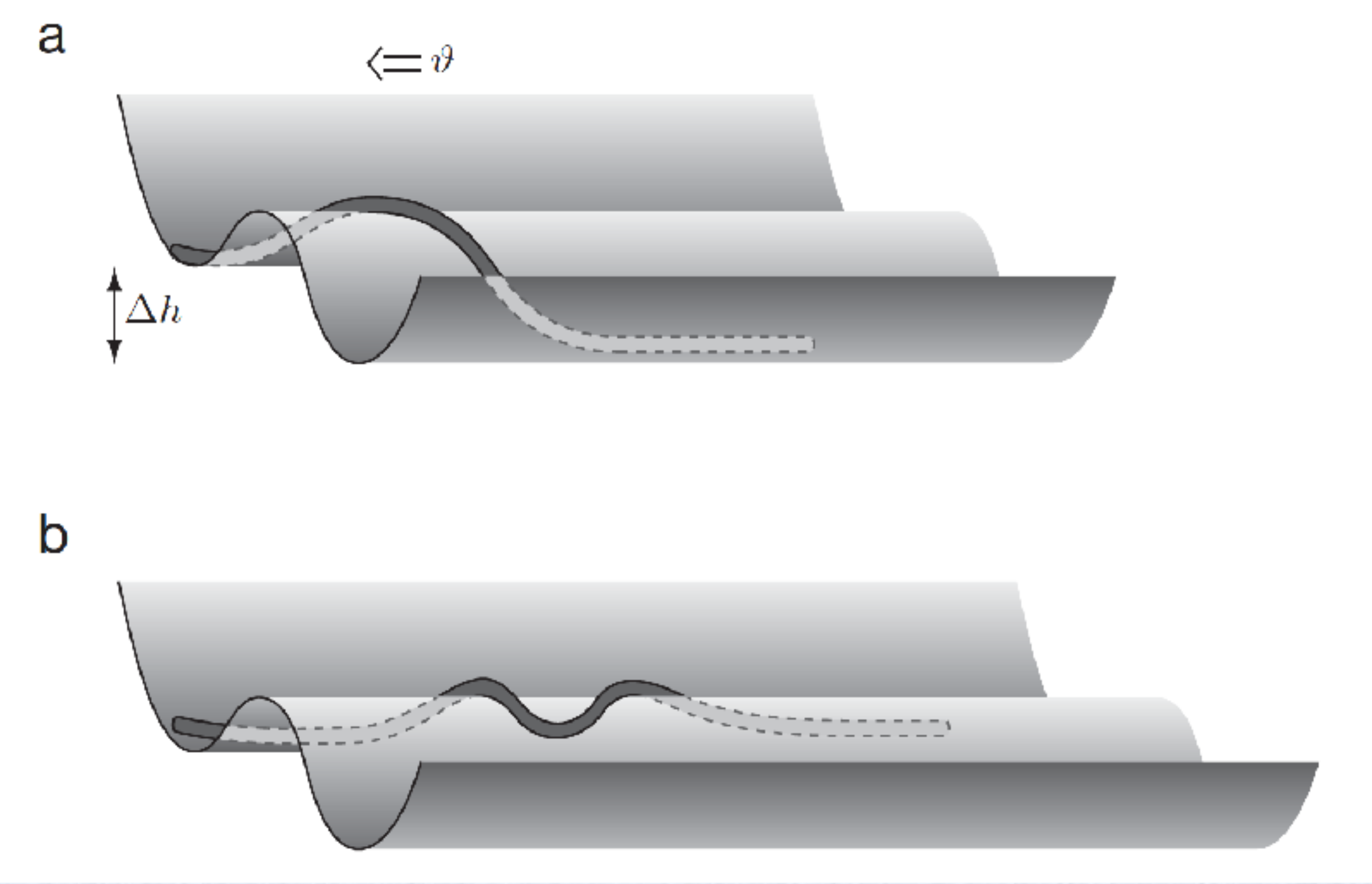
5.1.1 Mechanical solitary wave



From Nelson, *Biological Physics.*

Phil Nelson

5.1.2 Chemical waves

How could anything like that possibly happen?

Phil Nelson

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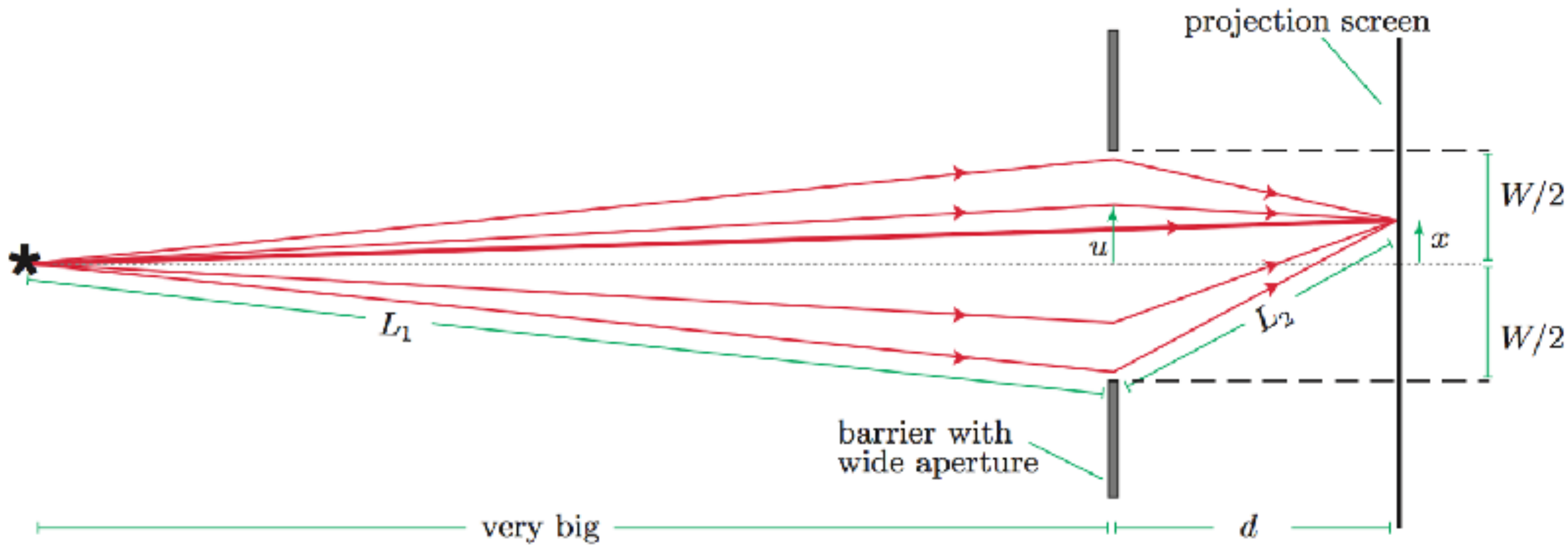
6.1.1 Diffraction: One wide slit

Bring in an adjustable slit. When it's 2 mm wide, you just get a shadow image. When it's 0.2 mm wide, you get a broad blur of light on the screen. In between you get interesting patterns.

How could anything like that possibly happen?

Back to the single, wide slit:



Everyday experience says that we'll see light on the screen between x = -W/2 and W/2.
That fits: If x is in that range, as shown, then there's a stationary-phase path (*heavy line*). That is, there's a path with *no kink*; nearby paths all have nearly the same phase.
If x is outside that range, there's no stationary-phase path.

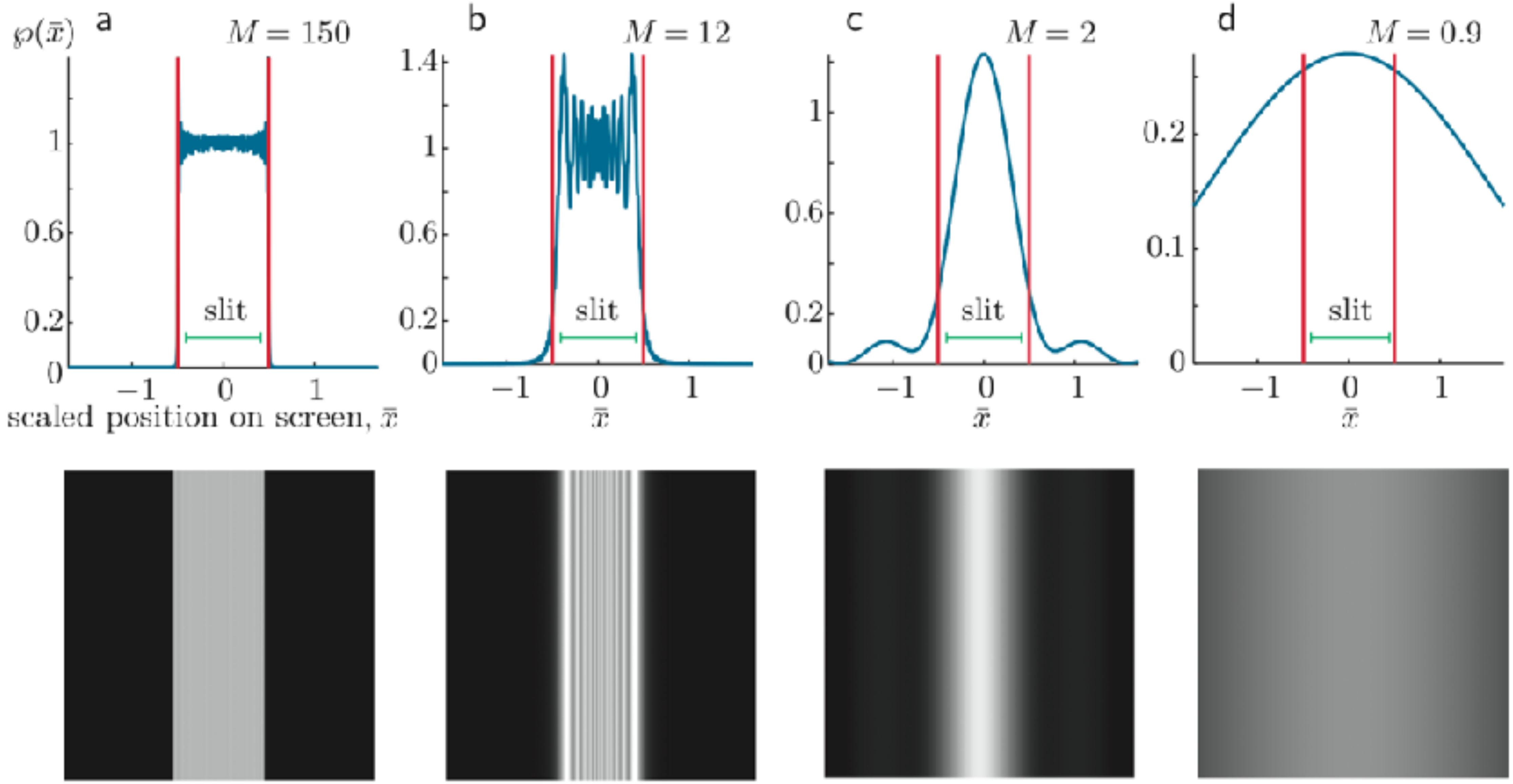


Figure 14.13: [Mathematical functions.] **Diffraction as aperture width decreases.** *Top:* Each panel shows the probability density for photon arrival (a constant times $|\Psi|^2$), as a function of $\bar{x} = x/W$, for various values of the parameter M defined in Equation 14.15. Rescaling x in this way means that in each case, the image of the slit in ray optics would correspond to the same range $-\frac{1}{2} < \bar{x} < \frac{1}{2}$ (*red lines*). See Problem 14.4 for details of the calculation. The separate values of the parameters d, λ, and W are irrelevant for these graphs; all that matters is the single composite quantity M. *Bottom:* Each panel shows the same information as in the panel above it, but as a simulated diffraction pattern: The gray level corresponds to the value of $\wp(\bar{x})$, times an overall scaling factor.

6.1.2 Diffraction: 1D array

Surprise! Not one of these things contains a single speck of blue pigment. For example, butterfly wings are covered with scales made from a *transparent, colorless* substance.

http://www.npr.org/blogs/health/2014/11/12/347736896/how-animals-hacked-the-rainbow-and-got-stumped-on-blue

A clue from butterflies:

Figure 5.3: [Photographs.] **Structural color versus pigments.** (a) The dorsal (top) side of a male *Morpho rhetenor* butterfly (see also the photo on page 45). (b) The dorsal side of a male *Cymothoe sangaris* butterfly. In both photos, the wings on the right-hand side are in their natural state, but the wings on the left-hand side have been saturated with an index-matching liquid. The pigment-based color of *Cymothoe* is barely affected, while the structural blue of *Morpho* is lost. The effect is reversible: When the liquid evaporates, the color returns. [Courtesy Glenn Smith; see Smith, 2009.]

How could anything like that possibly happen?

The algebra gets a little involved, but basically we just use the *geometric series*.

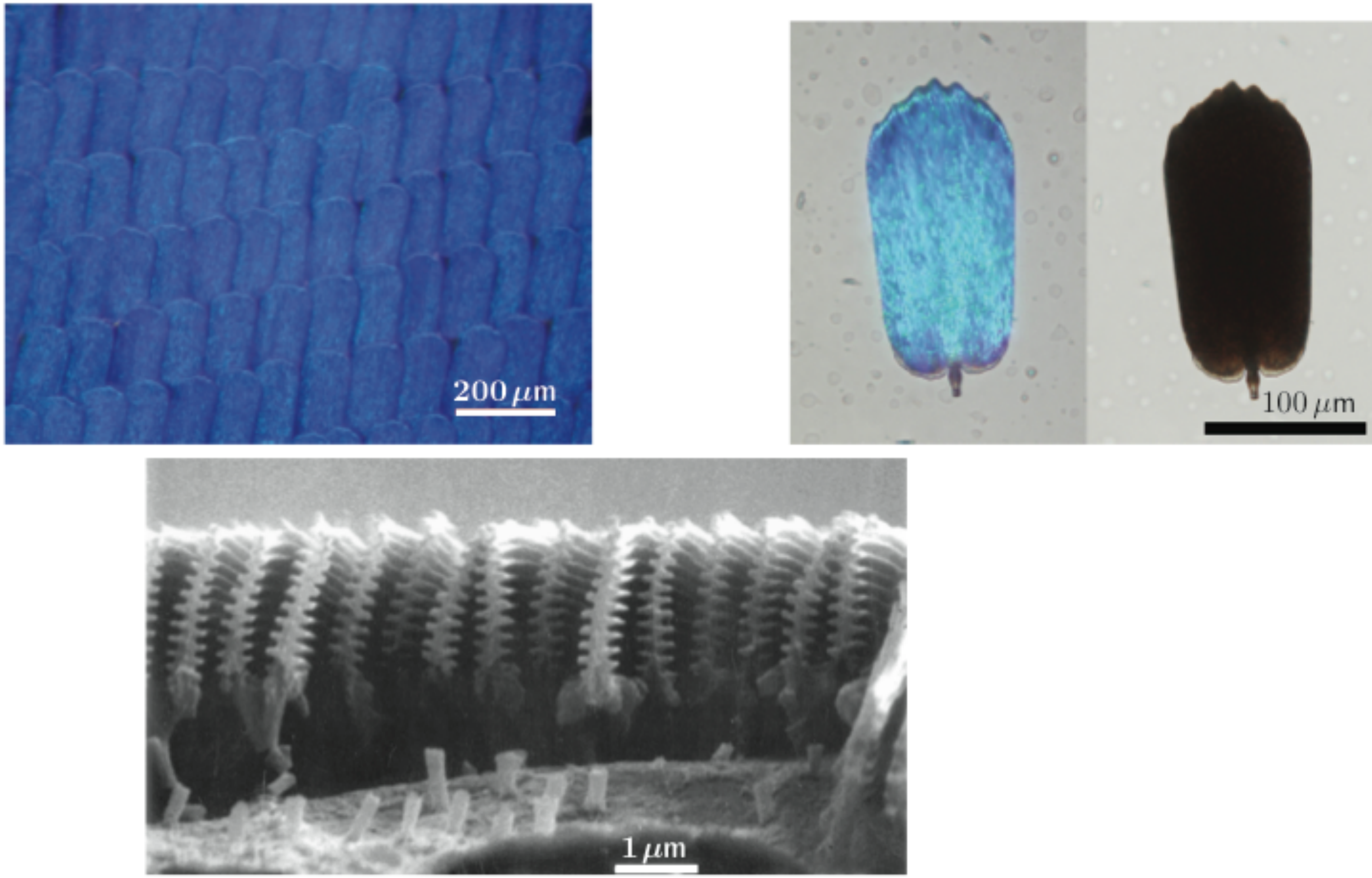
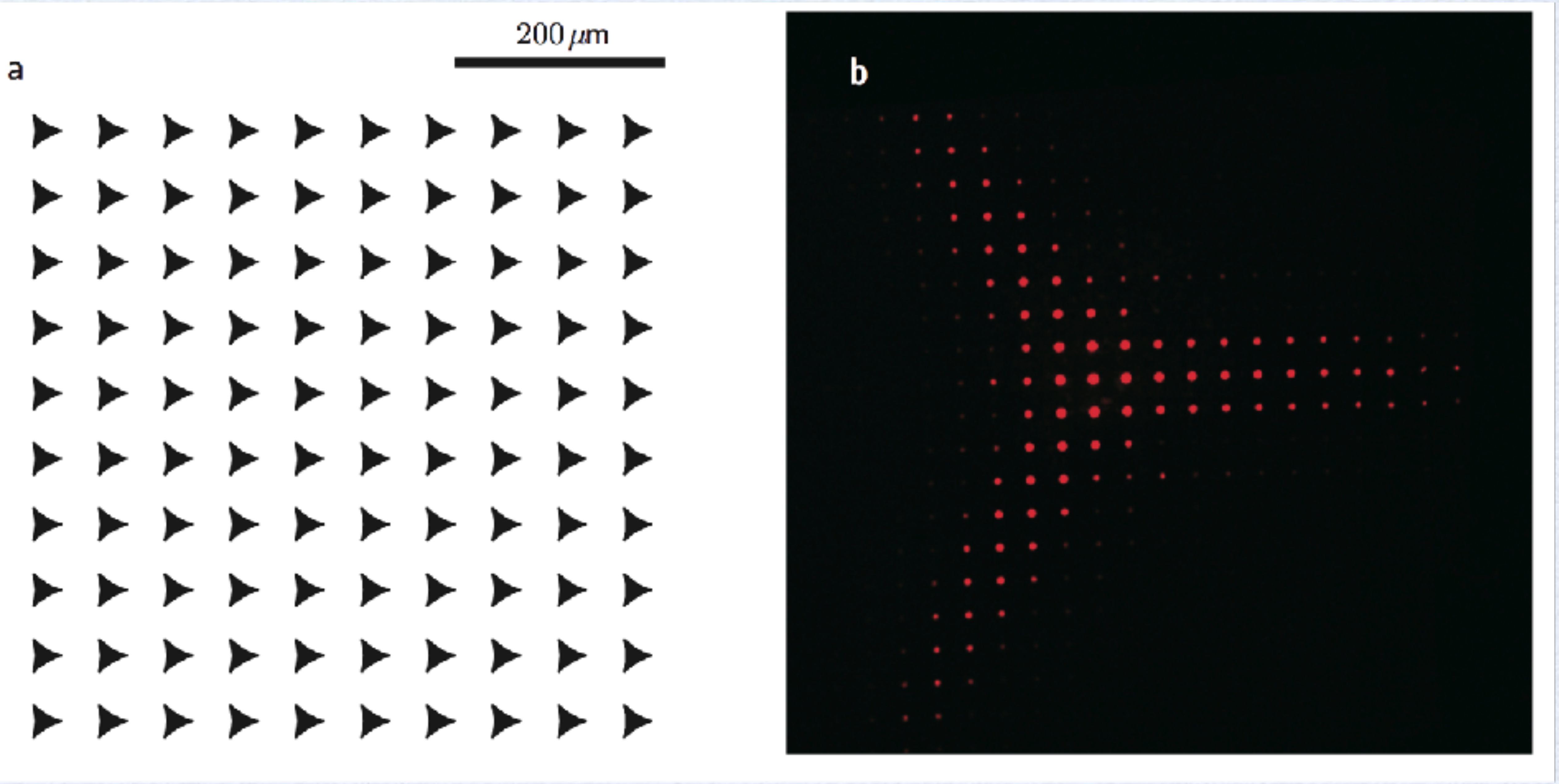


Figure 5.4: **Scales on the wing of the butterfly *Morpho rhetenor*.** (a) [Light micrograph.] Overall arrangement of scales. (b) [Light micrograph.] Individual ground scales observed via reflection (left) and transmission (right) microscopy. (c) [Scanning electron micrograph.] Cross section of a scale. [(a,b): From Kambe et al., 2011. (c): From Kinoshita et al., 2002.]

6.1.3 Diffraction: 2D array



The angular size of the image (dimensionless) depends on the physical size of the pattern (a length) and the color of the light. By dimensional analysis, that color must transmute into a length.

How could anything like that possibly happen?

Oops.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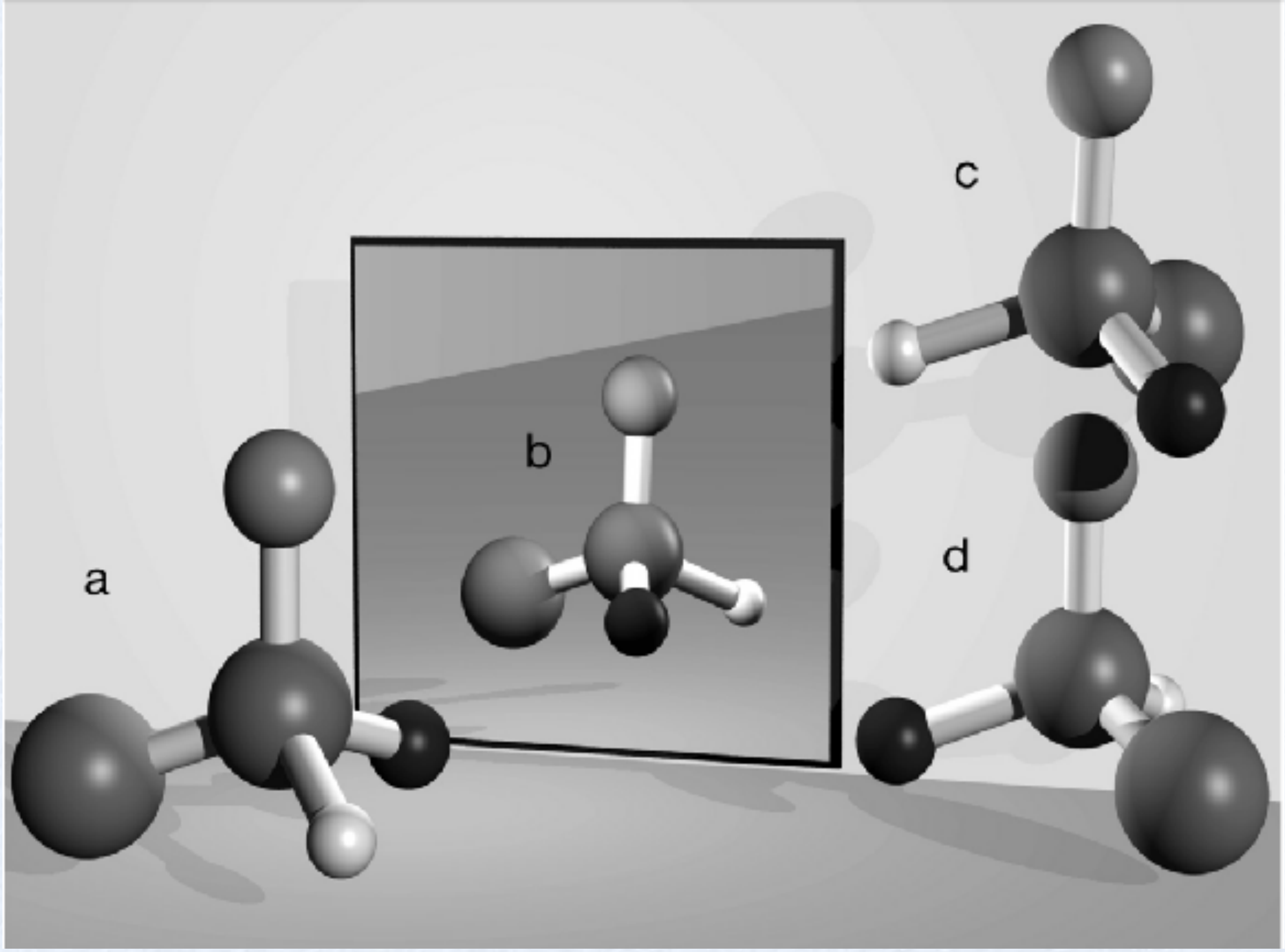
6.2 Geometry of molecules

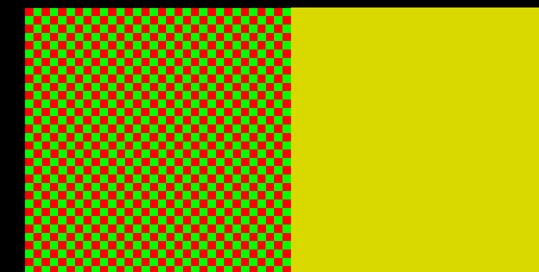
A solution of sugar rotates the polarization of incoming light. Water doesn't.



How could anything like that possibly happen? Specifically, how does the solution know *which way* to rotate the light?

6.3 Color perception

These two panels may look similar in color, particularly if you’re sitting in back (or remove your glasses).



But when I blow them up you see that actually the left panel consists of vivid green and red!

How could anything like that possibly happen?

I.e., How could your eyes be so bad that they can't even tell spectral yellow from red+green?

Thomas Young, 1802

An astonishingly modern chain of hypotheses:

1. Light comes in different flavors (let’s call them “spectral positions”).

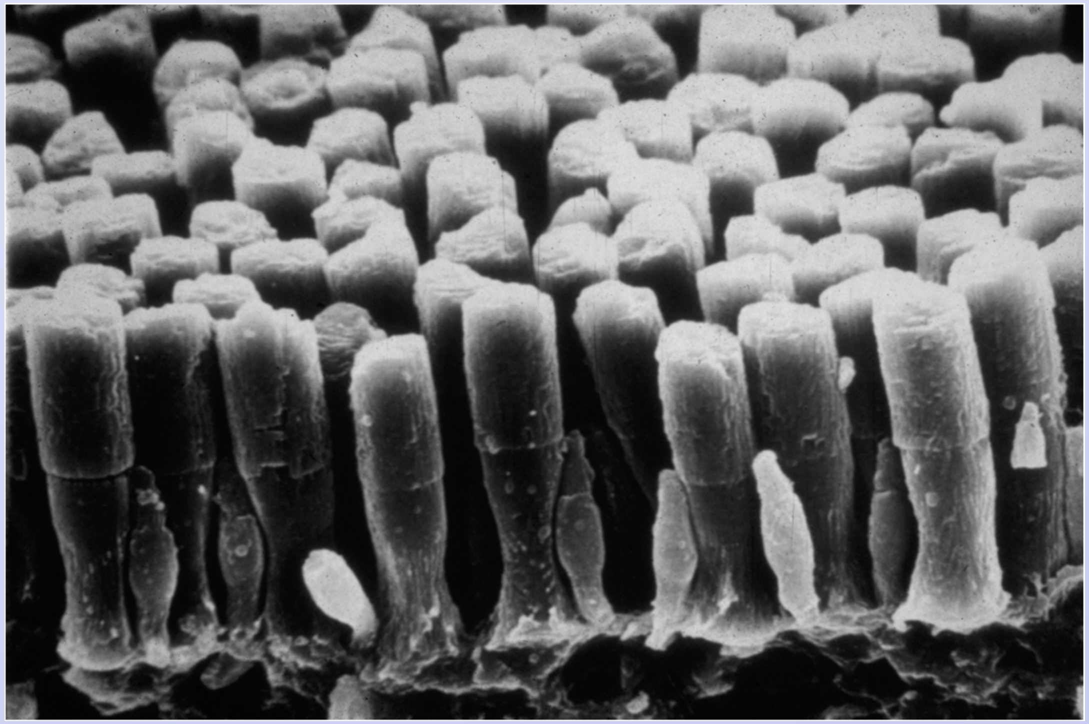
2. Even when mixed, those flavors retain their distinct character and can be re-separated.

3. “Color” involves the relative *amounts* of these flavors.

4. Our eyes contain a mosaic of “pixels” (“photoreceptor cells”).

5. *All the brain can know* about color is what it hears these cells saying.

And the key point: Each photoreceptor cell is *only sensitive to a particular range of color*: The cells are “tuned.”



Rod cells and cone cells in the retina of the tiger salamander. Image by Scott Mittman and Maria T. Maglio.

Thomas Young (continued)

Continuing Young's chain of reasoning,

1. Light comes in different flavors ("spectral positions").
2. Even when mixed, those flavors retain their distinct character and can be re-separated.
3. "Color" involves the relative *amounts* of these flavors.
4. Our eyes contain a mosaic of "pixels" ("photoreceptor cells").
5. *All the brain can know* about color is what it hears these cells saying.

6. Each photoreceptor has a distinct sensitivity range.

7. They come in just 3 classes. Each cell has exactly the same sensitivity range as all the others *in its class*.

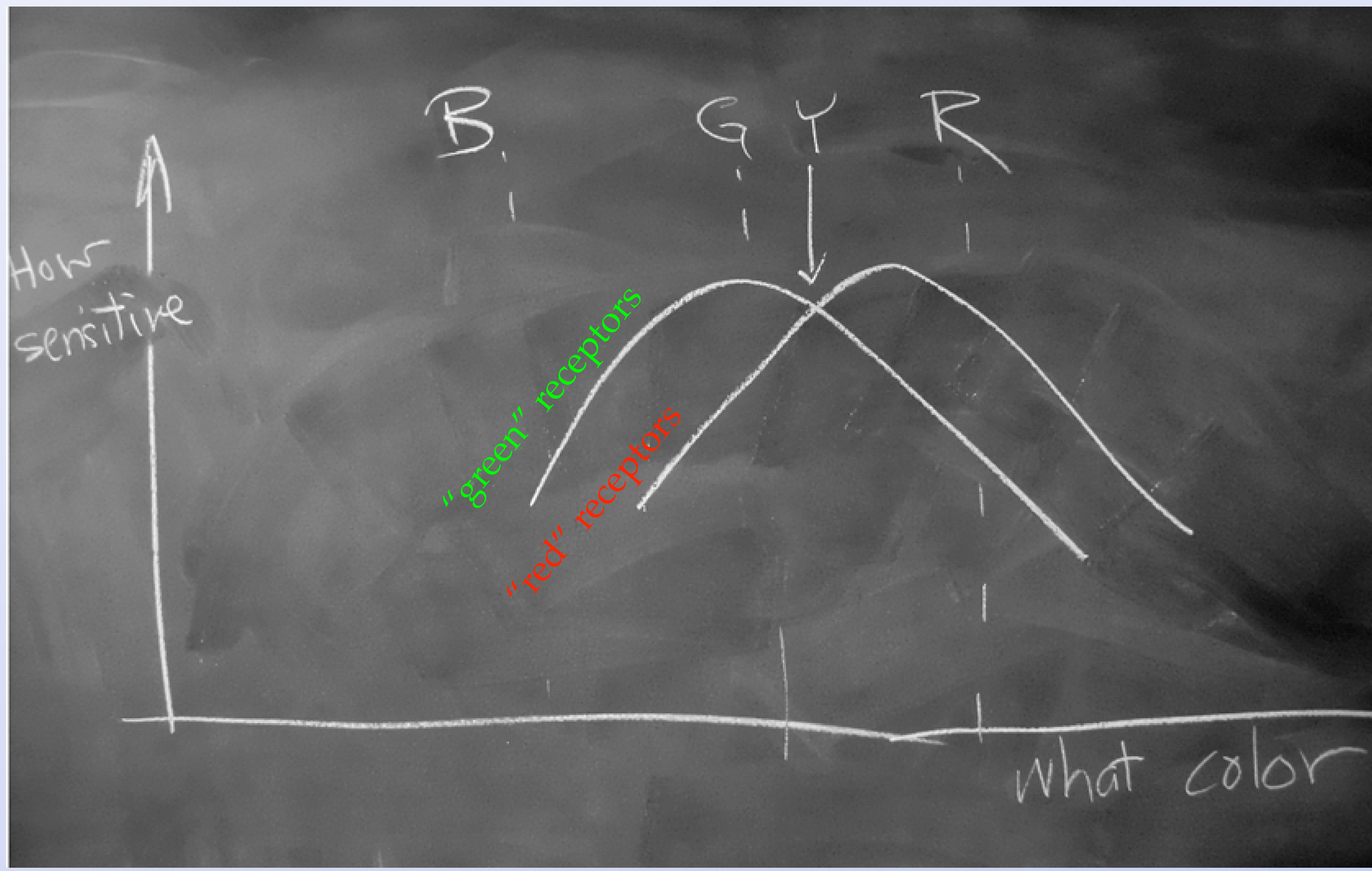
Proposed resolution of the R+G=Y paradox

This list of the sensitivities of a photoreceptor cell to light of various spectral positions can also be drawn as a graph. Unlike the light spectrum, which tells “how much is present,” this **sensitivity curve** expresses “how much is *needed*” to get a response to each kind of light.

Forget about blue and consider only red- and green-sensitive cells:

If the sensitivity curves *overlap*, then sending in pure spectral yellow will excite both the green-sensitive and the red-sensitive cells equally.

But the same result can be achieved by sending in equal amounts of pure green and pure red light!



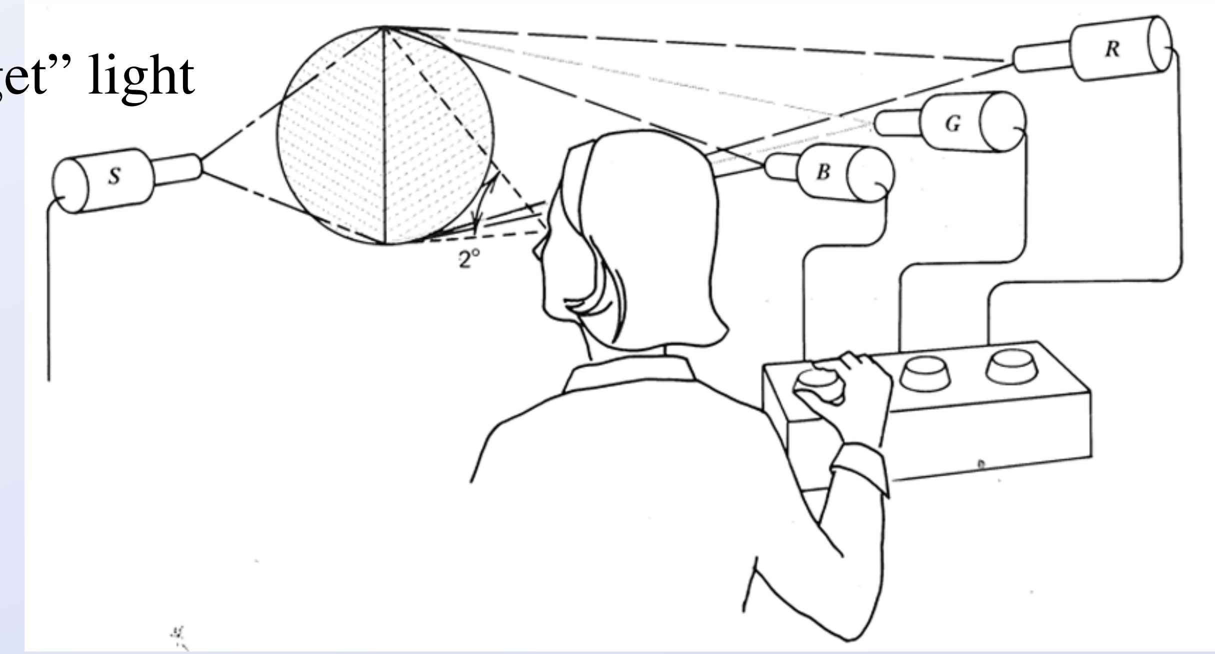
The brain can’t tell the difference because *all it knows is what the receptor cells tell it*.

A quantitative test

OK: better *nail the case* for Young hypotheses before we call the VCs.

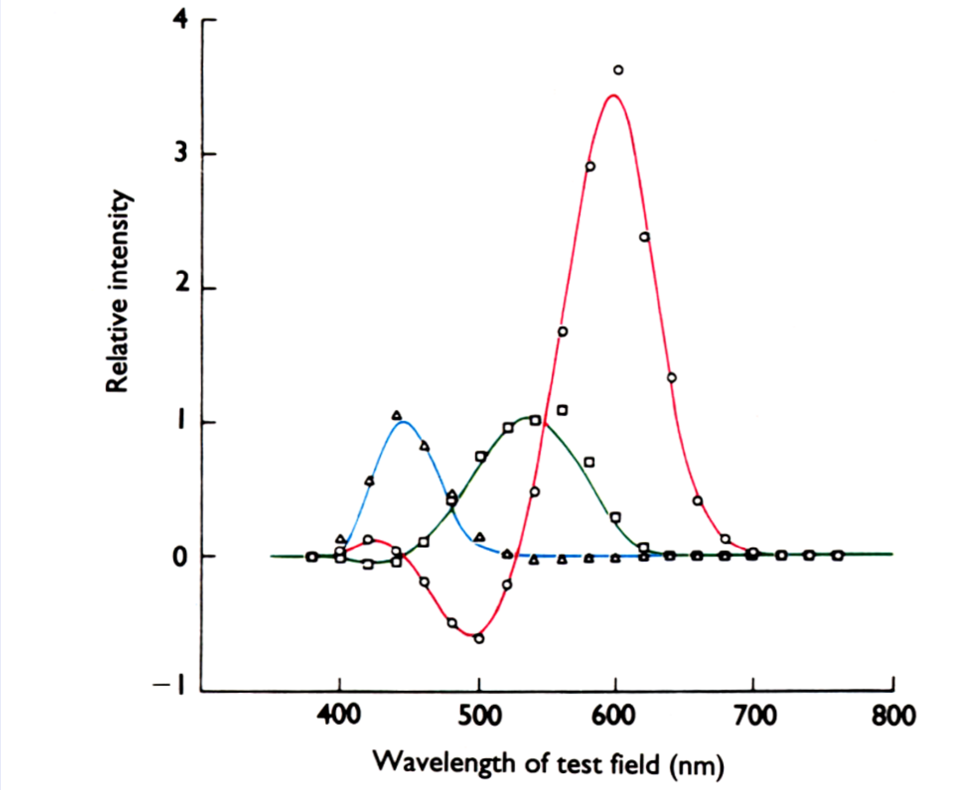
Quantitative, detailed, testable prediction is crucial.
That's our discipline: Don't go too far on a tangent without experimental *authority*.
Ideally we'd like a lot *more* experimental data points than unknowns (fit parameters).

"Target" light



3 standard lights.

Result: three "color matching curves":

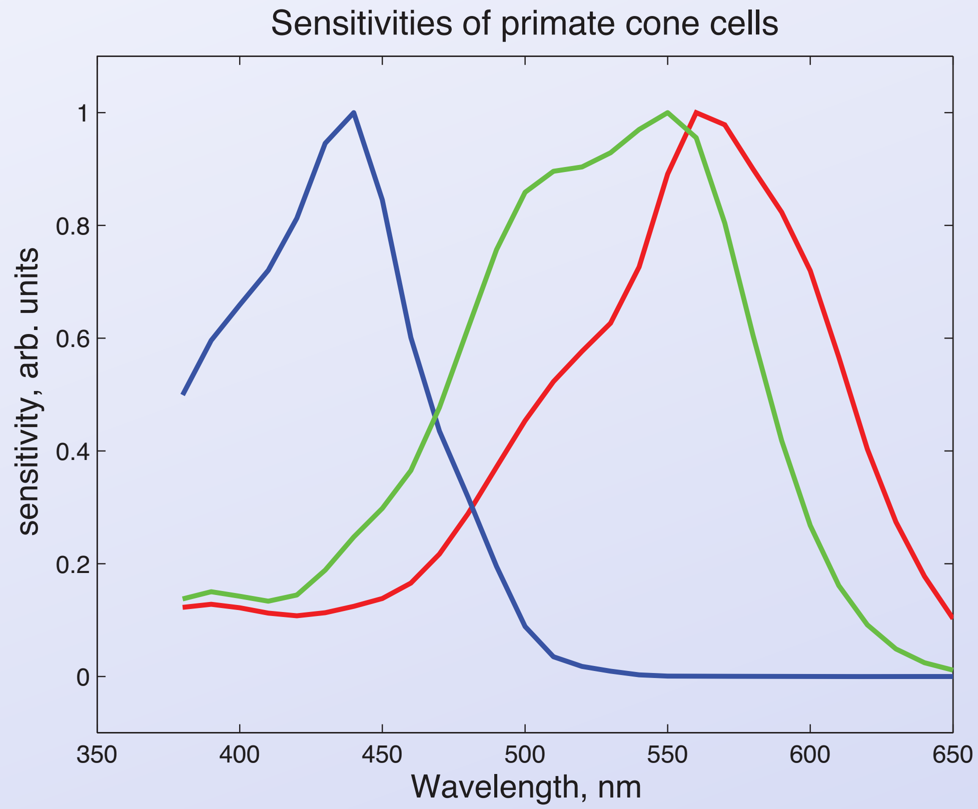


How the theory makes testable predictions

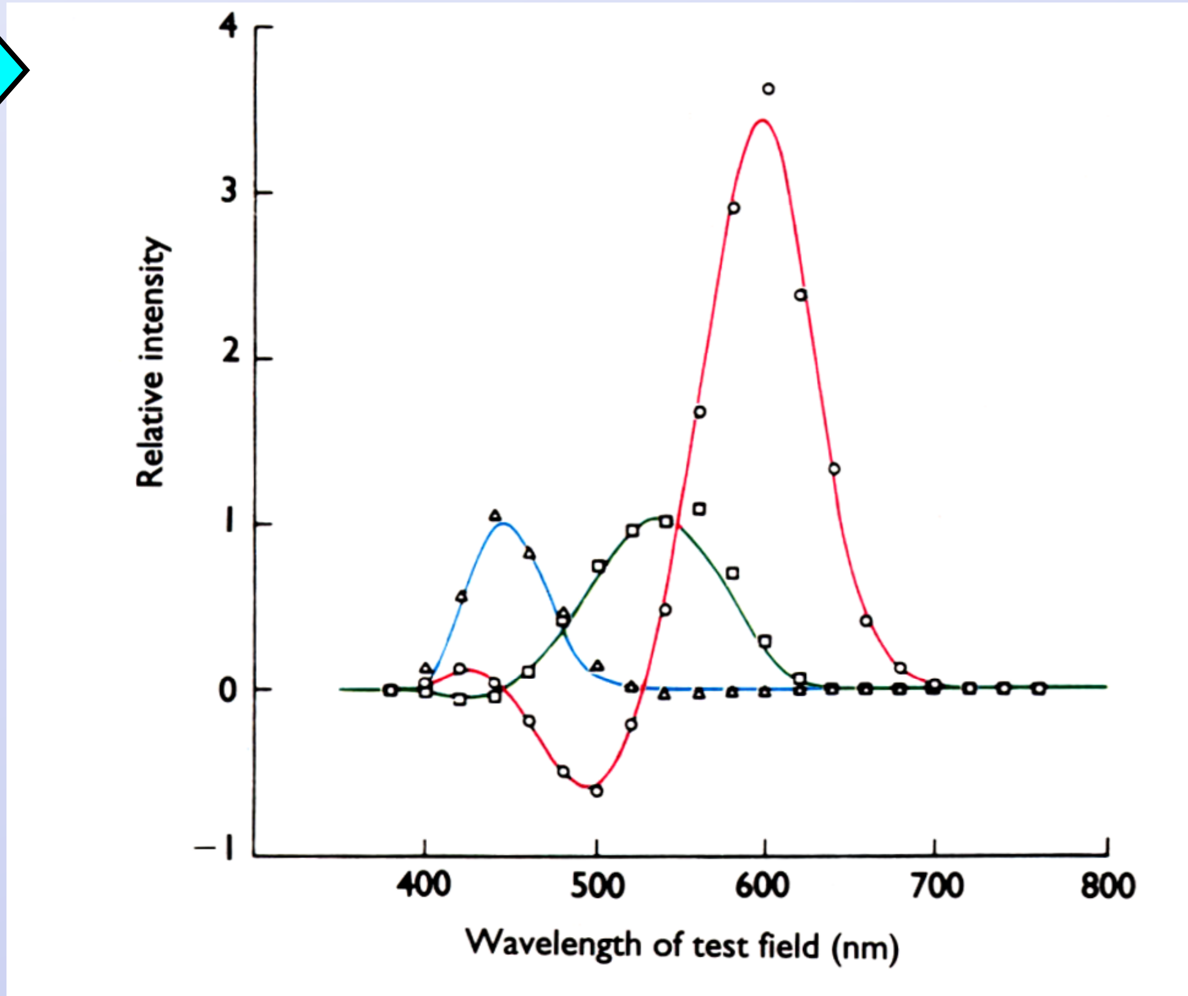
Once we measure the sensitivity curves, we can predict the response of each photoreceptor to any possible light spectrum. Then we can find out how much of each of the three standard lights is needed to *mimic* the response elicited by the target light, by solving *three linear equations*.

Left: The sensitivity curves of color photoreceptors indeed fall into three well-separated classes. Notice the big overlap between the "red" and "green" curves.

Right: Once those curves are known, the color-matching functions can be *predicted*, and *they agree with psychophysical measurements*.

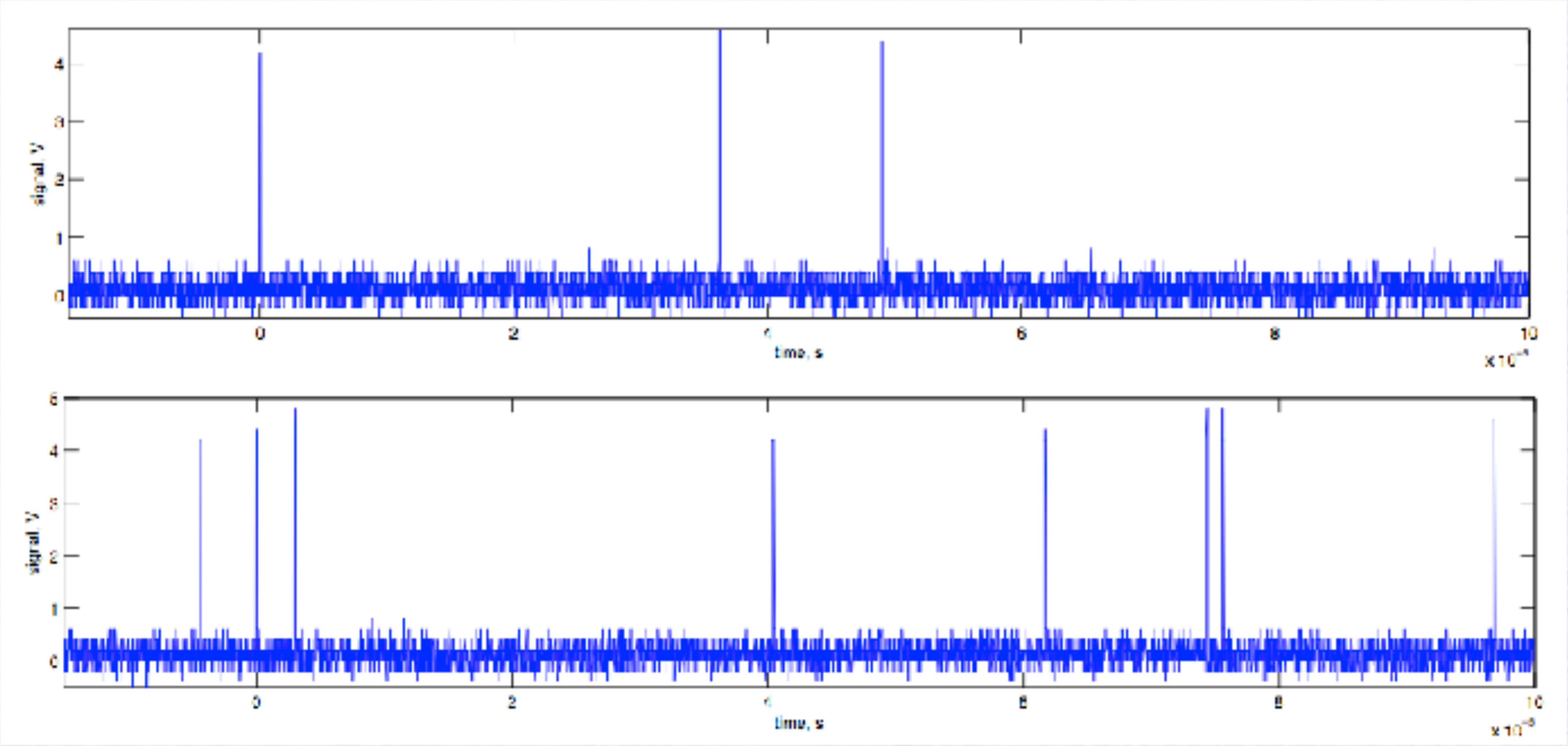


Curves: data from color-matching experiments.
Dots: predictions from theory.



Data from Julie Schnapf and Denis Baylor 1987.

6.4: Light is lumpy

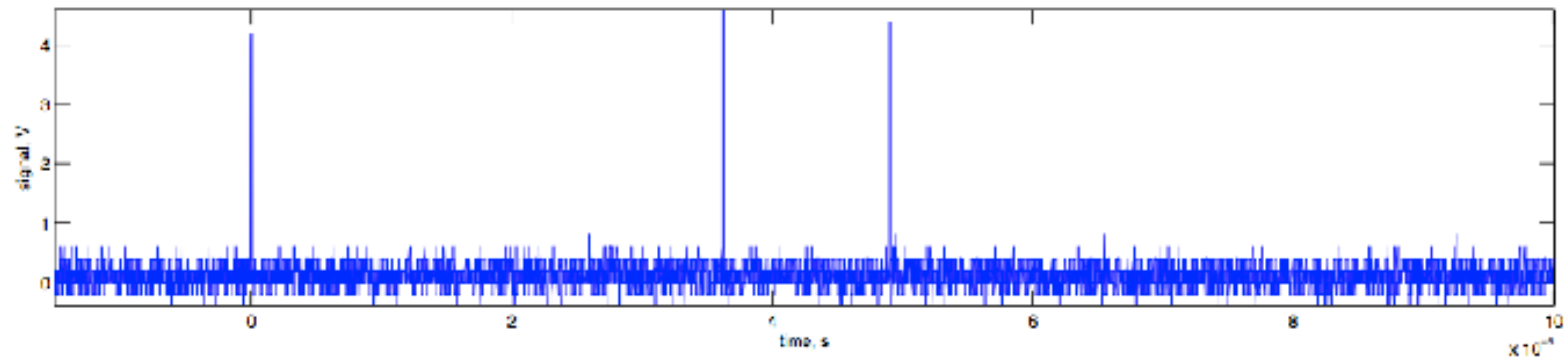


How could anything like that possibly happen?

Phil Nelson

We can detect very dim light with a photomultiplier tube or avalanche photodiode. Either way, light causes discrete clicks in the detector. ***Dimmer light gives equally big clicks, just less frequent***:

Dim illumination:



Slightly brighter (still very dim):

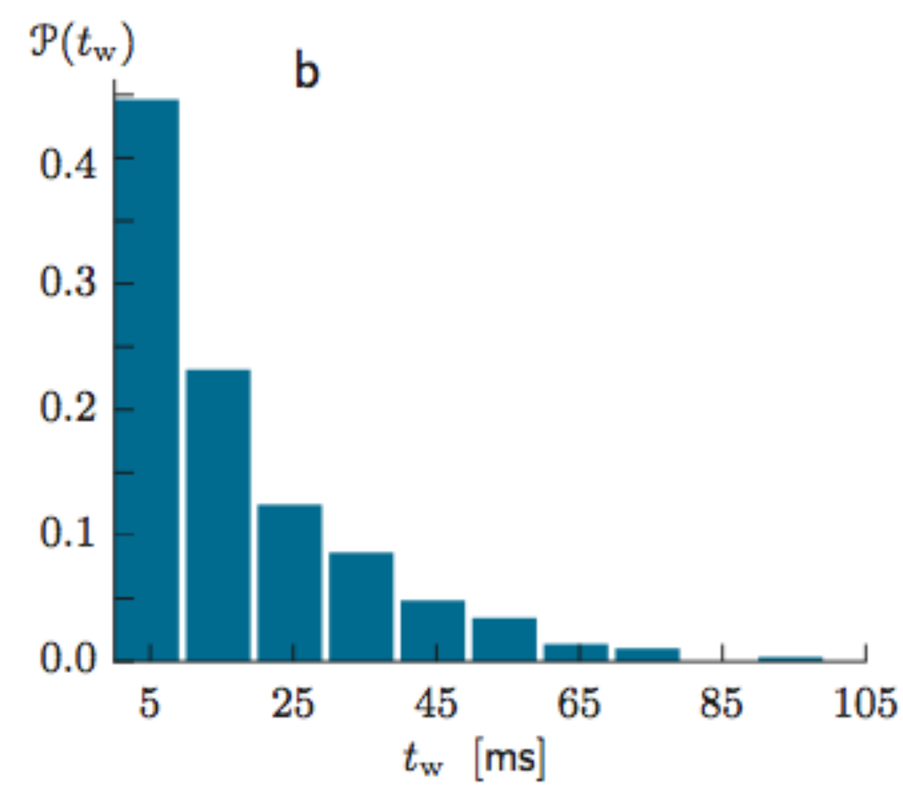
uniform blips audio clip

actual experimental data

simulated Poisson process

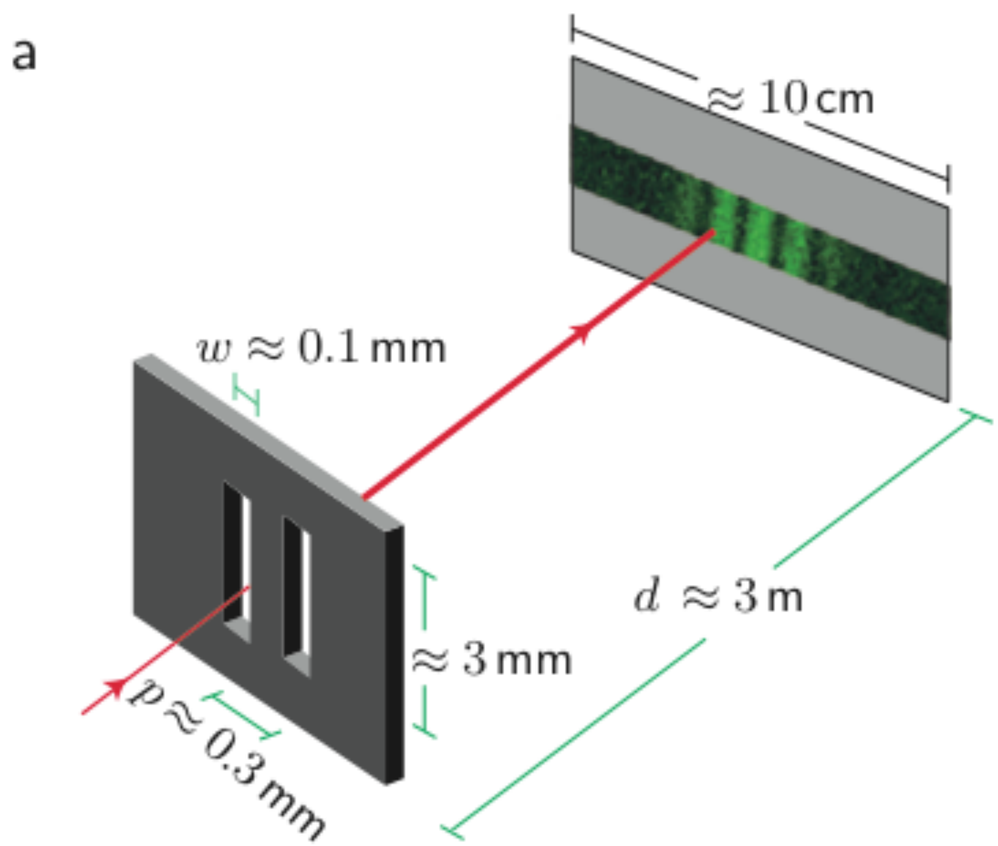
Experimental data courtesy J. F. Beausang.

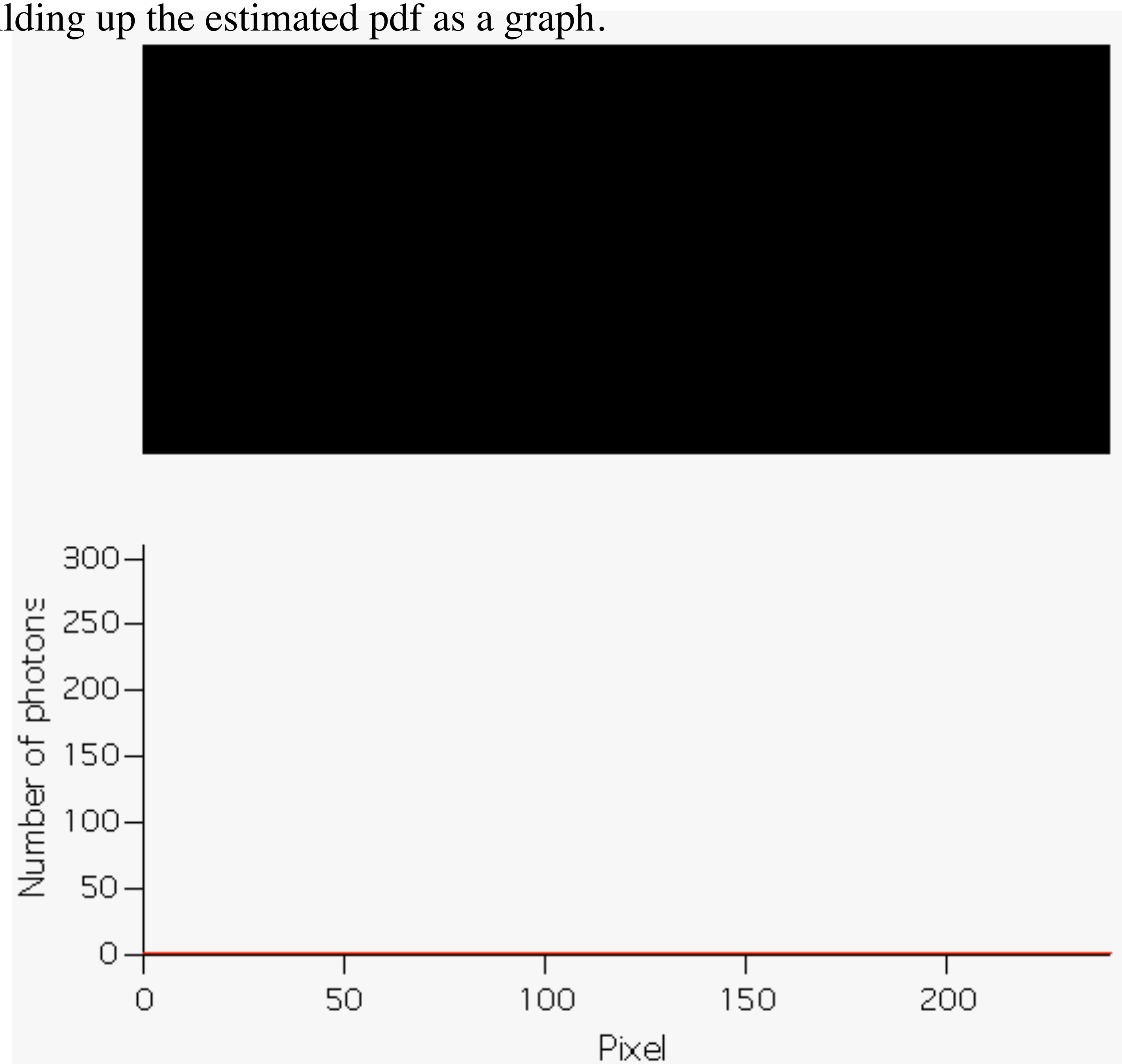
How can we learn anything from "just noise?" To get a handle on what's going on, notice that the absolute times of individual clicks aren't very significant, but the *intervals* between successive clicks are:



Hmm. That looks familiar. Could that stupid Geometric distribution have anything to do with the cosmic mystery of light? Which bugged Einstein all his life?

Every time a camera pixel recorded a blip, the corresponding pixel in the animation is turned on, and stays on. This way you can see the estimated pdf build up gradually. The final image is what you might see if all of those photons arrived in a short burst, too fast for you eye to resolve. Similarly in the histogram, for each photon the bin corresponding to the photon's *x* value is incremented, eventually building up the estimated pdf as a graph.





How could anything like that possibly happen?

http://www.physics.upenn.edu/biophys/Media/diffractbuildup/RochDiffractPhoton.mov

Phil Nelson

Fluorescence

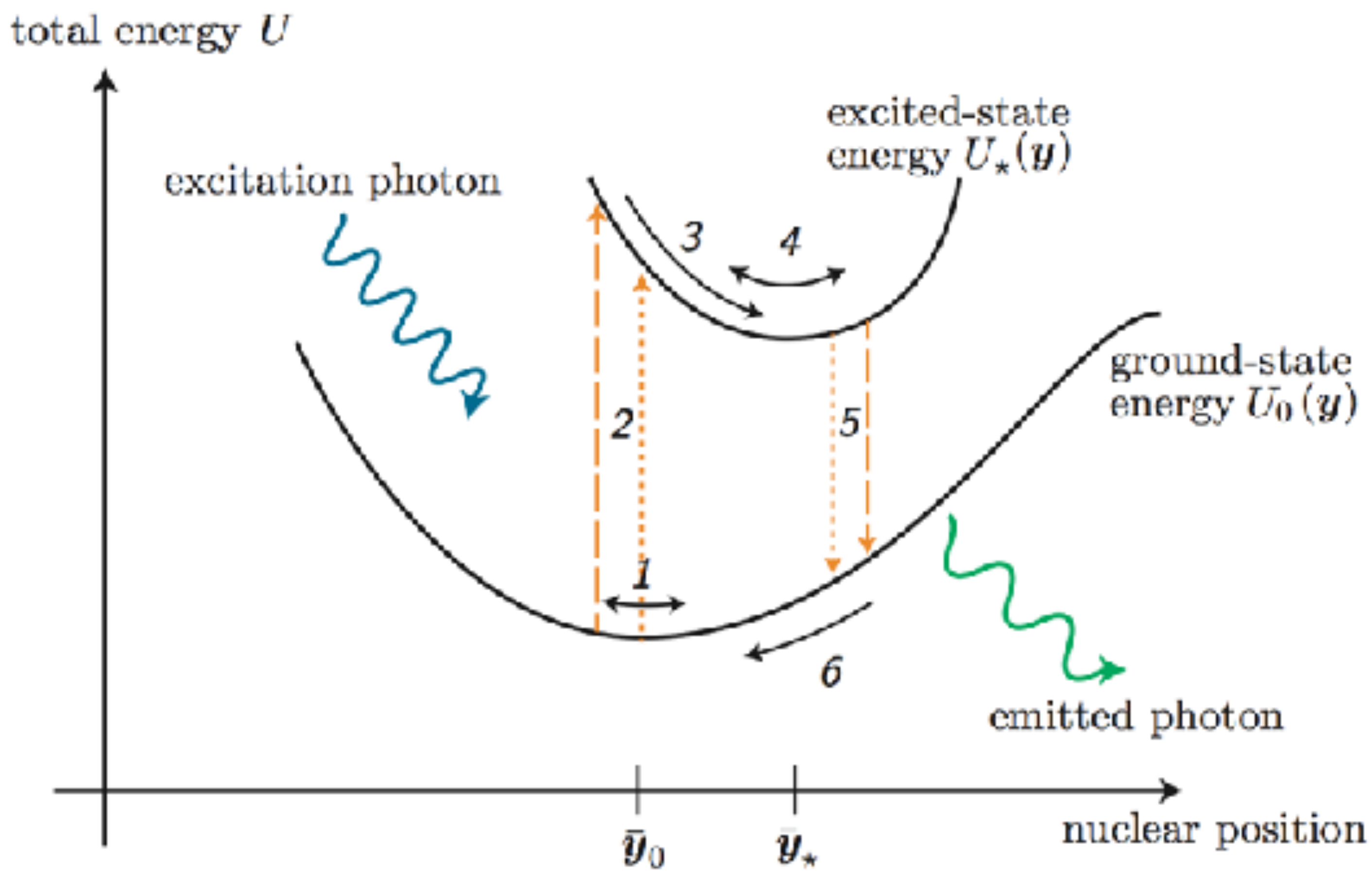


Figure 1.8: [Schematic energy diagram.] **Physical model for fluorescence.** *1*: The positions of the nuclei in a molecule fluctuate near $\bar{\boldsymbol{y}}_0$, the minimum of the energy function $U_0(\boldsymbol{y})$ appropriate for electrons in their ground state. *2*: Absorption of a photon (*left*) promotes the electrons to an excited state. The differing heights of the *dashed* and *dotted* lines indicate that the required photon energy depends on the momentary value of the nuclear position coordinate $\boldsymbol{y}$. *3*: The nuclei respond by moving toward the minimum of the new, excited-state energy function $U_\star(\boldsymbol{y})$. *4*: Then the nuclei fluctuate about the new minimum $\bar{\boldsymbol{y}}_\star$. *5*: Eventually a new photon is emitted (*right*), sending the electrons back to their ground state. The differing heights of the *dashed* and *dotted* lines again indicate that there is variation in the precise energy of the emitted photon. *6*: The nuclear positions then readjust back to the neighborhood of $\bar{\boldsymbol{y}}_0$. The difference in length between the ascending and descending arrows represents the Stokes shift, characterizing this fluorescent molecule (fluorophore).

Phil Nelson

We also get a...

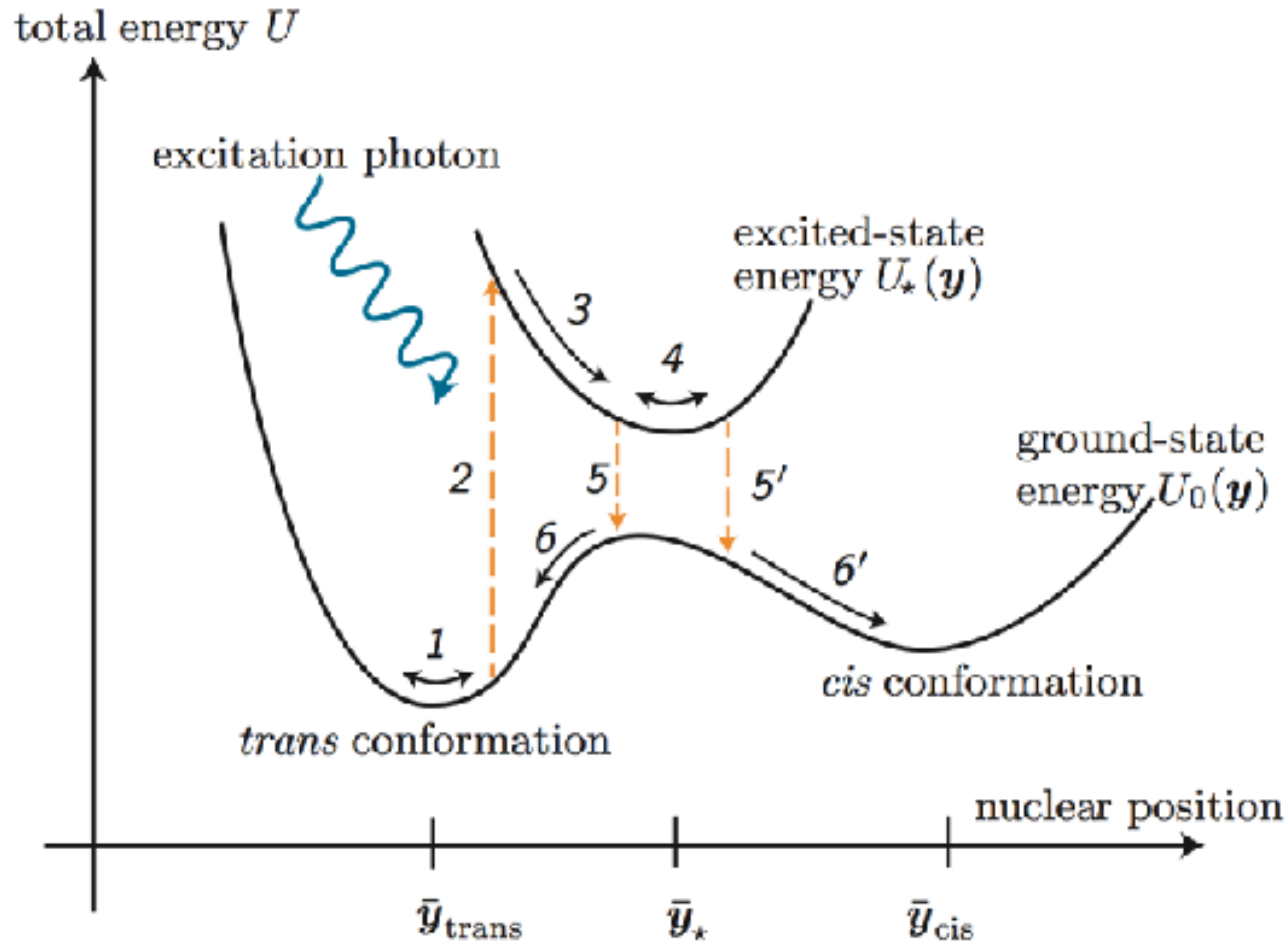


Figure 1.11: [Schematic energy diagram.] **Physical model for photoisomerization.** The first steps are analogous to those in Figure 1.8. Now, however, the ground-state energy function has two local minima, at $\bar{y}_{trans}$ and $\bar{y}_{cis}$. Promoting the molecule to its excited electron state sometimes enables it to fall back to a different conformation from the one in which it began (*5′–6′*), bypassing the ground-state energy barrier between the two conformations. Depending on the momentary configuration at the time of emission, however, the molecule may instead return to its initial conformation (*5–6*). Steps *5* and *5′* may or may not involve photon emission; for example, energy may instead be lost via collision.

Note that ordinary thermal jostling can in principle achieve the “activation energy” needed to make this conformational change occur spontaneously, without light. But in practice that will never happen at room temperature if the barrier is more than about 20 pN nm high. You should compute the energy of a visible photon and compare it to 4 pN nm, which is the typical magnitude of thermal energy at room (or body) temperature.

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Take it up another notch:

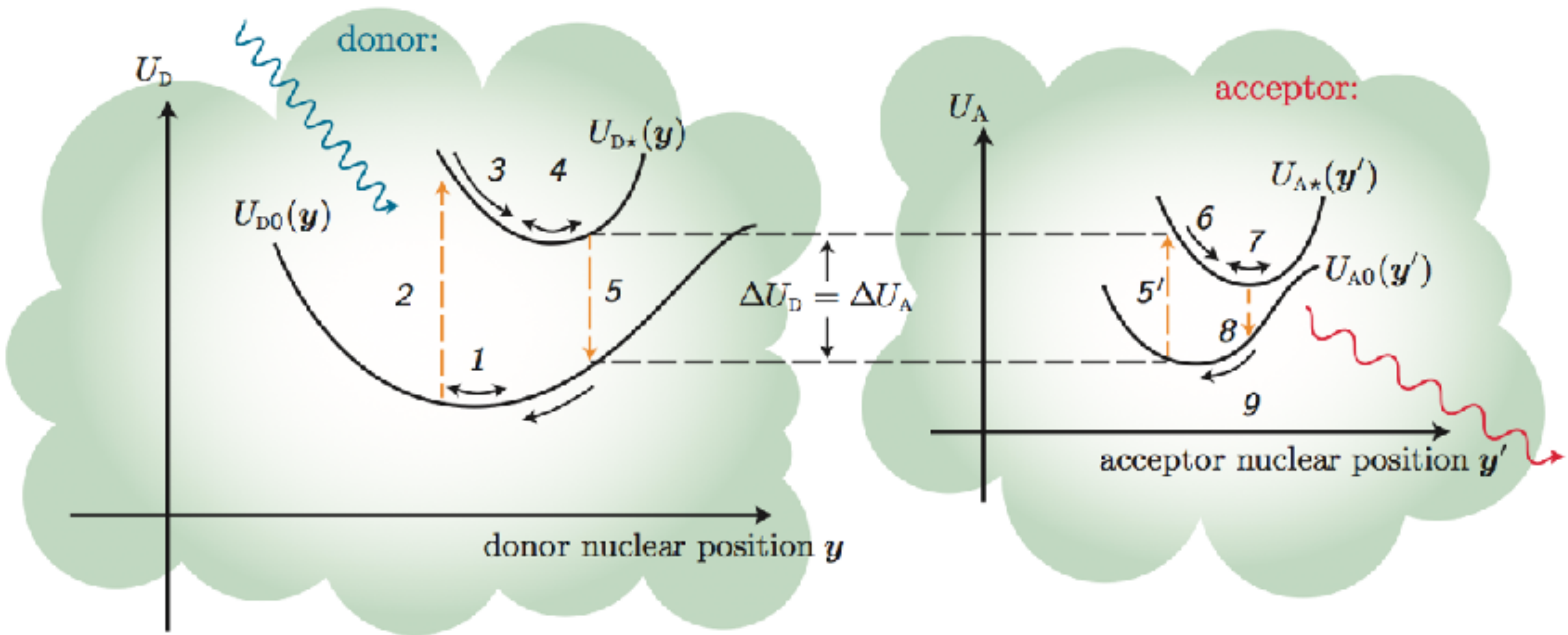


Figure 1.19: [Schematic energy diagram.] **Physical model of fluorescence resonance energy transfer (FRET), an elaboration of Figure 1.8.** *1–4*: Initially the donor enters its excited state as usual. *5,5′*: The donor's momentary configuration y determines an energy release $\Delta U_D = U_{D\star}(y) - U_{D0}(y)$ for return to the ground state. When the acceptor is distant, then the donor can release this energy by emitting a photon, as usual. When the acceptor is near, however, it can instead happen that its momentary configuration y' determines a ΔU_A equal to ΔU_D. In this case, the excitation can pass directly from donor to acceptor, without any intermediate photon. *6*: The excited acceptor delivers some excess energy to its surroundings as heat, preventing return of its excitation back to the donor. *7–9*: Eventually the acceptor emits a photon, with the same emission spectrum as if it had been directly excited.

6.5 Planetary climates

What is the most important scientific question of all time? Surely the answer is: Climate.

So, every academic discipline should be asking, "What can we offer students that is relevant to this question?"

Climate may seem distant from biophysics: The Earth system does not reproduce and hence did not evolve via descent with modification in the presence of natural selection. In that sense, planets are not “alive.” But planetary systems are complex and self-regulating, with many interesting feedbacks, so the subject has much in common with the physiology of living organisms. Moreover, our own planet hosts a biosphere that has itself made major modifications to the climate. So whether or not we call it “alive,” some of the concepts of biophysics turn out to be relevant.

The naked and the clothed

Some planets have atmospheres. But the atmospheres of Earth and Venus are mostly transparent to the solar spectrum, apart from the reflection that we already accounted for, so they have little effect on surface insolation, which is mostly in the visible band. Such radiation zips right through the atmosphere to the surface, warming it.

When we get quantitative, however, we see that story is missing a big part of the energy budget:

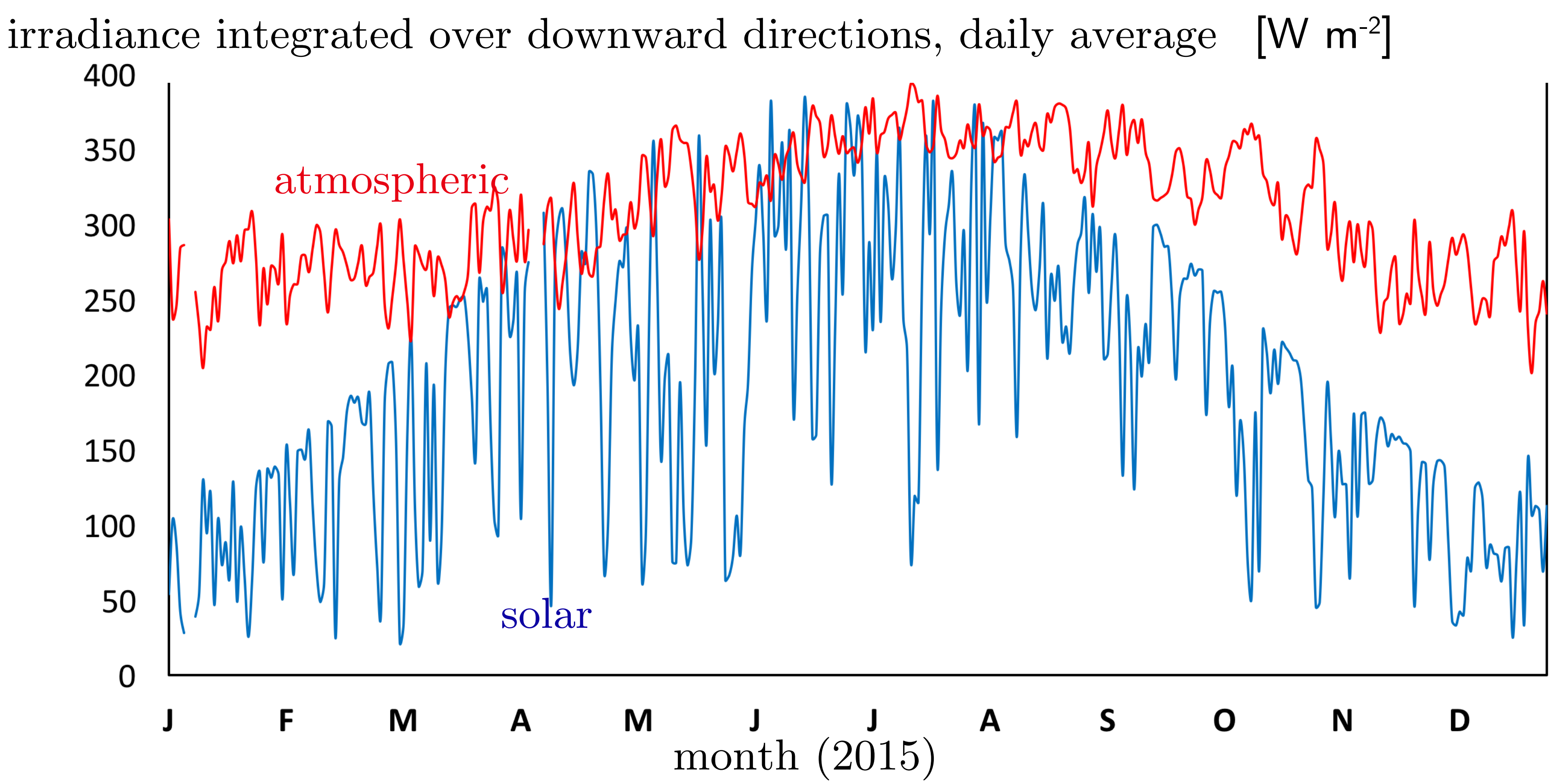
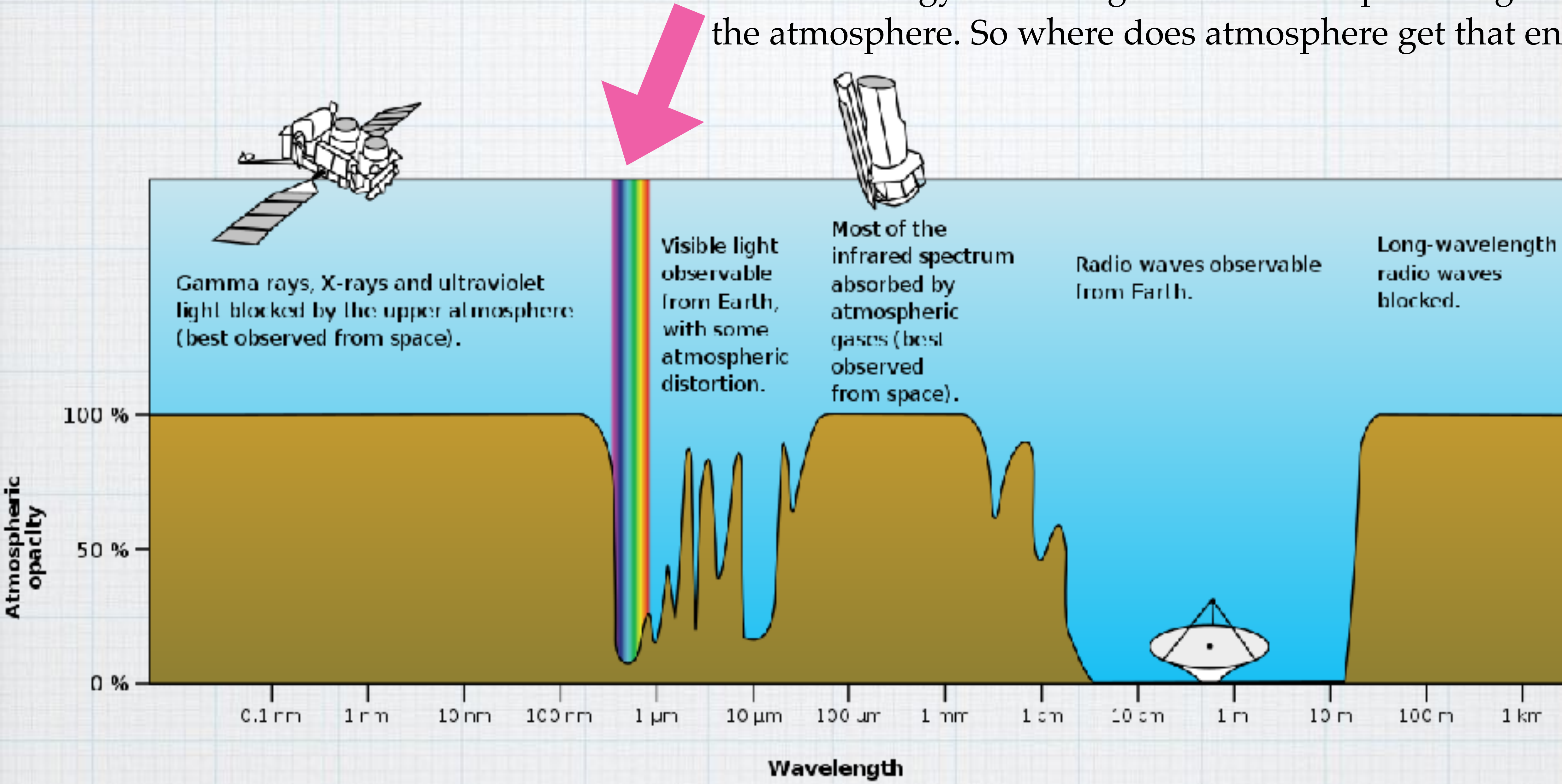


Figure 15.2: [Experimental data.] **Solar and atmospheric radiation arriving at one point on Earth surface.** The *lower (blue) curve* shows the irradiance integrated over all downward directions in the band 300 to 2800 nm, which includes nearly all light coming directly from the Sun but excludes nearly all thermal radiation at Earth's temperature (see Figure 15.1). The *upper (red) curve* shows the irradiance integrated over all downward directions in the band 4500 to 42 000 nm, which excludes nearly all light coming directly from the Sun but includes nearly all thermal radiation at Earth's temperature. [Data courtesy Peter Pilewskie.]

Where is all that extra radiation coming from?

Most solar energy is arriving in a band that passes right through the atmosphere. So where does atmosphere get that energy?



Well – when that light hits the surface, or penetrates the ocean, it *warms it*.
Then the surface radiates energy in a *different* wavelength band.
Then what?

Two coffee cans

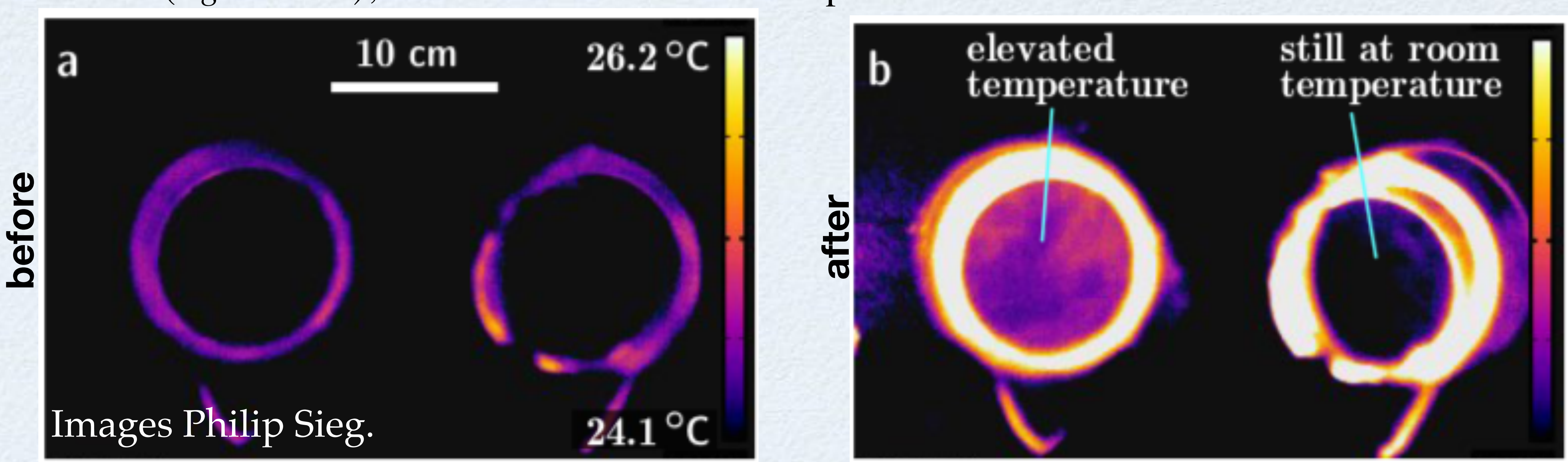
Two identical cylinders were prepared and sealed at the ends with thin plastic wrap. They looked the same to the eye.

https://youtu.be/0eI9zxZoipA

Phil Nelson

The can on the left contained air at room temperature. The one on the right was filled with carbon dioxide gas. Below *left* we are viewing them with a camera sensitive to the wavelength range 7.5–13 μm.
The color bar is a rough guide to what kind of light is being emitted. We see that initially they looked about the same. Reading the false-color scale gives apparent temperature 24°C, same as the wall behind them.

Each cylinder was exposed to a source of IR radiation through its thin window for two minutes, then the source was removed. Both cans got warmer, but the apparent temperature of the CO_2 was higher than the air (*right* below), and a measurable difference persisted even a minute later.



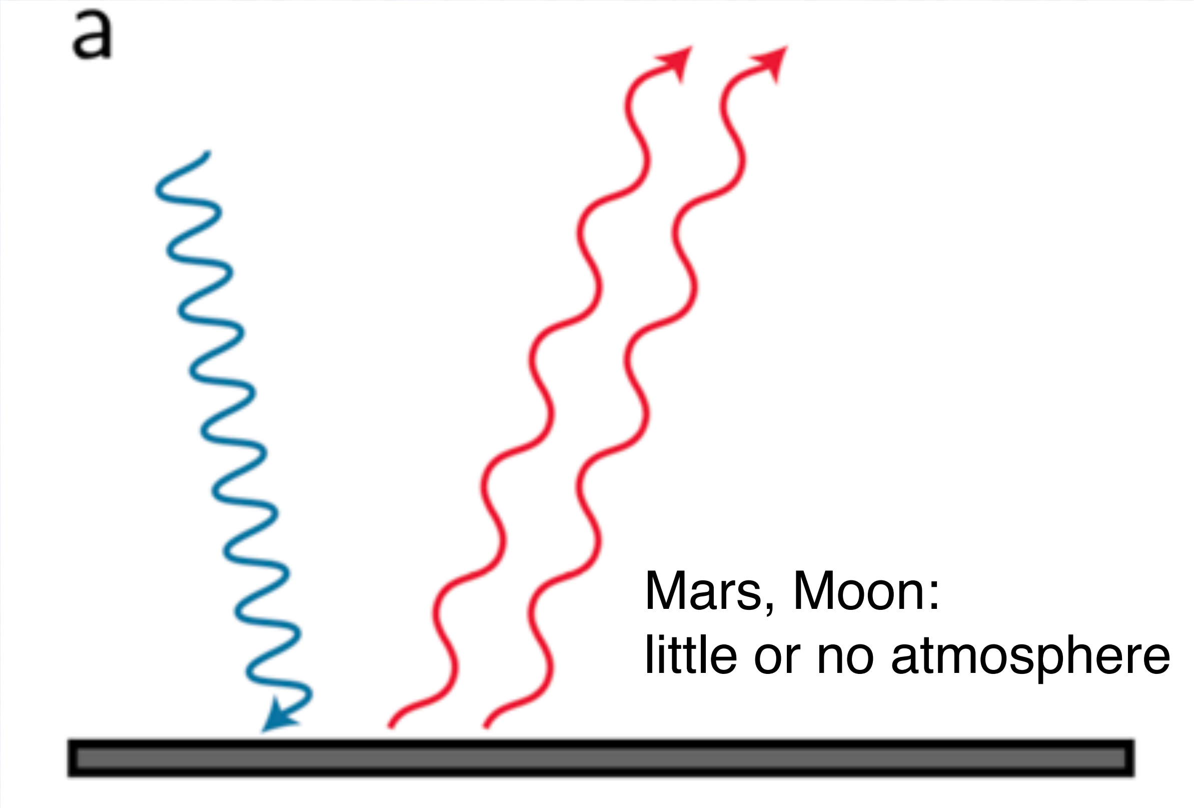
Images Philip Sieg.

How could anything like that possibly happen?

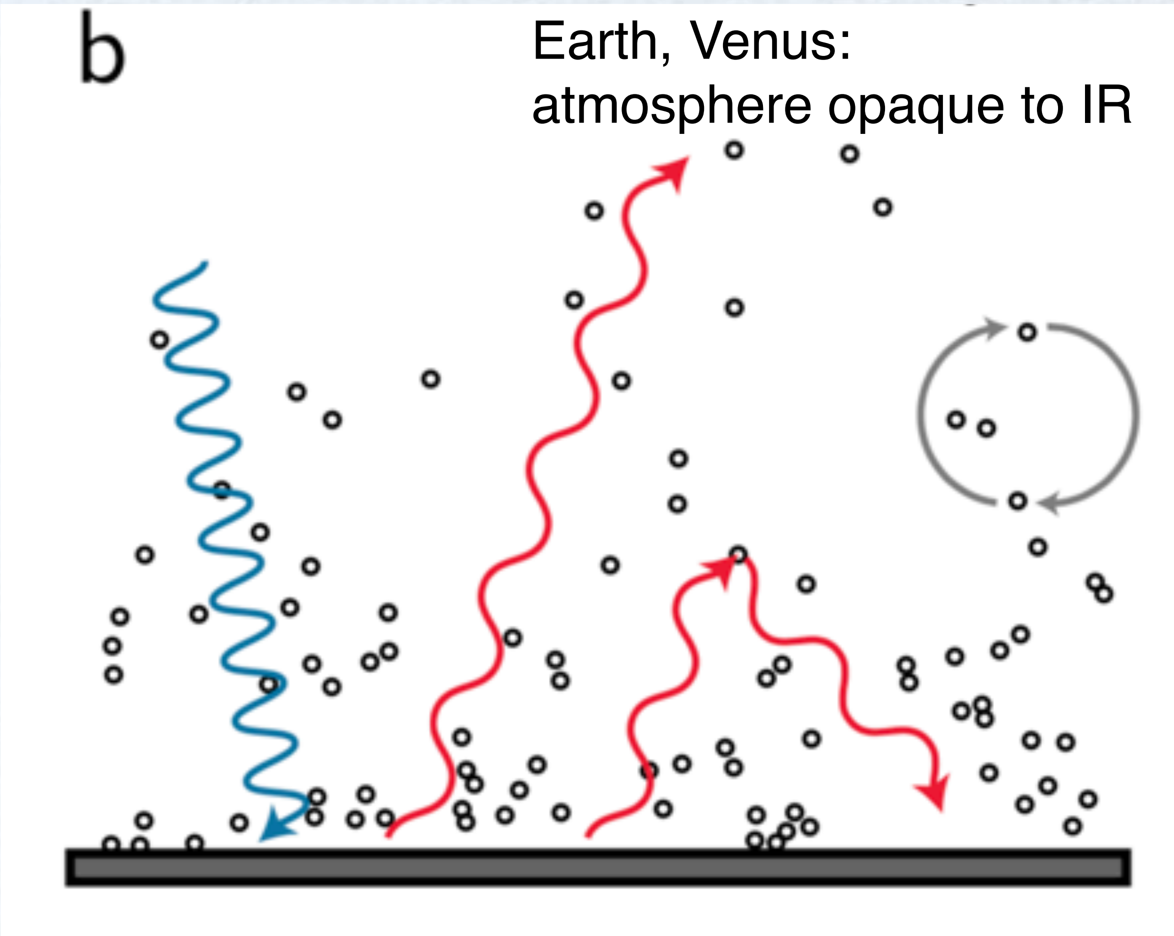
Phil Nelson

It's amazing: The climate of the *whole planet* hinges on two phenomena that cannot be understood without *quantum mechanics*, sometimes marginalized as a "theory of only very small things."

- All absorbed solar energy must be reemitted back to space, following the Stefan–Boltzmann law.



- Diatomic homonuclear molecules like oxygen and nitrogen (as well as noble gases like argon) cannot absorb or emit IR light because they can have no dipole electric dipole moment. But water vapor can because of the permanent dipole moment. And carbon dioxide can gain a dipole moment by bending. So these are IR-active gases, as seen in the demo.



7

1. Indoctrination
2. Skill set
3. Algorithmic thinking and data visualization
4. Some surprising phenomena: Materials
5. : Dynamics
6. : Optics
7. **Student assessment**
8. Outcomes

8

These courses aren't for most premeds. But there is a growing cadre of mathematically adept premeds who can handle them. What will they get?

1. Indoctrination
2. Skill set
3. Algorithmic thinking and data visualization
4. Some surprising phenomena: Materials
5. : Dynamics
6. : Optics
7. Student assessment
8. **Outcomes**

8: A few outcomes

Incredibly, 80 responses including students who took the course up to 7 years ago. See details at http://www.physics.upenn.edu/biophys/PMLS/pdf/141130survey_Report.pdf

2. My level of computer-math experience prior to taking this course was

#	Answer	Bar
1	1 = No prior experience	
2	2	
3	3	
4	4 = Extensive prior experience	

3. My level of computer-math facility after finishing this course was

#	Answer	Bar
1	1 = Inadequate for needs I encountered later	
2	Click to write Choice 2	
3	Click to write Choice 3	
4	4 = Adequate for needs I encountered later	

4. Completing this course benefited my work in later courses

#	Answer	Bar
1	1 = Not really	
2	Click to write Choice 2	
3	Click to write Choice 3	
4	4 = Significantly	

6. Completing this course led me to take more advanced science course(s) that I might not otherwise have considered

#	Answer	Bar
1	1 = Not really	
2	Click to write Choice 2	
3	Click to write Choice 3	
4	4 = Really	

8. Completing this course conferred skills that made me more attractive to research labs and/or graduate programs

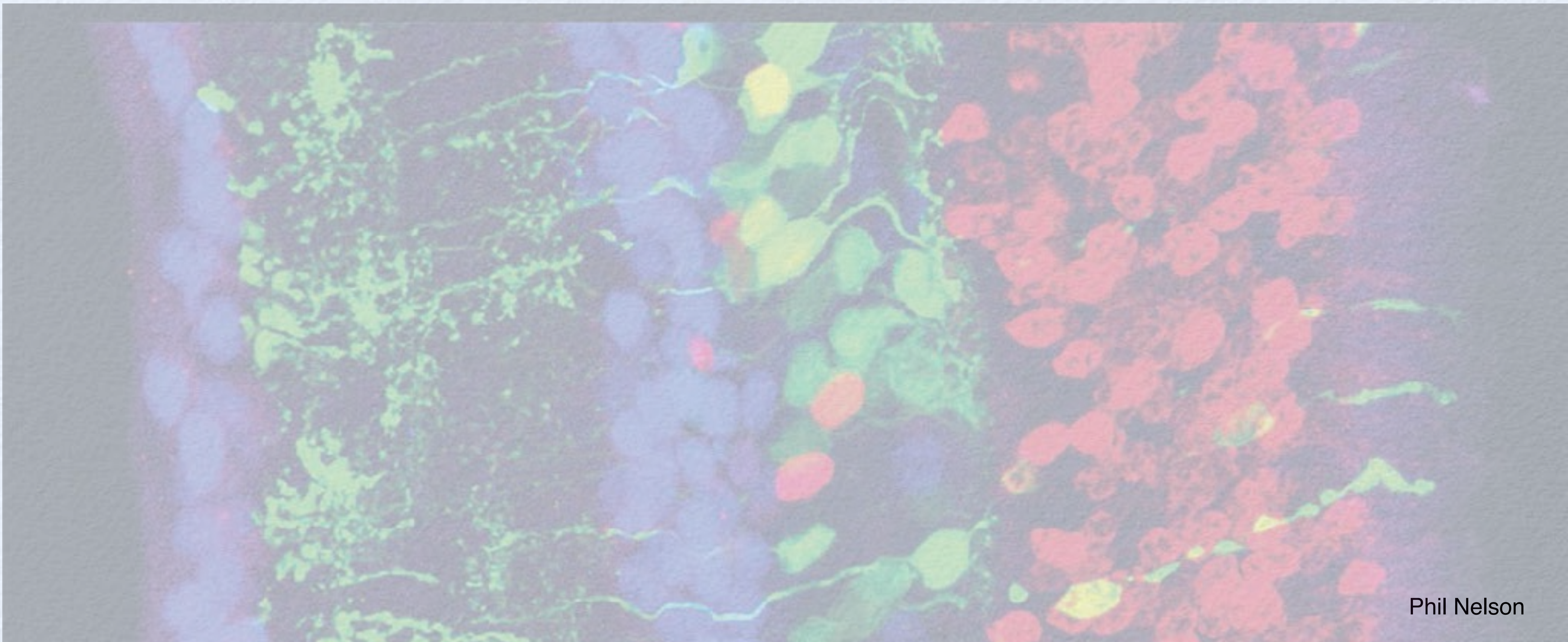
#	Answer	Bar
1	1 = I don't think so	
2	Click to write Choice 2	
3	Click to write Choice 3	
4	4 = I think so	

80 anonymous respondents, survey response rate about 80%.

Wrap

Excuse me… everybody says “modeling is super important.” But…

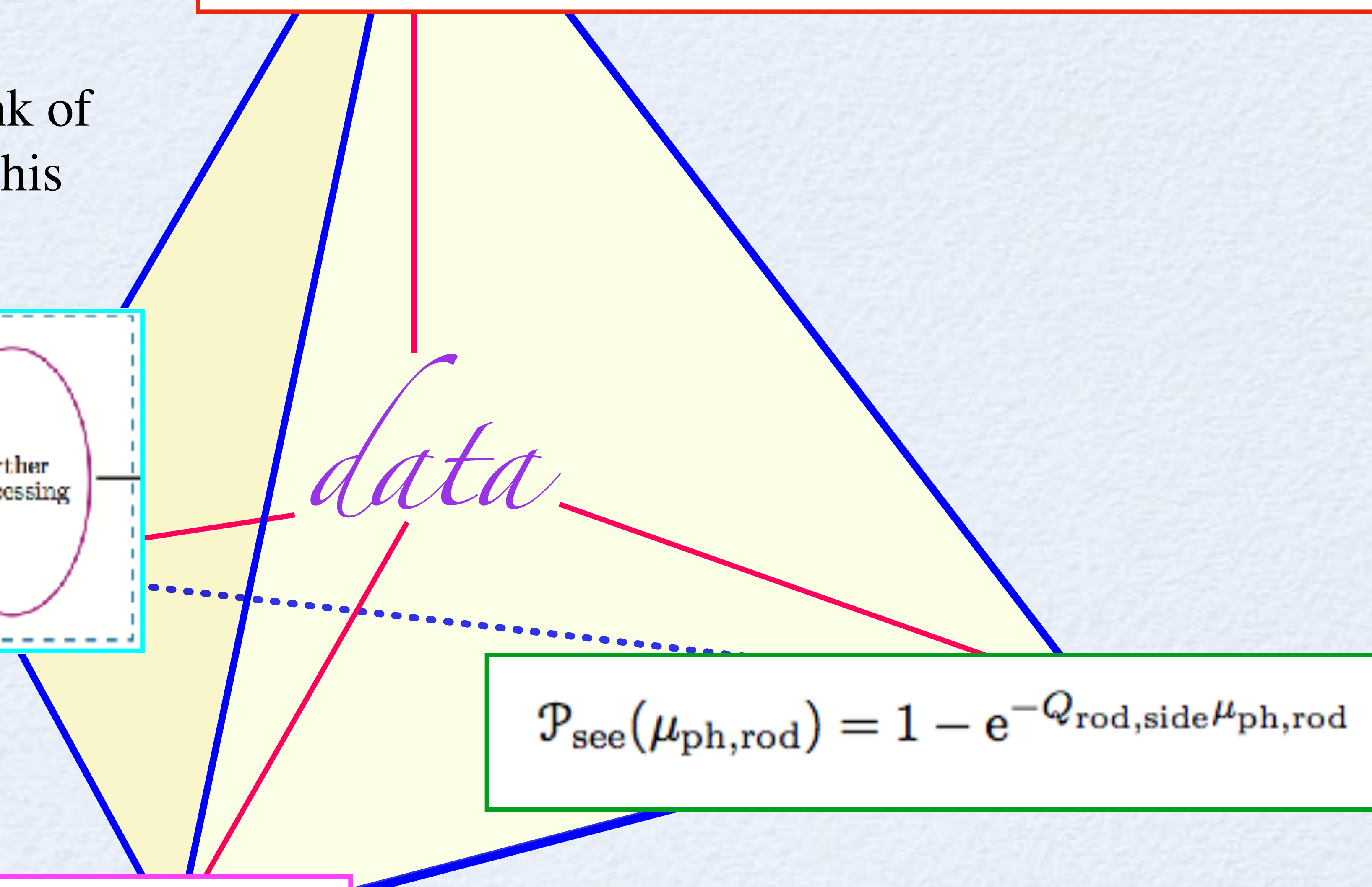
What is a “physical model” anyway? Is it distinct from a “mathematical model”?

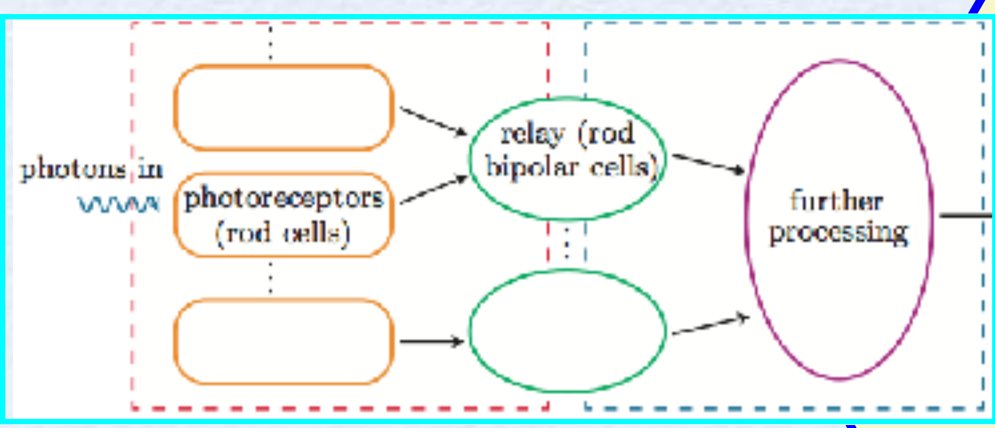


What is physical modeling?

Don't want to get all philosophical on you. I say, ***It's a Tetrahedron.*** Today I applied this approach to dim-light
vision, but it's useful to think of any modeling challenge in this way:

```
for j=1:46,
    photons=20+5*j;
    mbar=q*photons;
    total=0;
    for i=mstar:50
        total=total+exp(-mbar)*(mbar^i)/factorial(i)
    end
```





$$\mathcal{P}_{\mathrm{see}}(\mu_{\mathrm{ph,rod}}) = 1 - \mathrm{e}^{-Q_{\mathrm{rod,side}}\mu_{\mathrm{ph,rod}}}$$

"Yadda, yadda... photons, yadda,... cumulative Poisson distribution...

From Nelson, *From Photon to Neuron.*

Is it hopelessly difficult?

Luckily no. All you have to do is a slightly better job than you were doing before, and already you'll be way ahead of – say – other departments' courses.

Also there are books embodying these idea.

Remember to have fun yourself. Students feel it.

Thanks

University of Pennsylvania

NSF BIO and PHYS

This material is the subject of two recent textbooks:

From photon to neuron: Light, imaging, vision (www.physics.upenn.edu/biophys/PtN).

Physical models of living systems (www.physics.upenn.edu/biophys/PMLS).

Also see:

Biological Physics: Energy, Information Life (WH Freeman, 2014).

A student's guide to Python for physical modeling by Jesse Kinder and PN, updated ed. (Princeton University Press, 2018).

A student's guide to MATLAB for physical modeling by Tom Dodson and PN (free at **www.physics.upenn.edu/biophys/PMLS**).

For these slides see:
www.physics.upenn.edu/~pcn

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