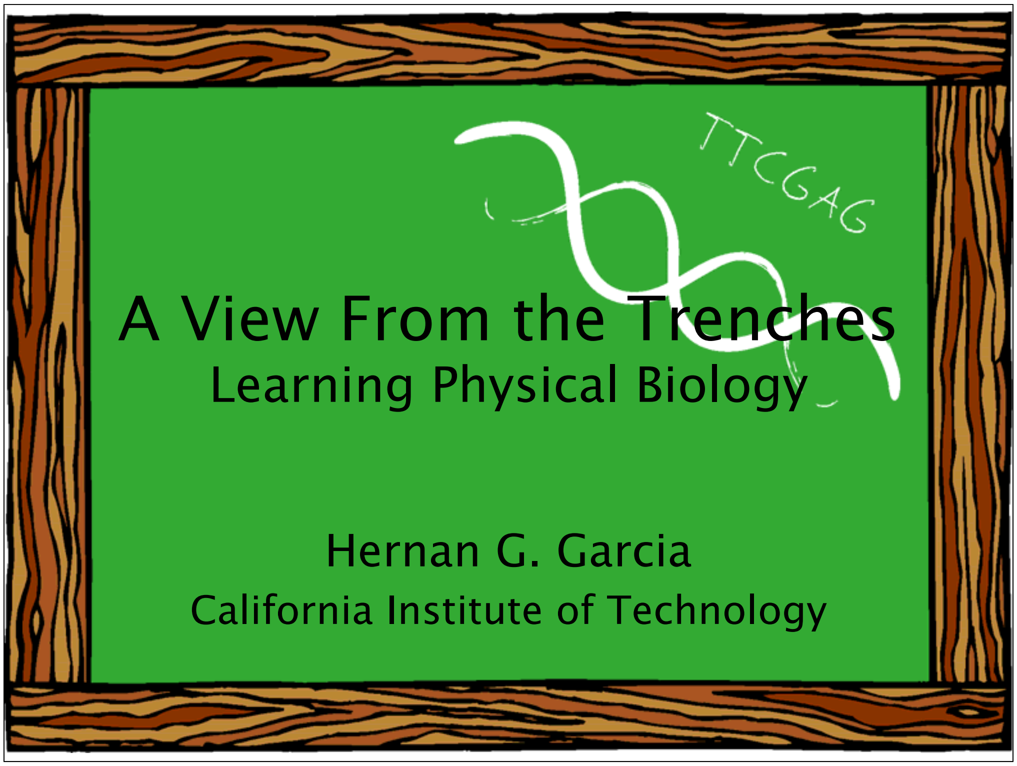


I've been doing this migration from "pure" physics to physical biology for the last 2.5 years, being at the very center of the issues that are being debated today. I hope that this view from the trenches will provide a unique perspective about the problem.

I want to apologize from the beginning if I happen to hurt anybody's feelings. I will try to provoke by emphasizing the points that I believe have potential for being more controversial.

Map of the Battlefield

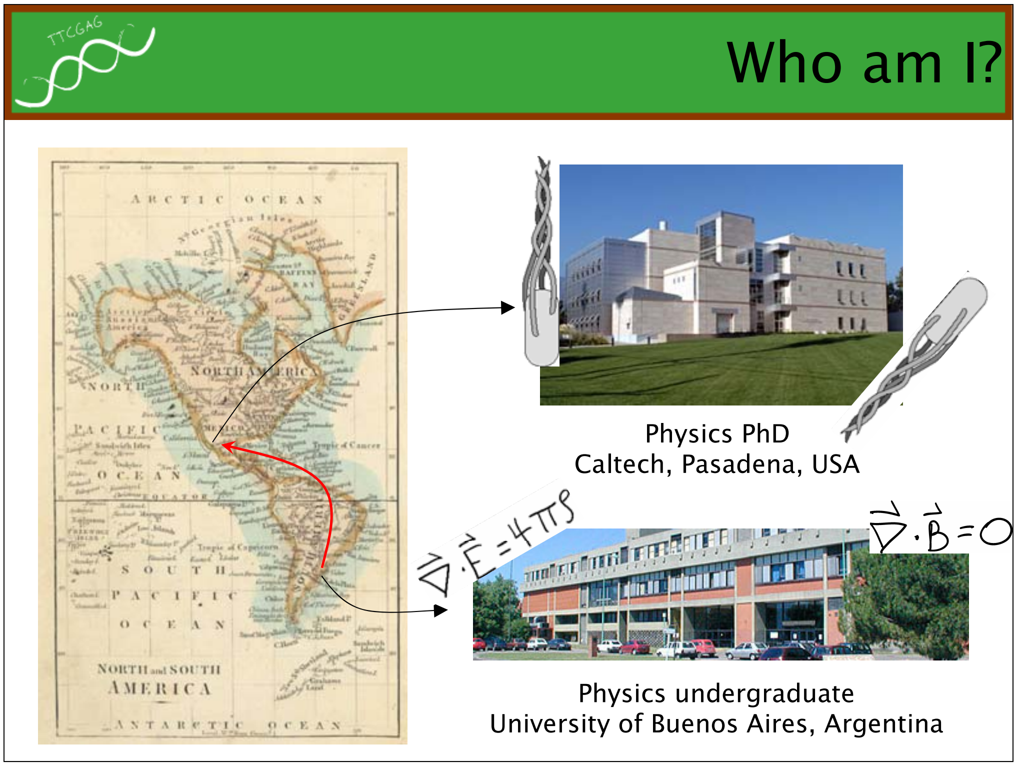
- Who am I?
  - A physics student goes biological.
- Biology taught from physics.
  - Courses I have taken and how they have let me down.
- Courses I have taught and how I have let the students down.
- MBL Physiology Course.
  - Life at the biological front.
  - Real experiments for real biologists.
- Some ideas.
  - Making a physical biologist.

I have organized the talk almost in chronological order trying to pick the best and the worst about my experiences in this transition to Physical Biology.

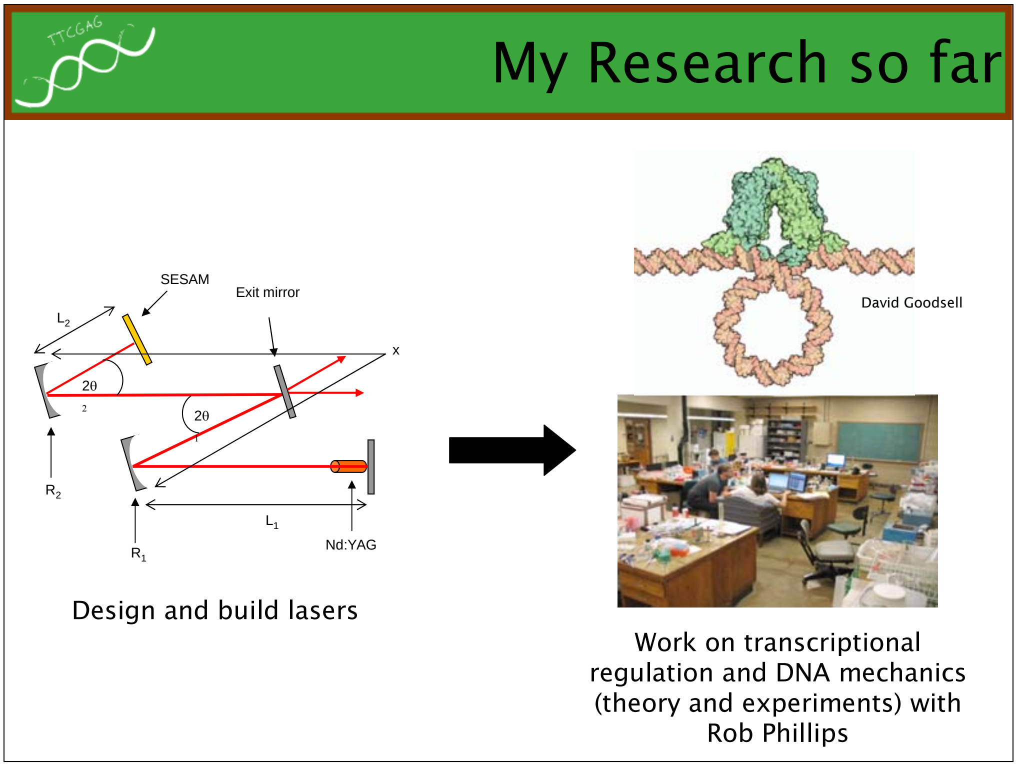
I will go over the different courses I have taken and describe how they have let me down. At the same time I'll go over how I have let students down in the courses I've taught.

I'll go over one of the experiences that changed the way I do research and teach the most: the MBL Physiology course at Woods Hole. This was my most direct exposure to real biology I've had so far to conclude with my views of what are the parts required are to make a physical biologists.

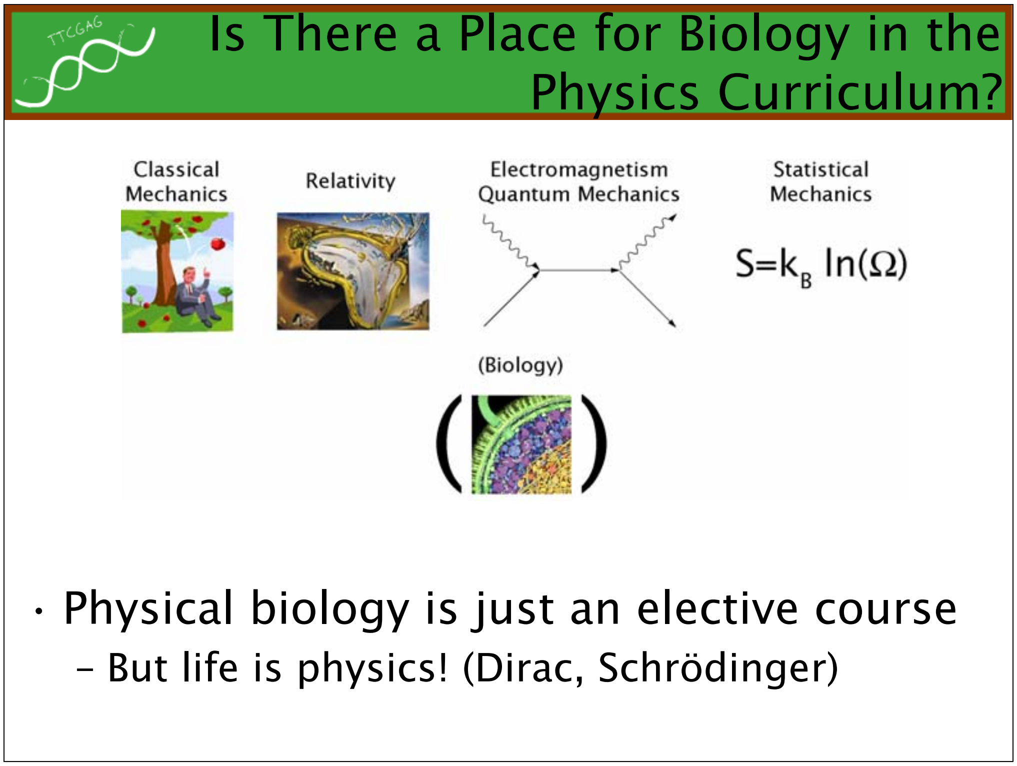
Real Biology Problems: Physical Biology → ASCB



<u>I did my undergrad as a Physicist in Argentina. 27 Courses that were only either on Math or Physics. For my PhD I moved to the Physics department at Caltech. I'm now working with Rob (APh) in the Broad Center, a building full of biologists....</u>



Basically I've made the transition of working on lasers, which is what I did for my undergraduate thesis, to being interested in how cells work by trying to understand transcriptional regulation and how DNA mechanics play an important role in life.



<u>**To my knowledge, Physical Biology is viewed in Physics curricula as an elective course.**</u>

<u>**I think that saying that the study of living matter is something independent of Physics is completely shortsighted (and Dirac and Schrödinger would agree as well). Biology should be more than just an elective course.**</u>

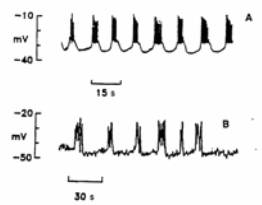
<u>**The potential from learning about Biology in the context of Physics might be higher than taking, for example, a solid state physics course. Just because of the world it would open in front of the student, a world of different problems and very conceptually different tools (or even new tools which will have to be developed) to approach them.**</u>

<u>**KEY IDEA: Biology deserves far more attention in Physics curricula than it's actually getting.**</u>

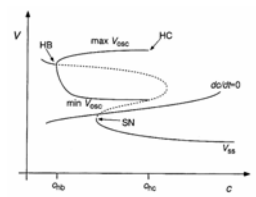
Learning Biophysics 1.0

- UBA: Biophysics
  - Based on mathematical physiology, centered on dynamical systems.
  - Example of electrical bursting in pancreatic cells:

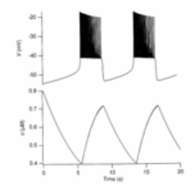
Show a phenomenon



Write a model and analyze its behaviour



Check that it reproduces the experimental data



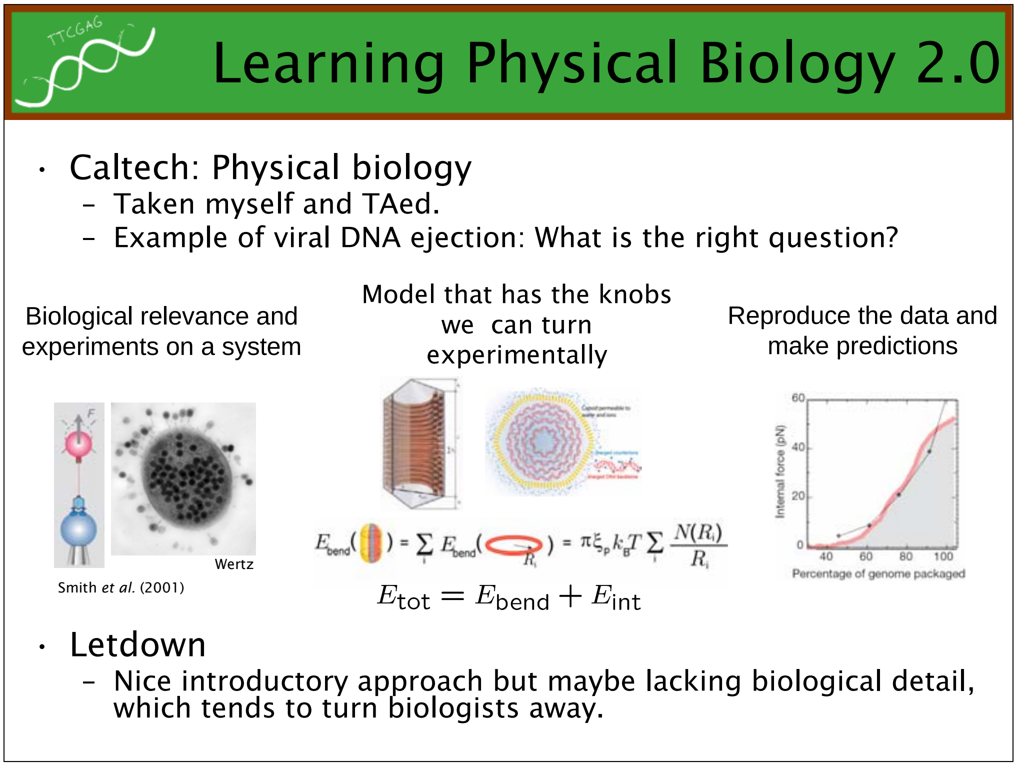
Keener and Sneyd (1998)

- Letdowns
  - This is insufficient! biology as a pretext: “Look, physics works!”.
  - Biological motivation: critical or mundane?
  - This is not talking to biologists!

One world view of biology from the stand point of physics is to use biological phenomena as a pretext to say that physics works. In the course I took in Buenos Aires, for example, a phenomenon like bursting activity of pancreatic cells motivated writing a set of equations. The dynamics of this system were then analyzed to see which parameters allowed for bursts, how we could reproduce the observation... And then we moved on.

This is at the heart of Bruce’s argument about deciding what’s mundane and what is critical: the failure to put this question in context makes it just a physics homework no biologist would be ever interested in addressing.

KEY IDEA: Biology can’t be just an excuse to solve different HW problems in Physics. It has to answer questions Biologists would be interested in.



On the other hand, at Caltech, I took and also TAed the Physical Biology course Rob designed. This course was more based on the biological motivation, on the art of figuring out what we want to ask through our model. As an example, by looking at different representative quantitative experiments on bacteriophage DNA ejection we made a simple model in terms of the mechanical and electrical properties of DNA which led to very particular predictions when changing the capsid size or the genome length. This is definitely more appealing to biologists.

However, there's the risk of "throwing out the baby with the bath water", of oversimplifying in such a way that biological detail is lost. As Physicists we have to be careful not to want make things simpler when they actually are just because there is a more elegant solution. It is arrogant from our part to think that the level of complexity biology has is just because biologist like complicated stories.

KEY IDEA: Building the model around the biological story is definitely a better approach, but we have to fight our desire for oversimplifications in the search for elegant solutions.

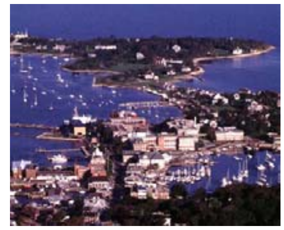
Reality determines the tools we will use.

Emphasizing the generality of a process does not mean that we shouldn't learn about the particulars (however, risk of not starting at the beginning).

"Did we throw out the baby with the bath water?"!!!

The Best of Molecular Biology's Traditions: A Summer at Woods Hole

- Physiology Course @ MBL
  - Seven weeks with biologists and physicists doing research level experiments side by side with professors.
  - Talks every morning from pretty much everybody in biology.
  - Great not only for learning hardcore biology, but also for developing collaborations
  - Show Dyche's movie.
  - This is ideal for people like me, not a term-long course that meets twice a week!



This is an intensive course that has been going on for 107 years. The idea is that professors bring experiments they want to do for their research. There's little to loose and a lot to gain and the professors are happy to be surrounded by people who will think about their experiment pretty much 24/7. In addition, the talks 6 out of 7 days every week really help to get a feeling for what is hardcore biology.

Just to give you a feeling about this course I want to show you a 3 minute movie Dyche Mullins made. It's kind of silly, but it shows very clearly how a mixture of hard work with a lot of fun is reached.

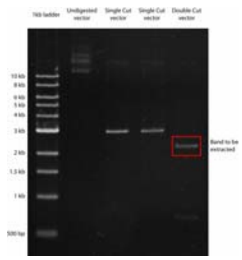
Going to Woods Hole was definitely one of the most important experiences I've had so far. The reach of this "science summer camp" goes beyond anything that can be done with regular curricula at Universities. This is what people like me need to go understand how to do real biology. You just cannot expect to gain the same thing from canned experiments in a class that only meets twice a week!

KEY IDEA: An intensive course like this is what is needed for students like me going into biology. A term-long course that only meets twice a week is likely to fall short, to be shallow.

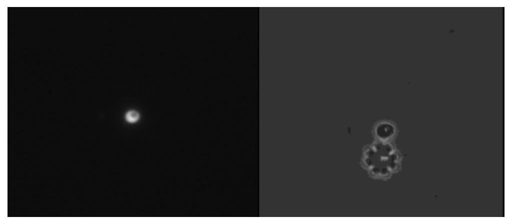
What I got out of Woods Hole

- Work with biologists on real biology problems.
  - Learn the tools as you need them in the context of a bigger research problem.

Learn how to run a gel to show how cloning is done



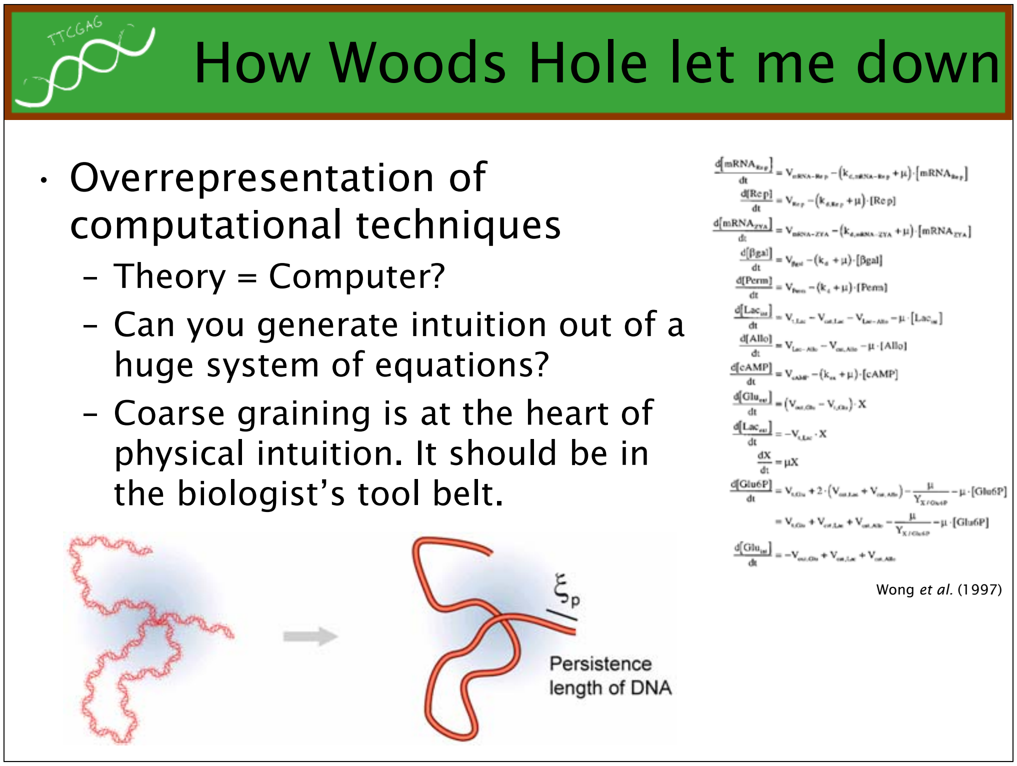
Learn how to track single cells + ask something new about a metabolic pathway



At Woods Hole I learned how to do real biology from real biologists. A combination of passionate people, state-of-the-art equipment and a "nothing to lose, but much to gain mentality" made it an extremely successful course.

In any student lab you would start by doing cloning just because, without a bigger objective. In Woods Hole, for example, once I asked a particular question about the phosphate pathway of Yeast I had to come up with a way of looking at it, which lead me to learn how to make movies of single cells over time and extract information out of them.

KEY IDEA: Centering on techniques is good, but it's much better in the context of a real problem.



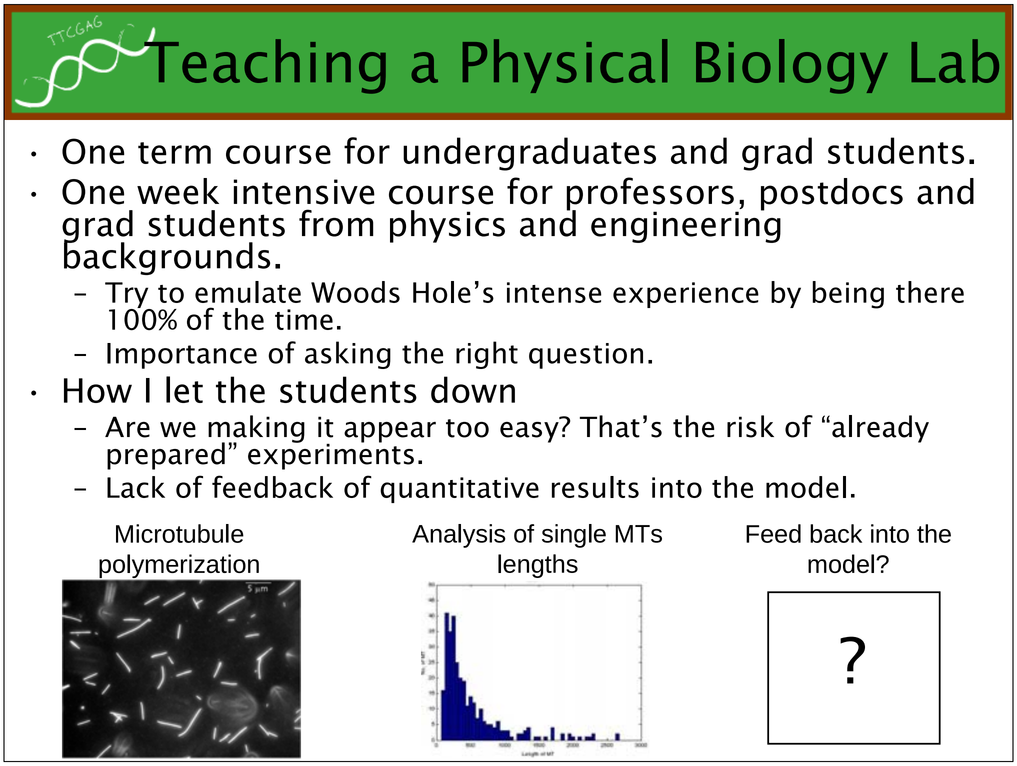
Biology students are let down by being taught just the computational side of physics.

However, I must say, that computational techniques were overrepresented being pretty much the only modeling approach the students encountered. I don't want to suggest that you can't learn from these techniques, but I certainly do not think that you can generate intuition about a system by describing it with 13 coupled partial differential equations.

Coarse graining has a lot to offer in this sense. I don't necessarily need to know the forces on each atom of a DNA molecule in order to describe a biological process. It might be enough with just describing it as an elastic rod which has only one parameter: its stiffness.

We hope to balance that when we teach there in this year's course!

KEY IDEA: Doing huge computations is not sufficient to develop intuition. You need coarse graining!



In the context of the theory course we started working on a Physical Biology lab, a lab centered on quantitative data. One version of it is a term long course, whereas the other one is an intensive one week course for professors, postdocs and grad students from physics and engineering backgrounds.

We've been successful at emphasizing the importance of asking the right question. For example, when solving a problem with a genetic approach cloning is relatively straightforward, it's about what you ask using that tool!

The complaints to the management here are that we are still making these experiments too canned, they give the impression of being really easy to prepare.

Finally, the biggest complaint is related to what we do with the quantitative data. It's not enough to measure the length distribution of single microtubules, you have to be able to feed that back into the model.

Julie and Ashok and the Listeria and what was going on behind the scenes.

KEY IDEA: Obtaining quantitative data isn't good enough and we haven't managed to go beyond that successfully yet.

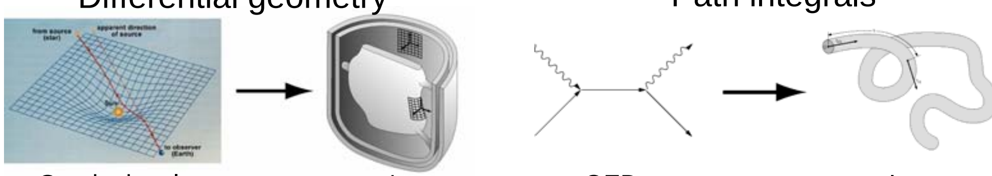
Importance of asking the right question: With the current development of molecular biology, for example, we have almost all the tools we might want. We need to combine them in a meaningful way in order to answer a meaningful question.

Shallow because of qualitative conclusions. Maybe that's as good as it gets for a course where time is a constraint.

Winning the War: Conclusions

- Universities *must* find a way of reproducing the intensity of Woods Hole.
- Physics Curriculum *must* teach physical biology – the physics of living matter.
- Physicists *must* convince biologists that their quantitative data *must* be addressed with quantitative models.
- “Life sciences majors *must* acquire a much stronger foundation in the physical sciences (chemistry and physics) and mathematics than they now get.”, Bio2010.

Differential geometry | Path integrals



Gravitational lensing → Membrane mechanics | QED → Polymer mechanics

<u>You can learn differential geometry to understand membrane mechanics rather than gravitational lensing, or path integrals in order to describe a biological polymer instead of quantum electrodynamics.</u>

Acknowledgements

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