# What Is Science?

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Cancer Research UK

EASE, Split
June 2014

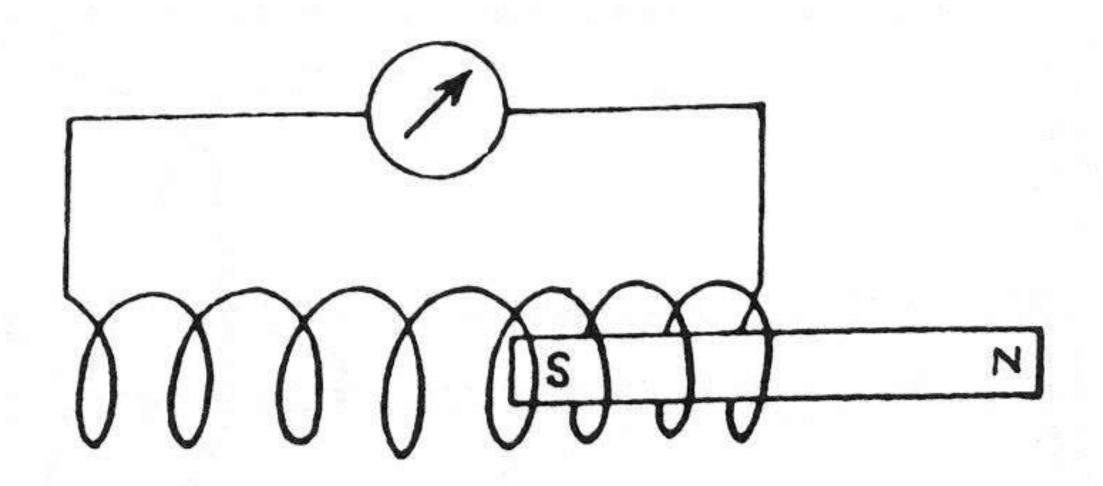


# Celia's question:

Daddy, why is the ceiling opaque?

"We come into this world, we live, and depart from it, without our thoughts being called to consider how all this takes place; and were it not for the exertions of some few inquiring minds, who have looked into these things, and ascertained the very beautiful laws and conditions by which we do live and stand upon the earth, we should hardly be aware that there was any thing wonderful in it."

# Faraday's magical experiment



Although we know no-

thing of what an atom is, yet we cannot resist forming some idea of a small particle, which represents it to the mind; and though we are in equal, if not greater, ignorance of electricity, so as to be unable to say whether it is a particular matter or matters, or mere motion of ordinary matter, or some third kind of power or agent, yet there is an immensity of facts which justify us in believing that the atoms of matter are in some way endowed or associated with electrical powers, to which they owe their most striking qualities, and amongst them their mutual chemical affinity.



Katherine & James Clerk Maxwell

# A Dynamical Theory of the Electromagnetic Field James Clerk Maxwell 1864

The general equations are next applied to the case of a magnetic disturbance propagated through a non-conductive field, and it is shown that the only disturbances which can be so propagated are those which are transverse to the direction of propagation, and that the velocity of propagation is the velocity v, found from experiments such as those of Weber, which expresses the number of electrostatic units of electricity which are contained in one electromagnetic unit.

This velocity is so nearly that of light, that it seems we have strong reason to conclude that light ... is an electromagnetic disturbance in the form of waves propagated through the electromagnetic field according to electromagnetic laws. If so, the agreement between the elasticity of the medium as calculated from the rapid alternations of luminous vibrations, and as found by the slow process of electrical experiments, shows how perfect and regular the elastic properties of the medium must be when not encumbered with any matter denser than air. If the same character of the elasticity is retained in dense transparent bodies, it appears that the square of the index of refraction is equal to the product of the specific dielectric capacity and the specific magnetic capacity. Conducting media are shown to absorb such radiations rapidly, and therefore to be generally opaque.

#### How Can We See Distant Stars?

"According to the assumption to be contemplated here, when a light ray is spreading from a point, the energy is not distributed continuously over ever-increasing spaces, but consists of a finite number of energy quanta that are localized in points in space, move without dividing, and can be absorbed or generated only as a whole."





## The Hamiltonian Operator

$$-\frac{\dot{h}^2 \nabla^2}{2m} + V(x)$$

"The problem of getting the interpretation proved to be rather more difficult than just working out the equations"

P.A.M.Dirac

## QED: The Jewel in the Crown

• Such an accurate theory of the interactions of photons and electrons that if you were measuring the distance from New York to Los Angeles, it would be specified to the width of a human hair.

#### How does science work?

Where do Karl Popper's "Falsifiable hypotheses" come from?

#### There is only one way to find things out...

"You know, the proper method for inquiring after the properties of things is to deduce them from experiments"

Isaac Newton, 1672

"Rationality was not forever the hallmark of human thought... other systems remain in favour...

To this day, there continue to be conflicts between the two dominant and antagonistic patterns of thought we have inherited—one based on the acceptance of supernatural forces, authority, or revelation to explain the phenomena of Nature, and another relying on observations, data, hypotheses, and verifiable conclusions'

John A. Moore: Science as a Way of Knowing 1993

# Great Discoveries are — by Definition — Unexpected

"In forecasting the future of scientific research there is one quite general law to be noted. The unexpected always happens.

So one can be quite sure that the future will make any detailed predictions look rather silly."

J.B.S.Haldane, The future of biology, 1927

"If politics is the art of the possible, research is surely the art of the soluble.

(No scientist is admired for failing in the attempt to solve problems that lie beyond his competence)."

Peter Medawar, reviewing "The Act of Creation" by Arthur Koestler

Perhaps the most important single step in the research process is choosing a question to investigate. What most distinguishes scientists noted by posterity is not their technical skill, but that they chose interesting problems.

In the late 1960s, a student told me that he wanted to go into general relativity rather than elementary particle physics, because the principles of the former were well known, while the latter seemed like a mess to him.

It struck me that he had just given a perfectly good reason for doing the opposite

Particle physics was where creative work could still be done.

Steven Weinberg, 2003.

In the real world, it's very hard to know which problems are important, and you never know whether at a given moment in history a problem is solvable...

#### How can we encourage creativity?

Max Perutz used to receive visits from earnest men and women armed with questionnaires and tape-recorders who wanted to find out what made the MRC Laboratory of Molecular Biology in Cambridge (where he worked) so remarkably creative ...

"I felt tempted to draw their attention to I5th-century Florence with a population of less than 50,000, from which emerged Leonardo, Michelangelo, Raphael, Ghiberti, Brunelleschi, Alberti, and other great artists." "Had my questioners investigated whether the rulers of Florence had created an interdisciplinary organisation of painters, sculptors, architects, and poets to bring to life this flowering of great art?"

"Creativity in science, as in the arts, cannot be organised. It arises spontaneously from individual talent. Well-run laboratories can foster it, but hierarchical organisation, inflexible, bureaucratic rules, and mountains of futile paperwork can kill it.

Discoveries cannot be planned; they pop up, like Puck, in unexpected corners."

Max Perutz

## The Pain and Suffering...

... of not understanding

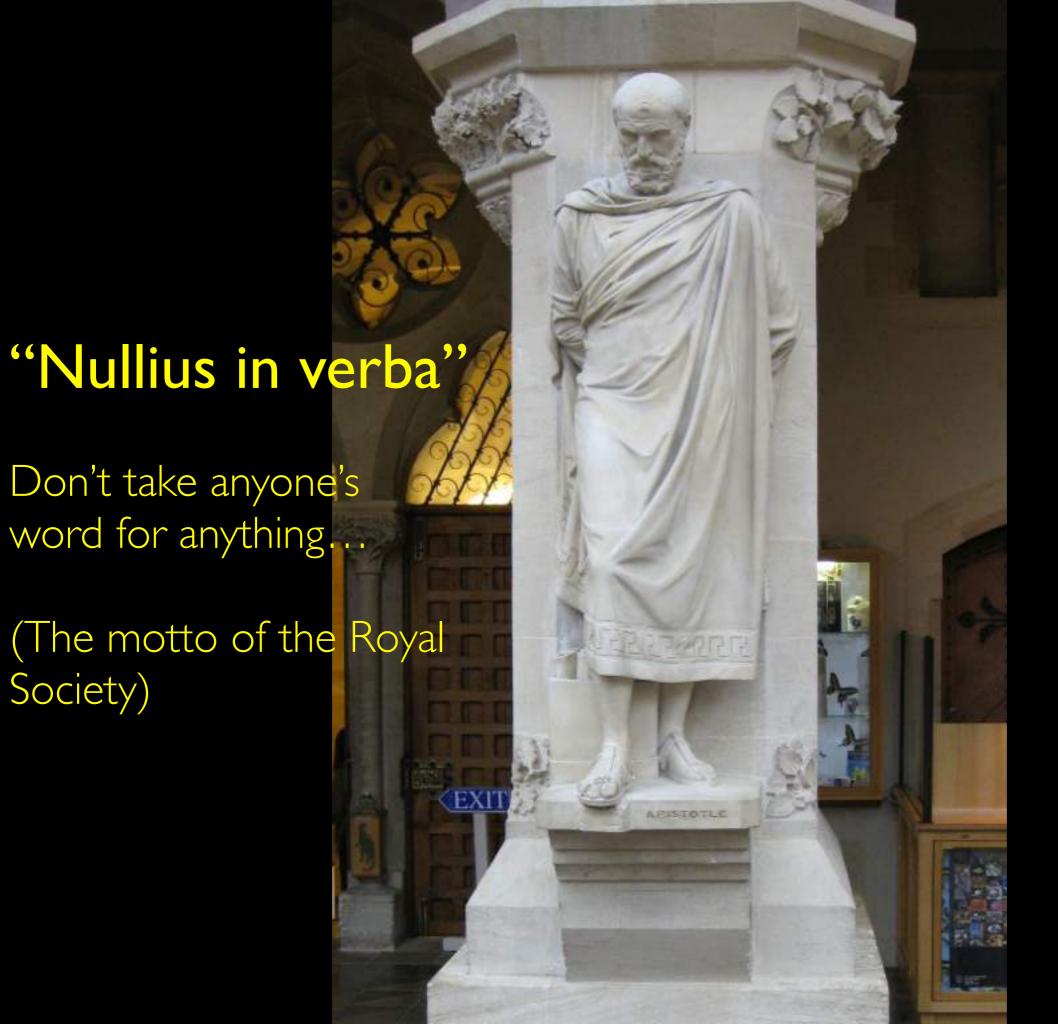
Stanley Cohen, Vanderbilt University, Nashville, Tennessee (Nobel Laureate in Physiology or Medicine, 1989)

# "Reading Rots the Mind"

(The motto written on Francis Crick & Sydney Brenner's office blackboard)

# "Study Nature Not Books"

(A saying of Luis Agassiz displayed prominently in the Library of the Marine Biological Laboratory, Woods Hole)



Society)

### Aristotle's Six Questions:-

- What is the nature of the vital principle?
- Is "being alive" basically the same for all living things?
- What is needed for the maintenance of life?
- What gives rise to the diversity of living creatures?
- What accounts for the existence of natural groups of organisms, and their organisation into hierarchies?
- What is responsible for like producing like? Why do offspring resemble their parents?

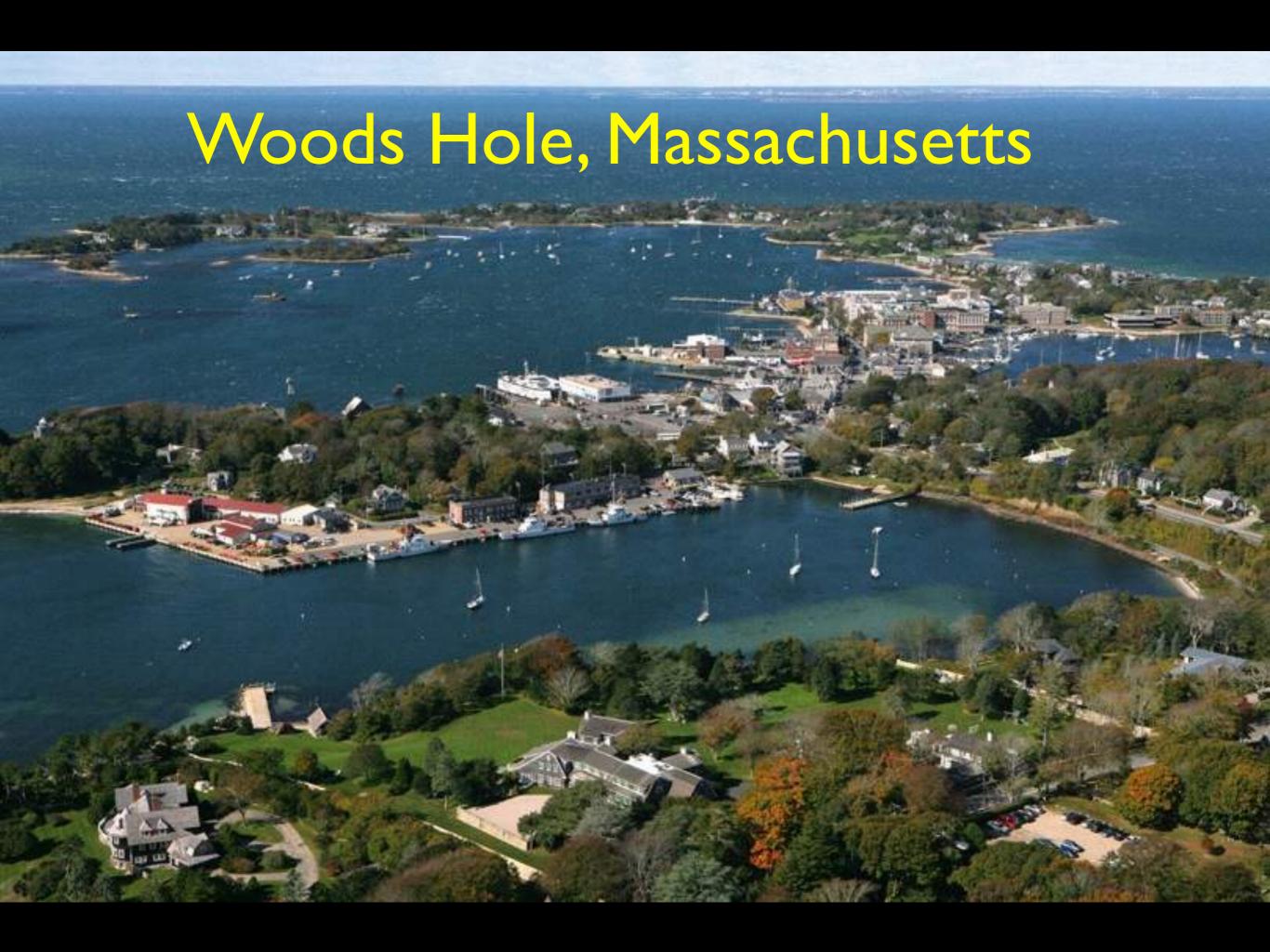
"It is important to remember that the answers to these questions are without practical consequences. No one in ancient Greece would have benefitted economically or politically from knowing the answers. The questions were asked, and answers sought by a very few individuals who could afford the luxury of speculation because of the intellectual joy it brought."

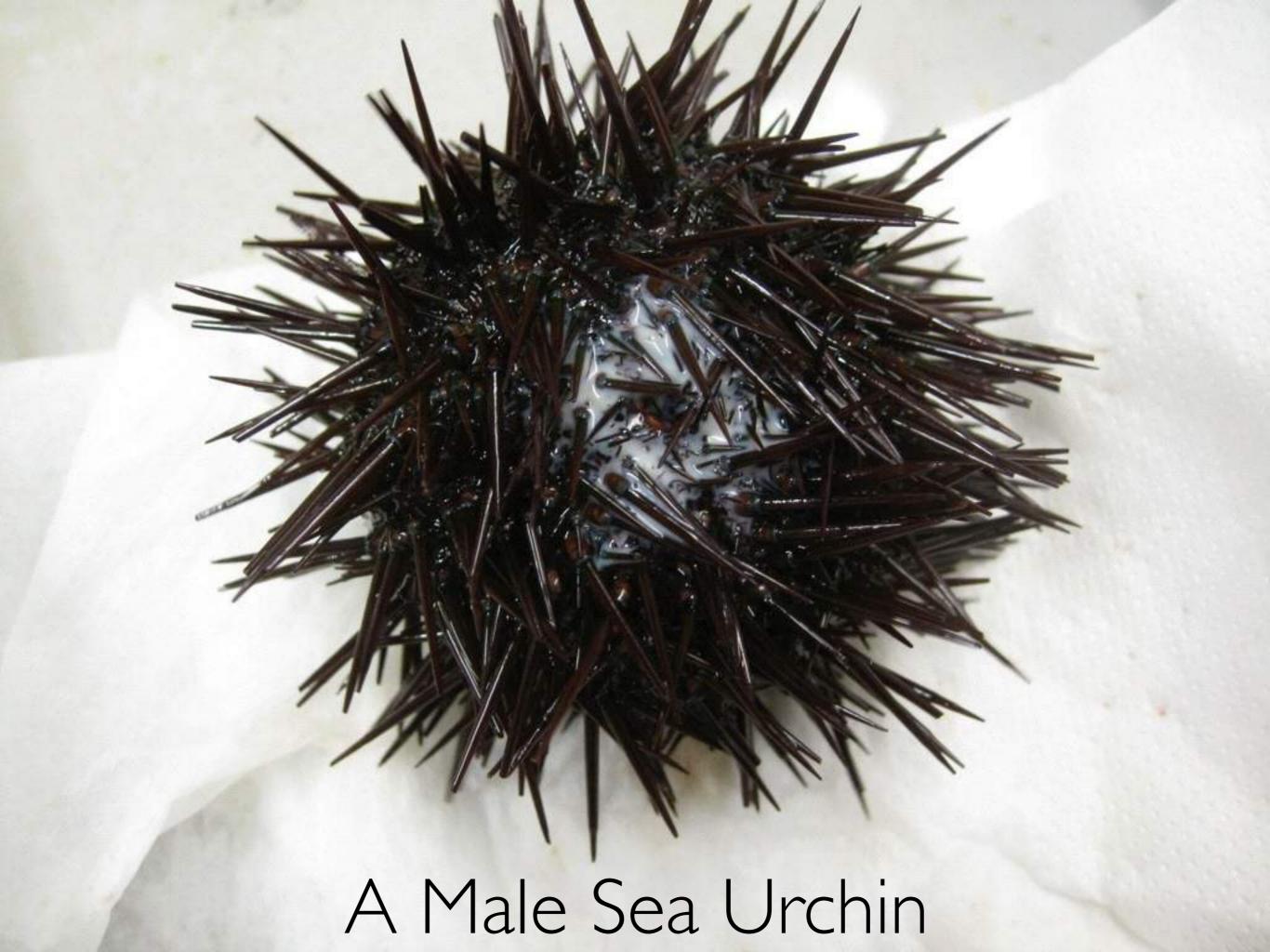
The great innovation of Galileo was to avoid trying to explain why objects fall (as Aristotle had) in favour of quantifying how they fall

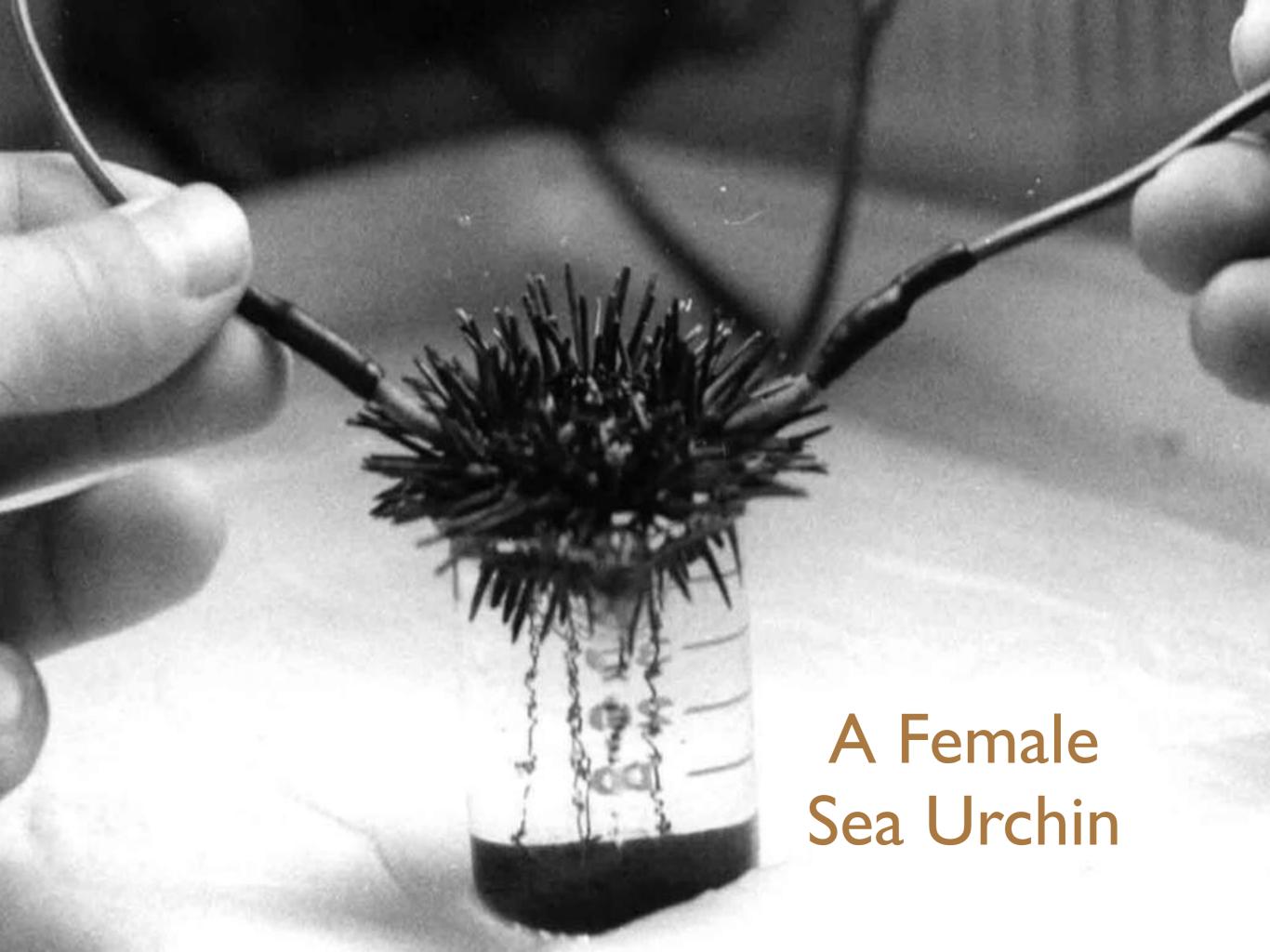
The great innovation of Vesalius was to do dissections himself and base his anatomy book on what he actually saw, rather than on the authority of Galen.

"If our civilization is to survive, we must break with the habit of deference to great men. Great men may make great mistakes..."

Karl Popper, Preface to The Open Society and Its Enemies





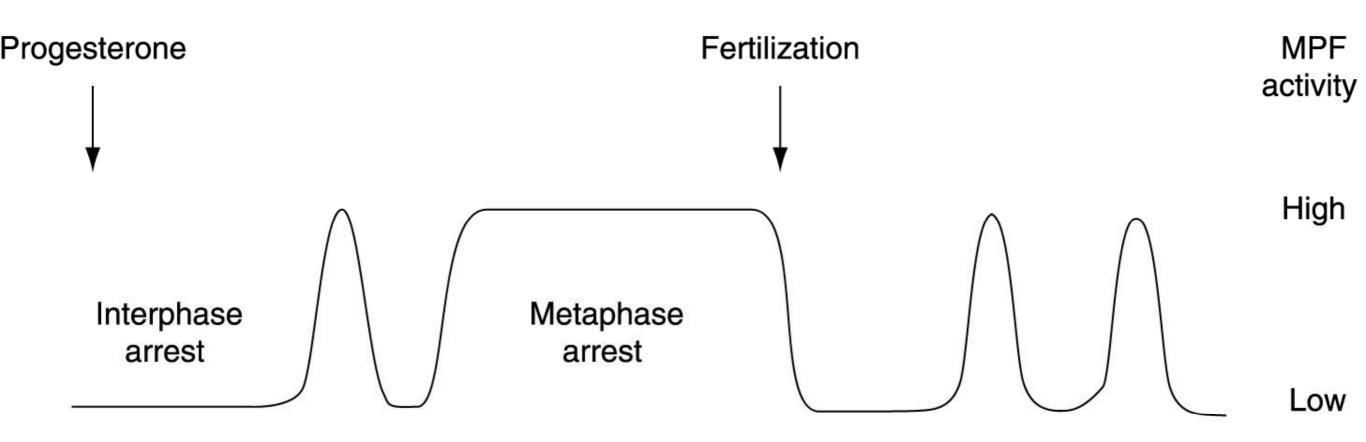


#### The First 4 Divisions of Fertilized Sea Urchin Eggs

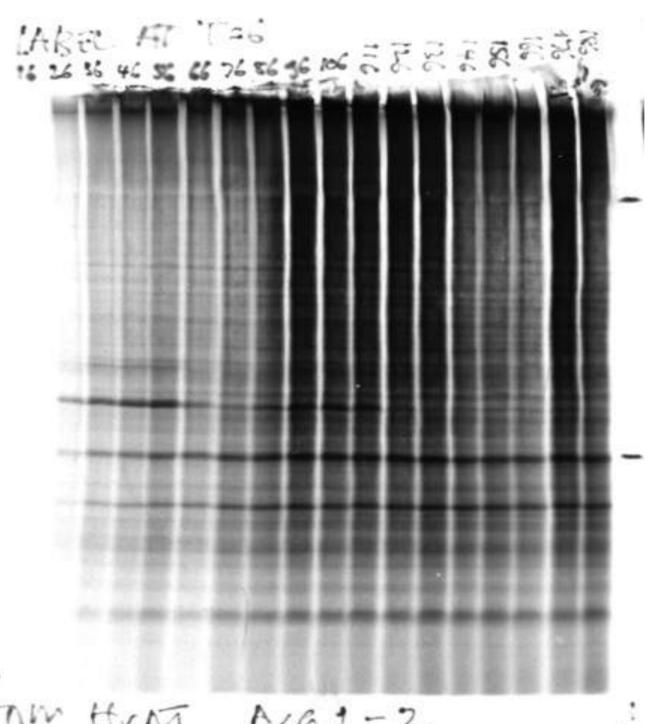


900X Speeded Up (by Christian Sardet)

## The Cell Cycle Oscillator - "MPF"

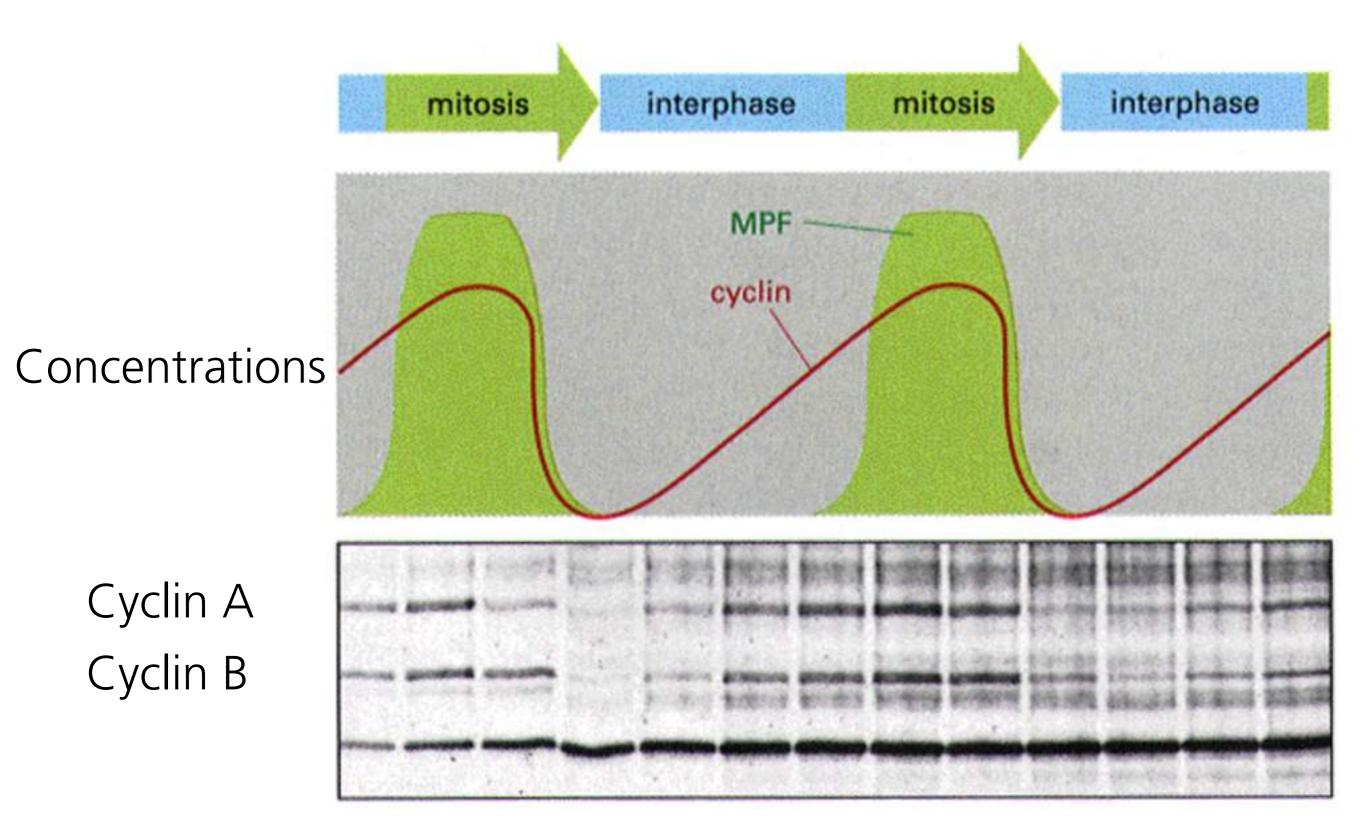


### The Nobel Prize-winning Experiment



1-Dimensional SDS-polyacrylamide gel

## Cyclins go Up and Down, a Bit Like MPF - Is There a Connection?



# "Wild Speculation Based on Faulty Logic"

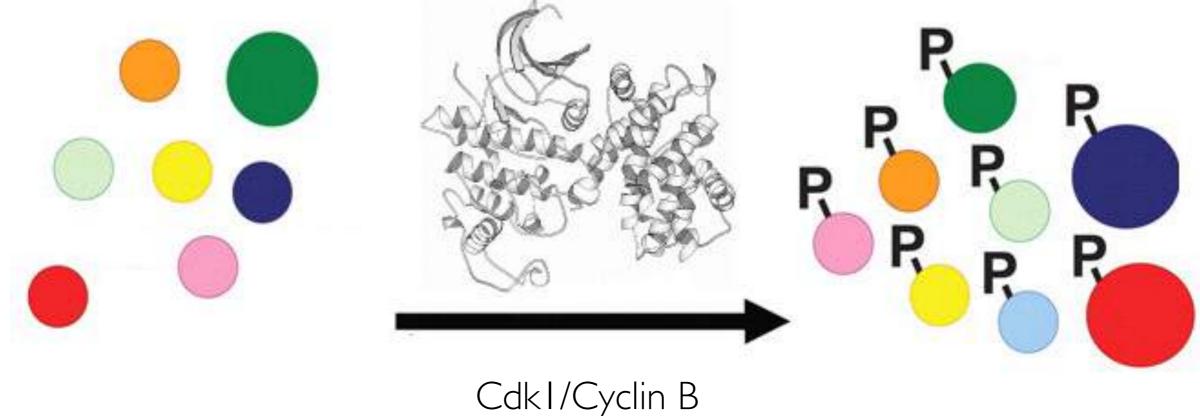
(unidentified referee's comments on the first version of the first paper about cyclin)

#### CDC2 + CYCLIN = MPF

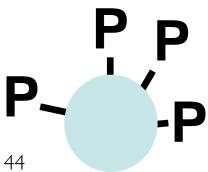


#### Interphase

#### Mitosis

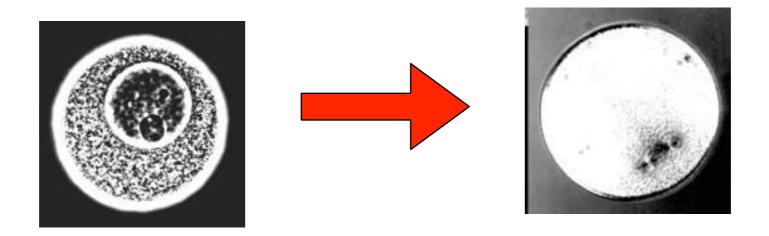


There are actually hundreds of substrates, many with multiple phosphorylation sites

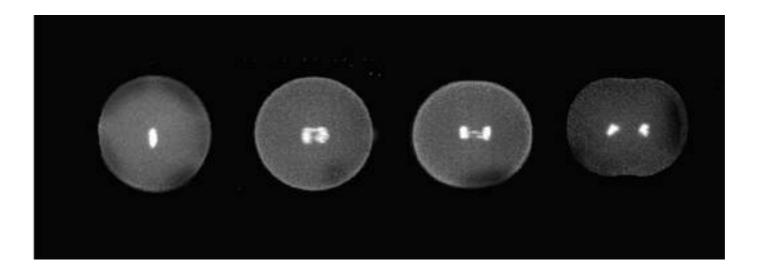


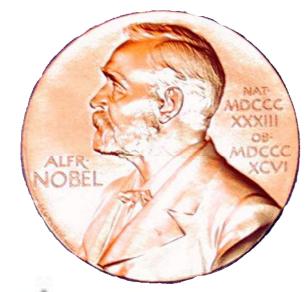
#### SO SIMPLE WHEN YOU UNDERSTAND!

Cyclin Accumulates, Cdc2 Turns On, Cell Enters Mitosis



Cyclin is Destroyed, Cdc2 Turns Off, the Cell Exits Mitosis





Åt dem som har gjort månskligheten den största nytta Nobels testamente (Nobelförsamlingen) Kårolinska institutet lur heslutat atl 2001 års

#### NOBELPRIS

i fysiologi eller medicin skall tillerkännas och gemensamt utgå till

(Tim Hunt)

LELAND H HARTWELL OCH

för deras upptäckter röninde kontrotlen av celleykeln

STOCKHOLD DESCRIPTIONS AND THE PROPERTY SOOT

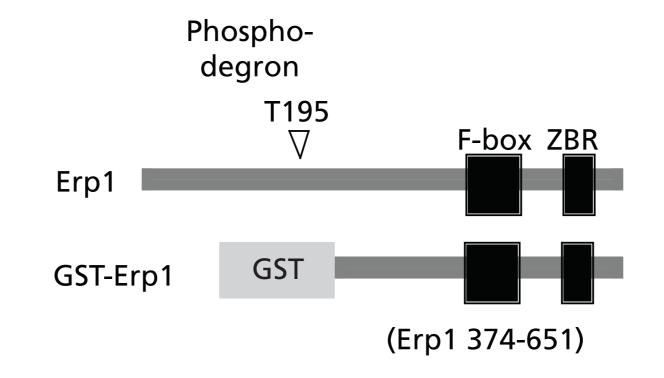
A.C. Ageir

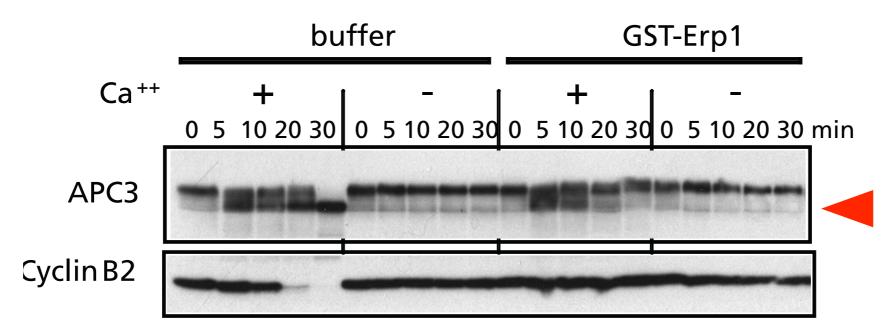


1 per Cinery



## Another Tiny Hint...

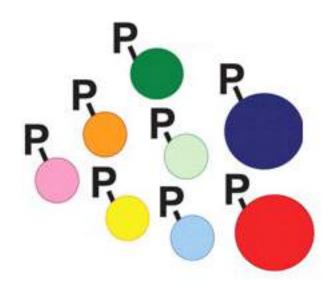




#### How Do You Get Out Of Mitosis?

#### Mitosis

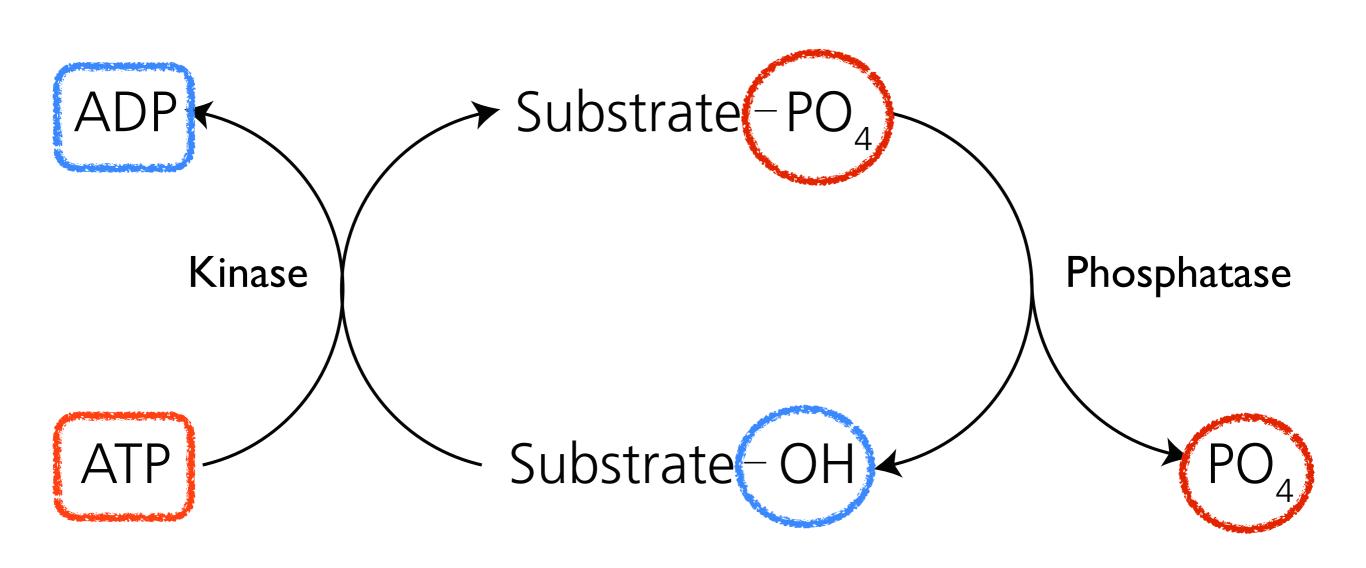
### Interphase



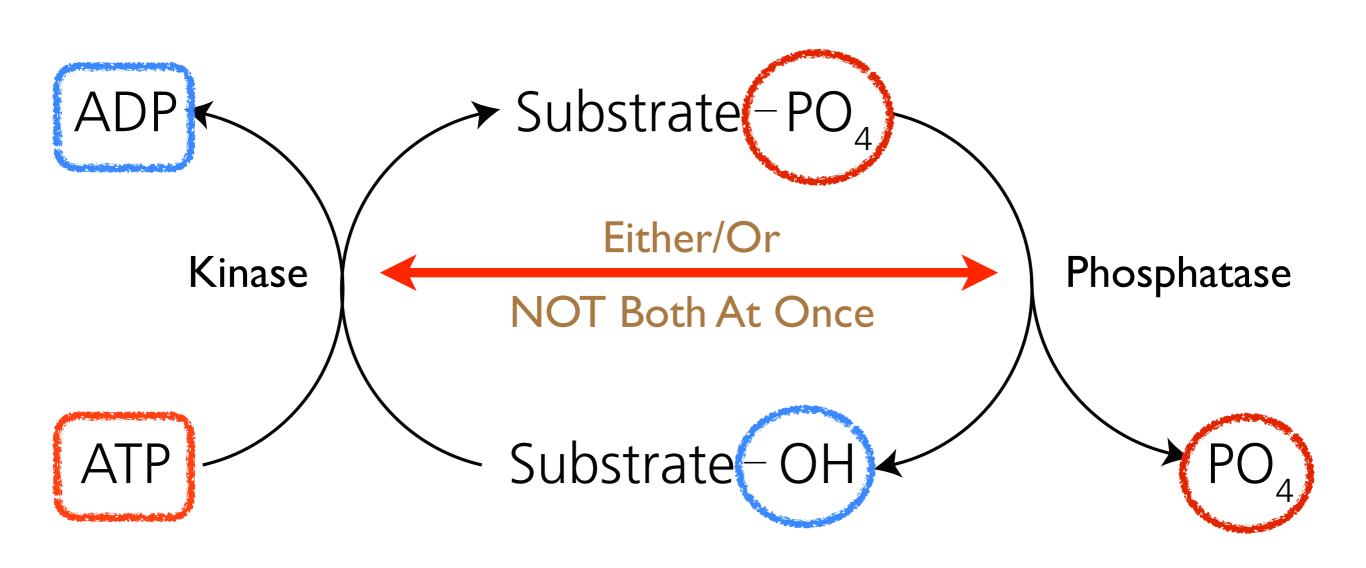
Who Does This?



### The Futile Cycle Problem...



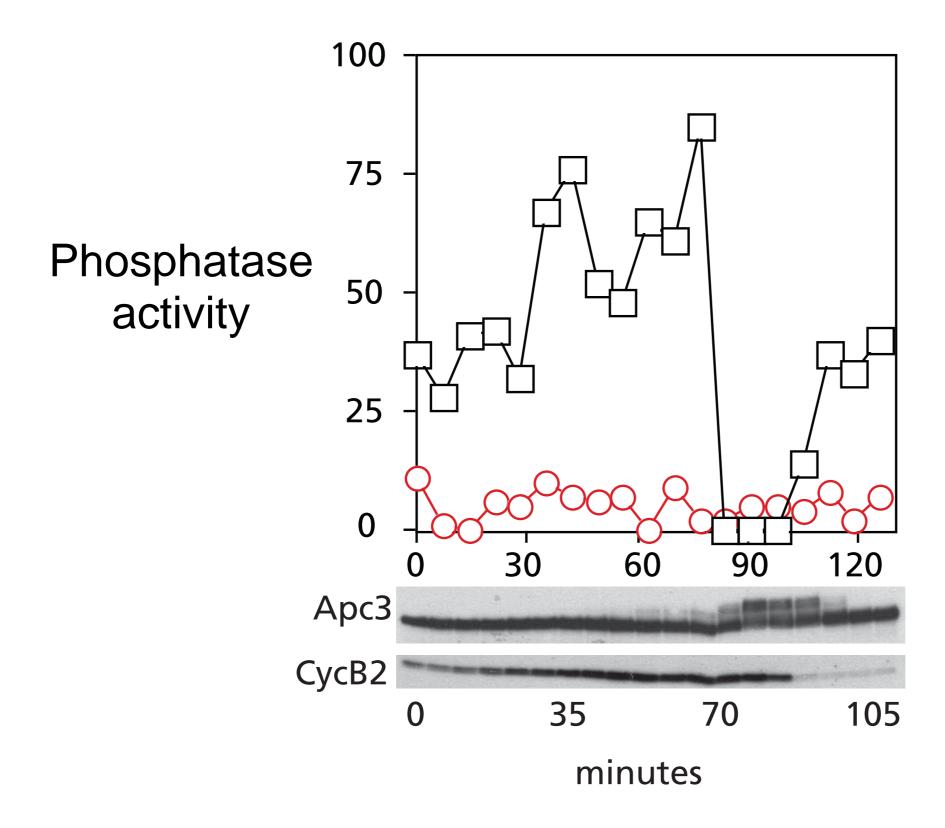
### The Futile Cycle Problem...



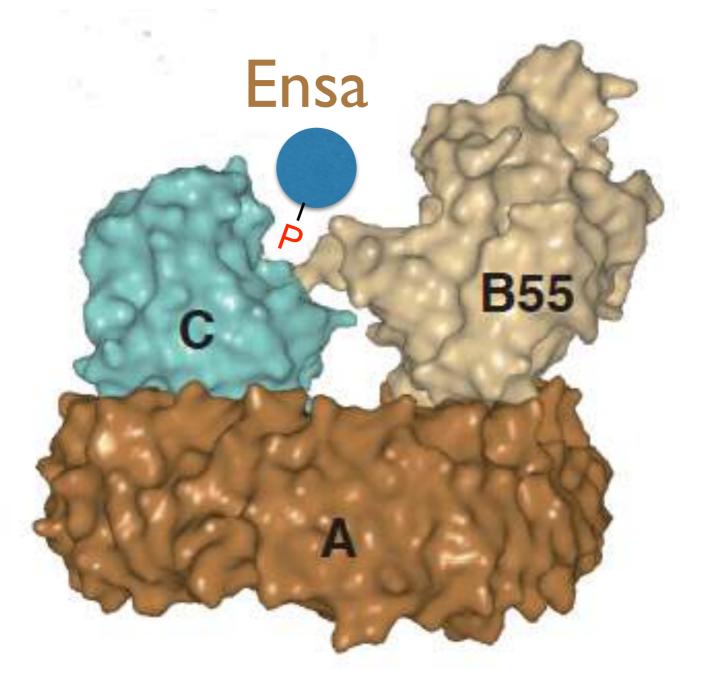




#### Phosphatase X Turns Off in Mitosis

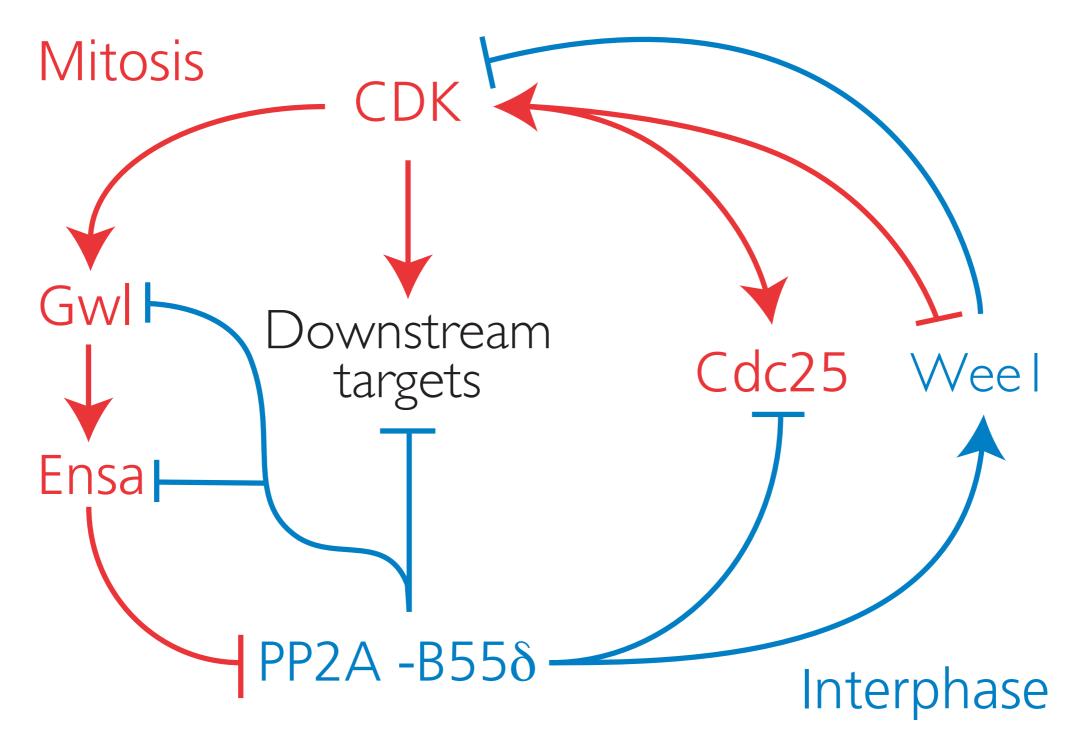


# PP2A-B55δ is inhibited by a pseudo-substrate



(A Phosphorylatable Phosphatase Inhibitor)

# A Tricky Ambiguity: Phosphatases Work Both Downstream And Upstream of CDK I



French students are inclined to think that theory is the thing, and experiments are some sort of lousy cookbook operation which you do hastily at the end of your work. But look at the numbers. For the wind in the willows, theory represented three months' work for four or five people; the experiments represented something like four years of work on the optical side, and four years of work on the surface side, done by different people. So experiments are really the stumbling block.

#### Notes on Style: Pierre Gilles de Gennes

Science is clearly a form of art, with the same invention and the same doubts. There are major differences, however: one is the difficulty of communication. An Indian playing his flute in the streets of Bogota invents a new tune: with ten seconds, and passerby may be struck by it – possibly for their whole life. But in our trade, a beautiful discovery can be transmitted only to people who have been through a long specialized education. We must do our best to keep in contact with our fellow citizens, but we often fail...

...Incidentally, the artistic professions suffer from many parasites: among others, the art critics, or commentators. Fortunately, we do not have the counterparts of art critic in our sciences (although some referees tend to mimic this style...).

# Being INTERESTING is more important than being right!

It doesn't matter if you get it slightly wrong (you can never get it completely right)

And if it's important, the next people will correct you.

The EDITORS' job is to create a journal where authors feel at home (for one reason or another)

• Fair

Friendly

Efficient

Browsing?

# The Problem of Libraries & Librarians

