

How to Win a Nobel Prize

Tim Hunt

“Thinking Big in a Small World”

Rigi-Kulm

20 January 2013



What's it worth?

Then

Now

2001

2012

£1,500

£7,000

0.7%

3.3%

1/3rd share was £213,000 in 2001

Alternative Title:

“Wild Speculation Based on Faulty Logic”

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

[Nobody really likes new ideas!]

The Ambassador Problem

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: within ten seconds, passers by 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 specialised education. We must do our best to keep in contact with our fellow citizens, but we often fail.

Pierre Gilles de Gennes, *Soft Interfaces*

Growing up in Oxford..



PERFORMING



Henry Parlier

TEACHERS

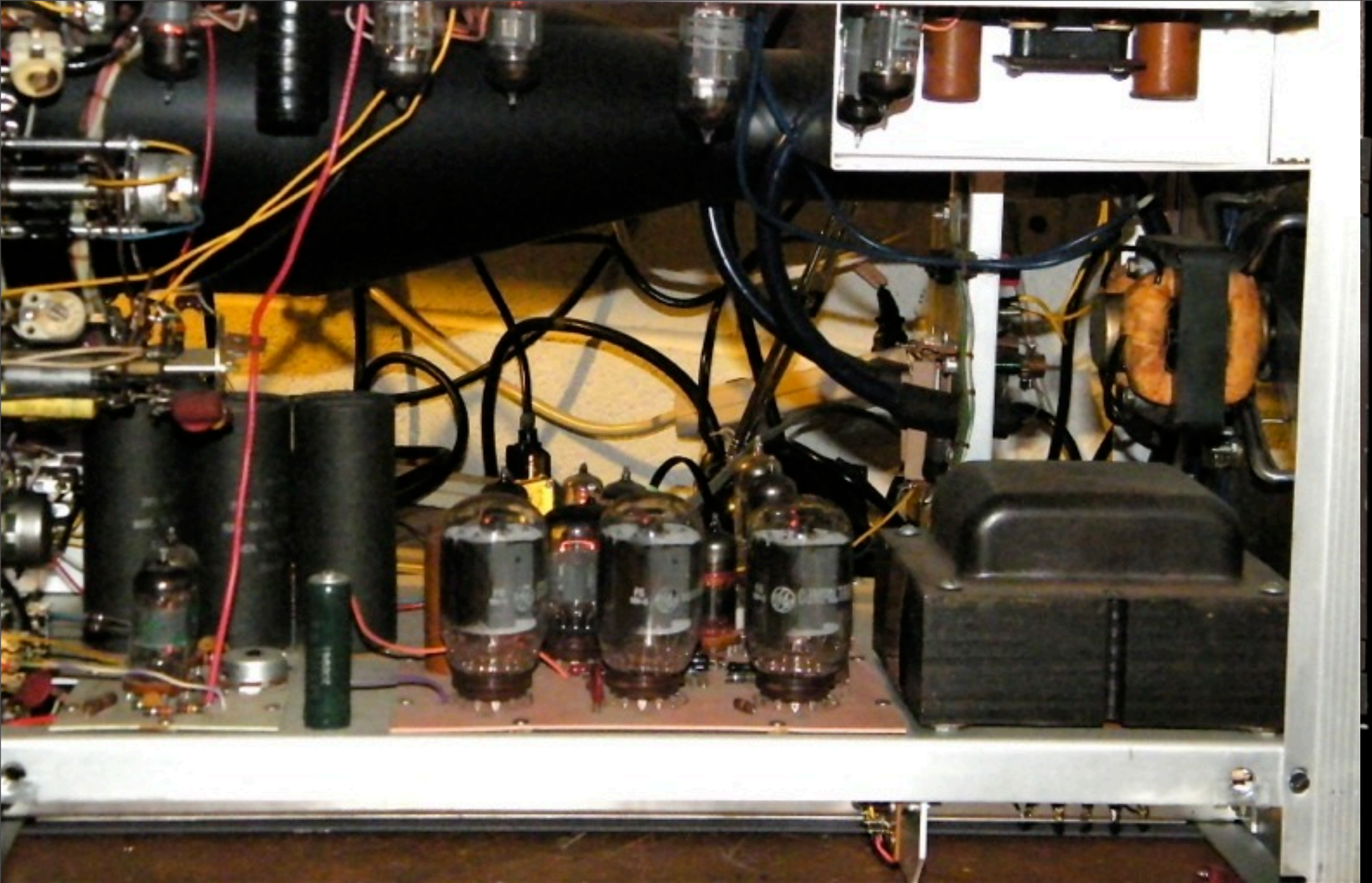


Gerd Sommerhoff: 1915-2002

No set curriculum and
examinations were required.

The only restriction was that the three terms should be devoted to
physics, chemistry and biology in rotation

“Just get them interested”
said Jock Lynam, the headmaster.



“Inventive children want to learn in a self-directed way and under their own steam. The best in them is stifled by pre-set routines...

Learning the skills, of course, is crucial, but the ideal time for that is after they have discovered the need for them in their own free endeavors”.

Gerd Sommerhoff “In and out of consciousness”, 1996

Cambridge

(learning to be a scientist)



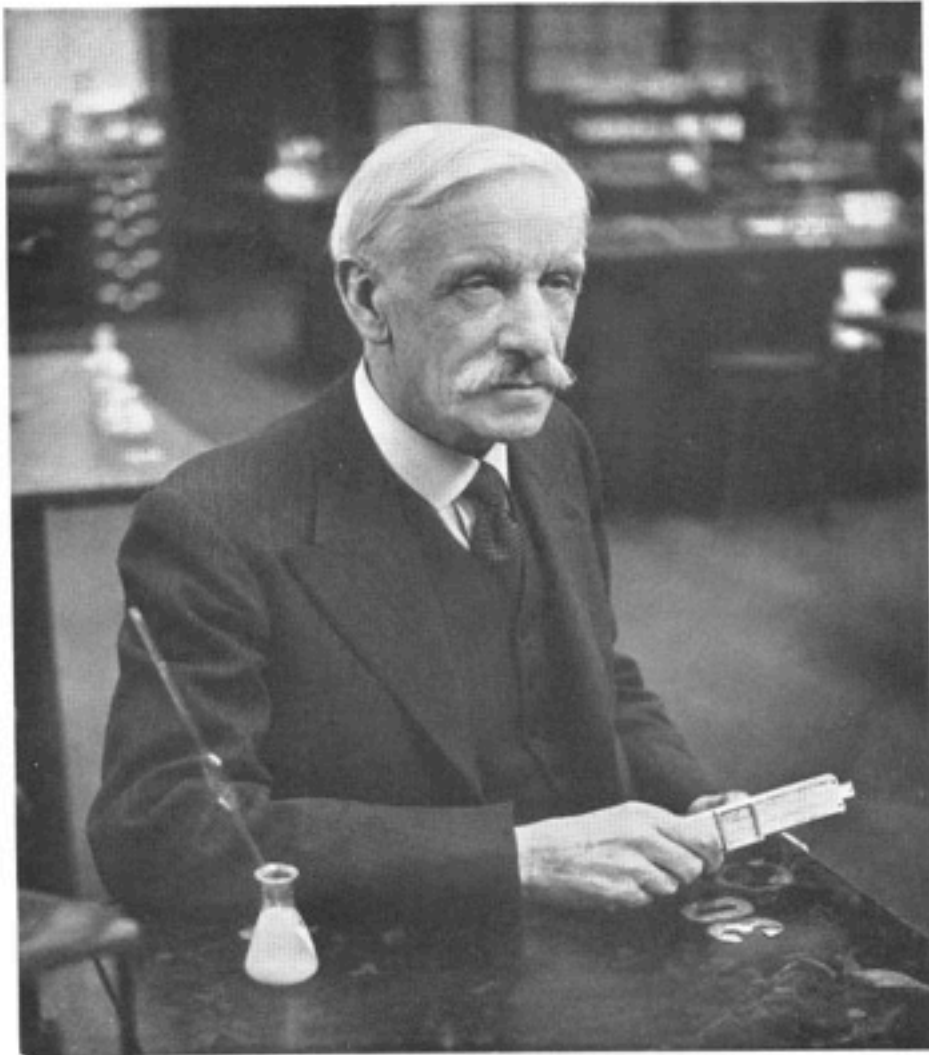
The Old Cavendish



Tuesday, 22 January 13

Newton's Laws
Maxwell's Equations
Thompson's Electron
Rutherford and Radioactivity:
The Atomic Nucleus
The Proton
The Neutron
Splitting the Atom
Watson & Crick - DNA
Kendrew & Perutz - Protein Structures

Good at Biology, and not bad at Chemistry...



FREDERICK GOWLAND HOPKINS

1937

Nobel laureate 1929 for vitamins

PERSPECTIVES IN BIOCHEMISTRY

Thirty-one Essays

presented to

SIR FREDERICK GOWLAND HOPKINS

*by past and present members
of his Laboratory*

Edited by

JOSEPH NEEDHAM

and

DAVID E. GREEN



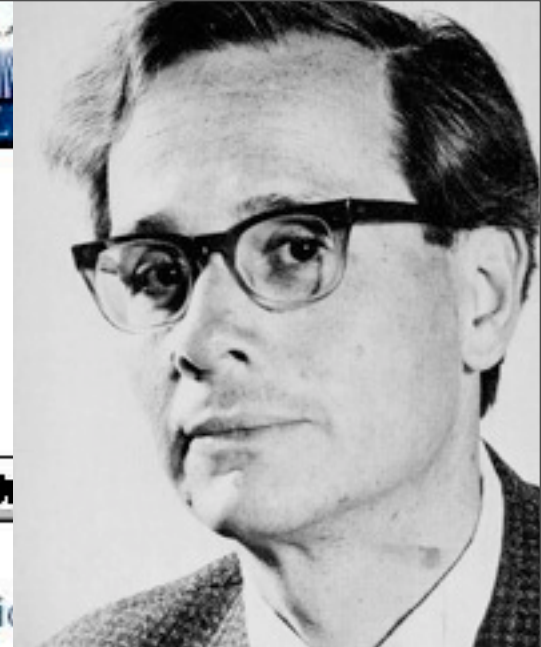
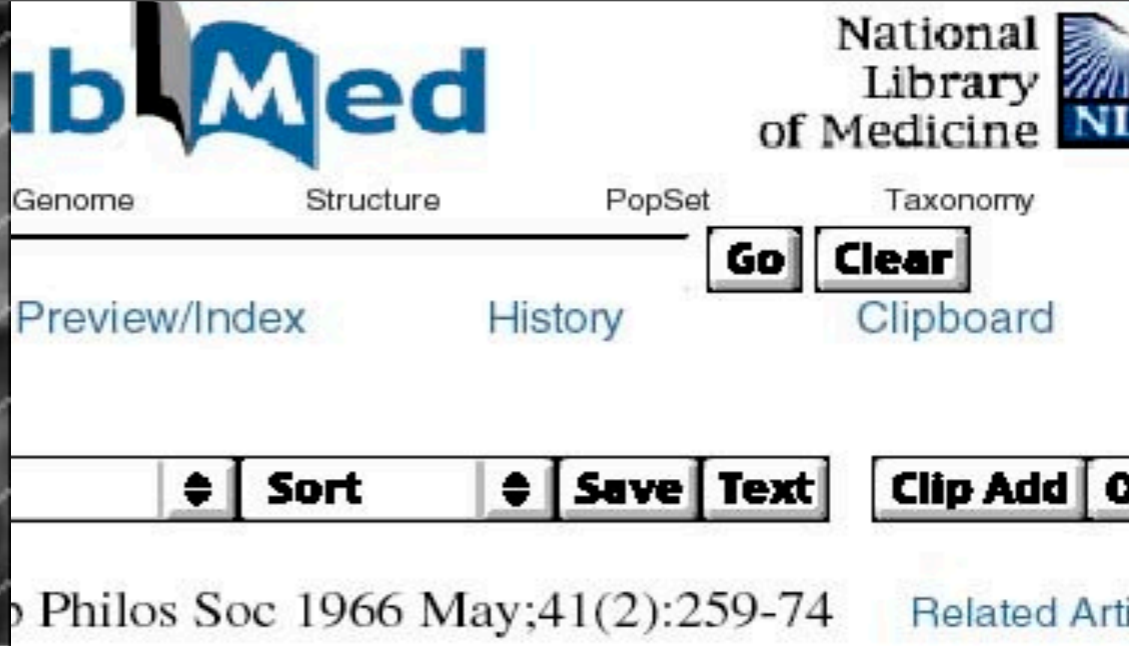
CAMBRIDGE
AT THE UNIVERSITY PRESS

1937

AMBITIOUS AIMS

CONTENTS

The Biochemistry of the Individual	<i>page 1</i>
By J. B. S. HALDANE, F.R.S. <i>Professor of Genetics, University College, London.</i>	
The Meaninglessness of the Terms Life and Living	11
By N. W. PIRIE, M.A. <i>Demonstrator in Biochemistry, University of Cambridge.</i>	
Recent Developments in our Knowledge of the Protein Molecule	23
By DOROTHY JORDAN LLOYD, D.Sc., F.I.C. <i>Director of Research, Leather Research Association, London.</i>	
Proteins and Cell-Organization	36
By R. A. PETERS, M.D., F.R.S. <i>Whitley Professor of Biochemistry, University of Oxford.</i>	
A Speculation on Muscle	45
By J. D. BERNAL, F.R.S. <i>Assistant Director of Research in Crystallography, University of Cambridge.</i>	
Chemical Aspects of Morphogenetic Fields	66
By JOSEPH NEEDHAM, Sc.D. <i>Sir William Dunn Reader in Biochemistry, University of Cambridge.</i>	
Molecular Forces, Orientation and Surface Films	81
By N. K. ADAM, F.R.S. <i>Professor of Chemistry, University College, Southampton.</i>	
The Economy of the Bacterial Cell	91
By MARJORY STEPHENSON, M.A., Sc.D. <i>Member of Staff, Medical Research Council, Cambridge.</i>	
Rigidification in Phylogeny	99
By ERNEST BALDWIN, Ph.D. <i>Demonstrator in Biochemistry, University of Cambridge.</i>	



Early development of the echinoid egg compared with erythropoiesis.

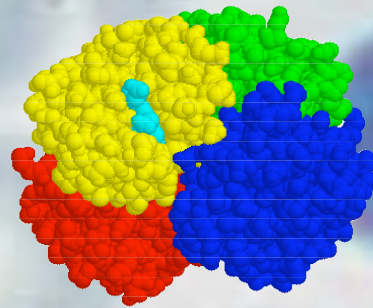
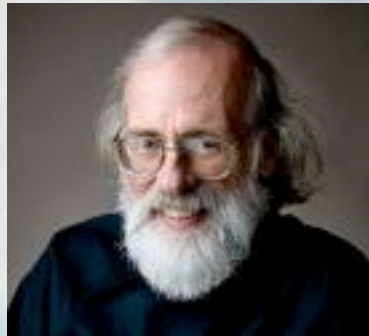
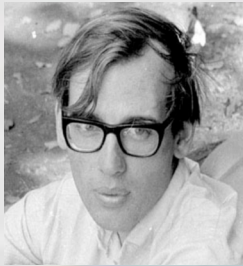
Borsook H.

MEETINGS: FOOD FOR THOUGHT (and Vernon Ingram gets it wrong!)

- Female
- Genetic Code*
- In Vitro
- Ovum*

PMID: 5205707 [PubMed - indexed for MEDLINE]

A GREAT 'MODEL' SYSTEM



Haemoglobin



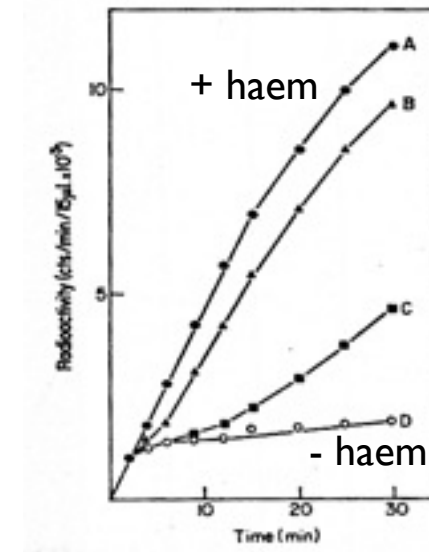
Haemoglobin Synthesis in Reticulocytes
Tony Hunter & Louis Reichardt

Travel Broadens the Mind

Globin Synthesis Needs Heme, and the Control is Reversible



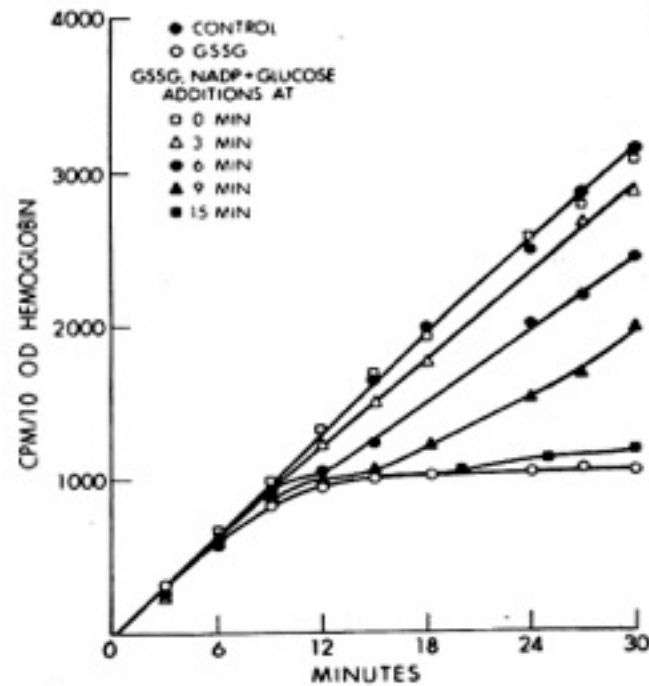
East 180th Street



Irving London in Thessaloniki, Woods Hole and New York
Summer 1966, and 1968 - 1970

HELPING OTHERS

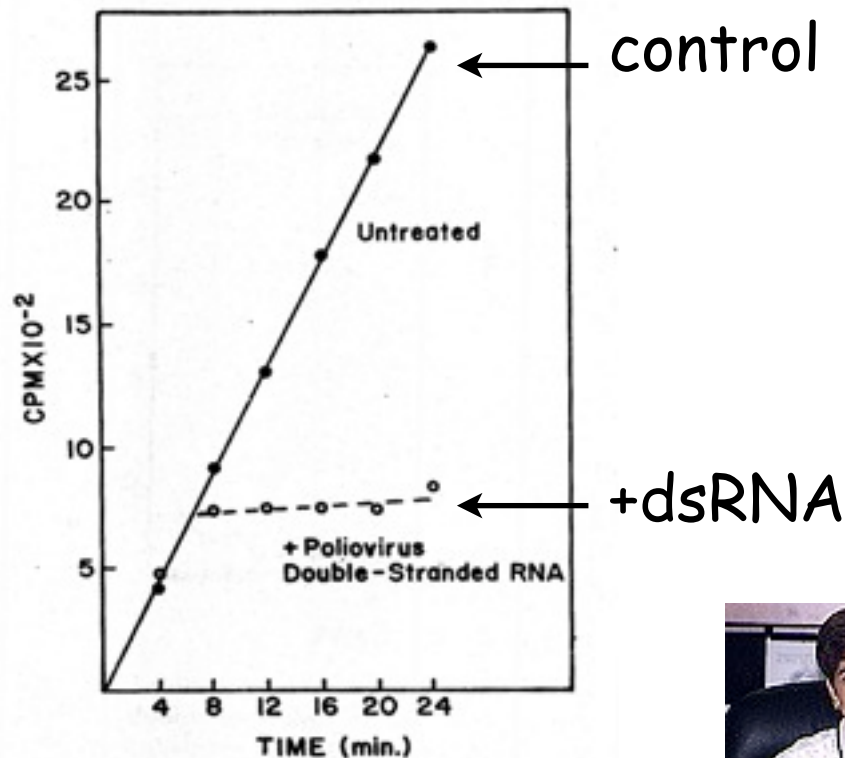
Tiny Amounts of Oxidized Glutathione Are Deadly



Nechama Kosower

Fun Collaborations

Tiny Amounts of dsRNA Kill Globin Synthesis



Ellie Ehrenfeld



Richard Jackson

CLEVER PEOPLE



Tuesday, 22 January 13

ORDEAL BY FIRE (over 1000°)



Unexpected Silver Linings

Purging the past: A clean break

New surroundings, new neighbours

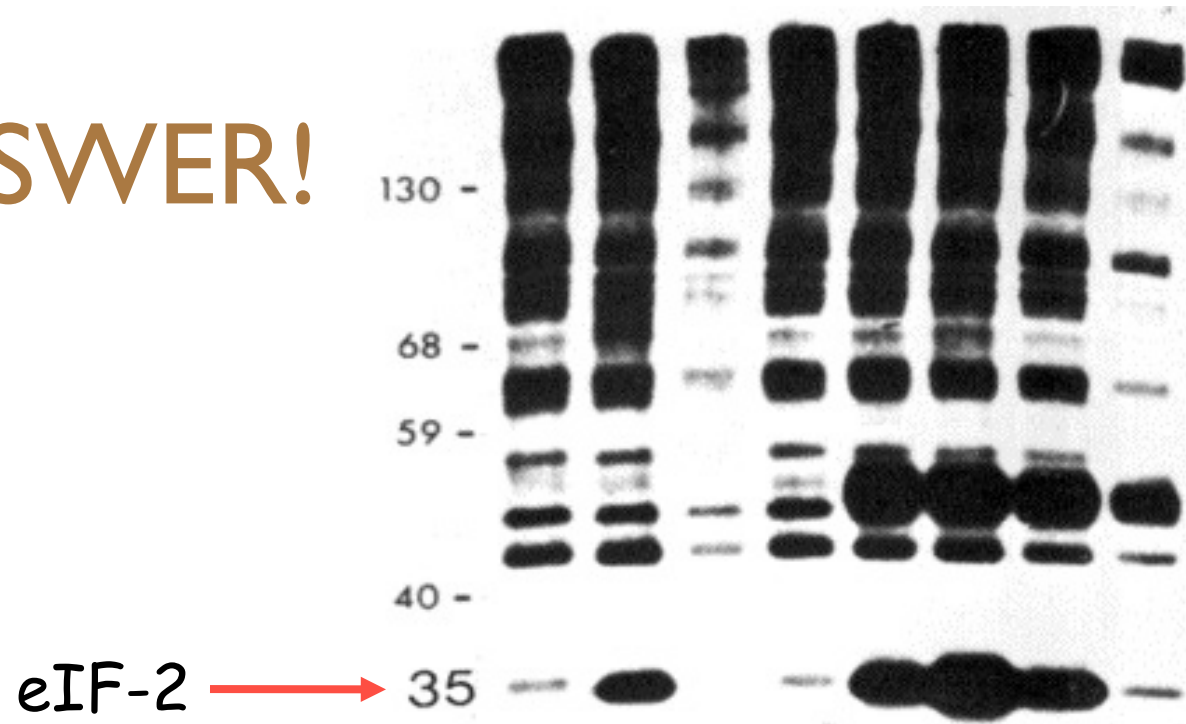
All new equipment

Wonderful stores (thanks to Max Perutz)

The MRC LMB canteen (thanks to Mrs Perutz)

dsRNA-dependent eIF-2 phosphorylation

The ANSWER!

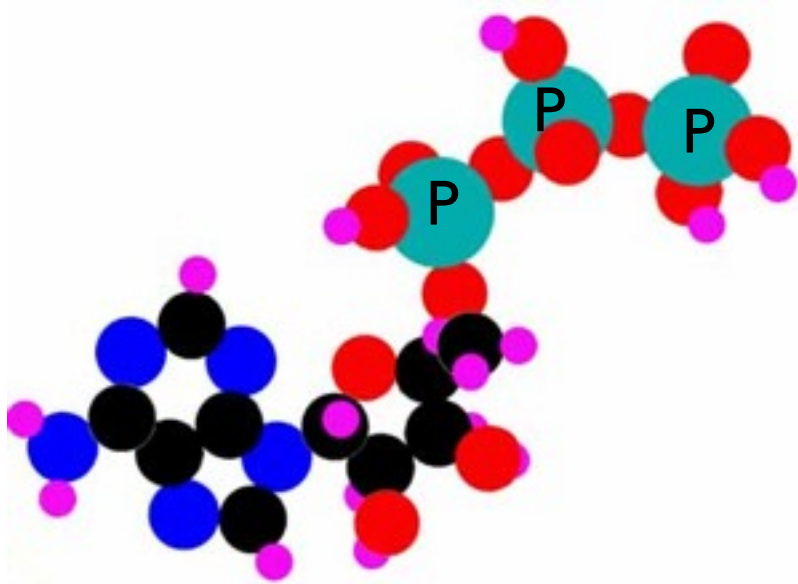


SDS-polyacrylamide gel

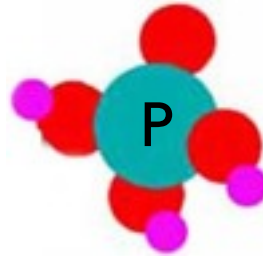
The ambassador's in trouble...

17 -

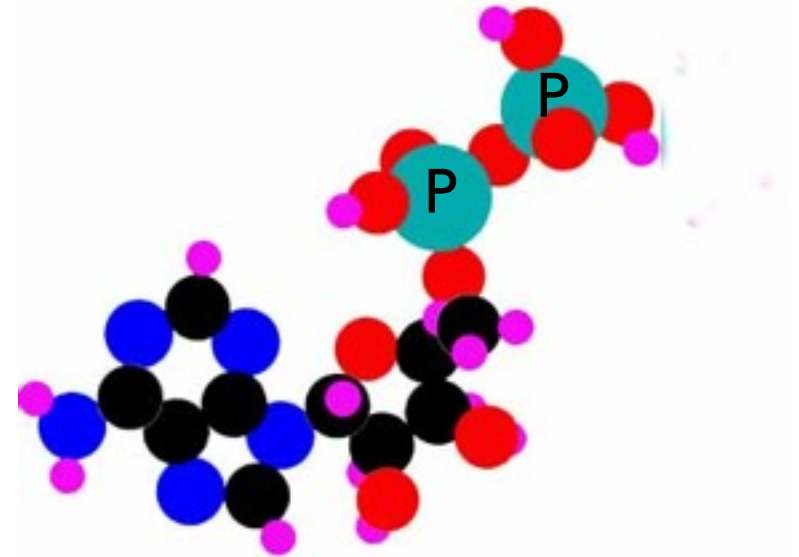
It's a PROTEIN KINASE!



ATP

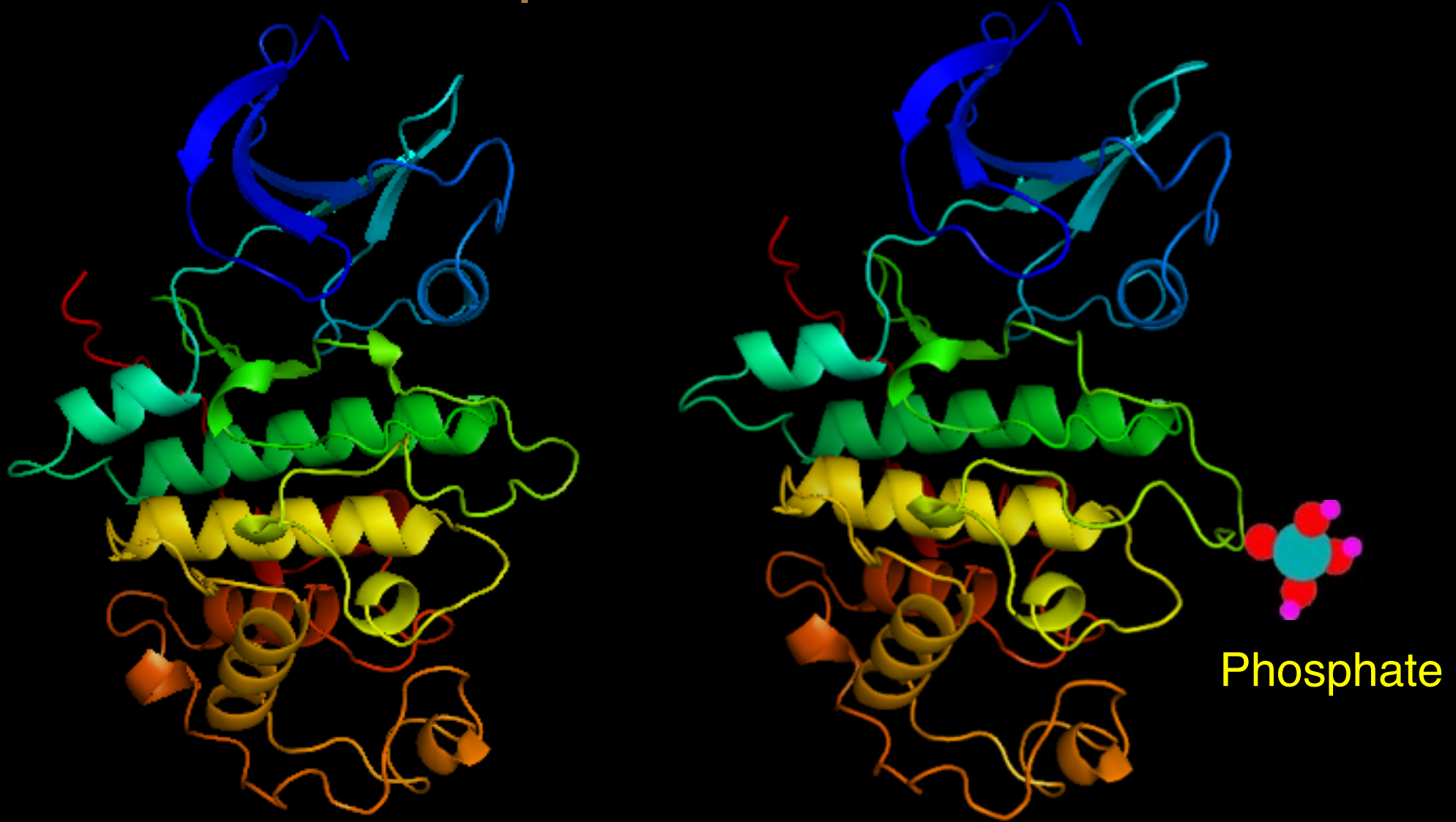


Phosphate



ADP

An Example of ACTIVATION



100X more active!

Phosphorylation...

Can also Cause INHIBITION,

Sometimes Sticks Proteins Together,

or may Blow them Apart!

(You Never Know Until You Look)

A Yellow Bicycle Changes my Life



FRIENDS & Colleagues



Tuesday, 22 January 13

Woods Hole, Massachusetts



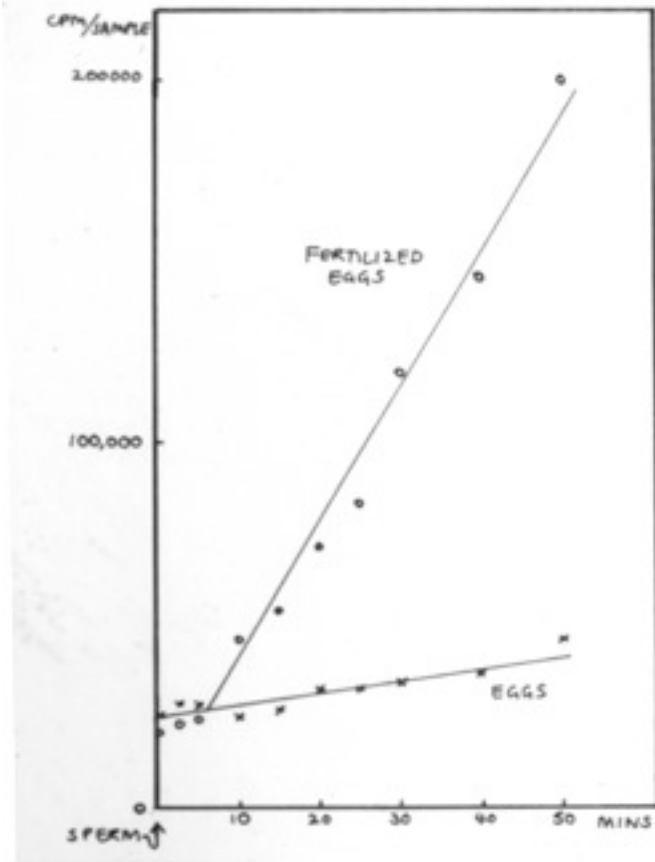
Tuesday, 22 January 13

A NEW START: Sea Urchin Eggs

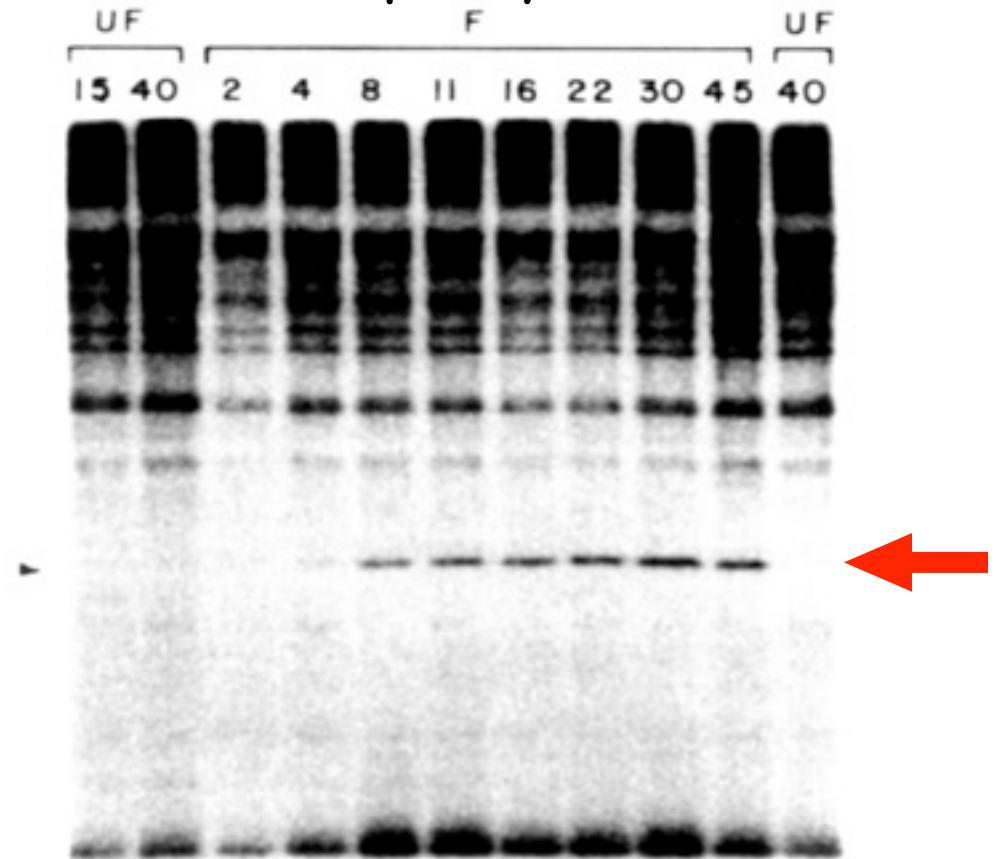


DYNAMICAL THINKING

Protein synthesis



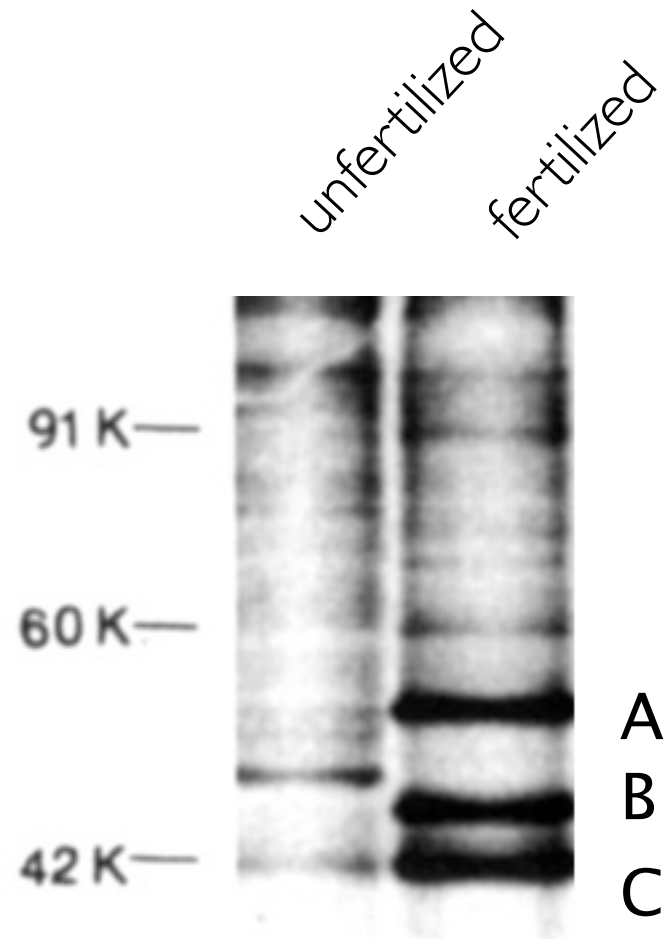
Phosphorylation



SDS-polyacrylamide gel

Translational Control

Clam eggs,
1979



Eric Rosenthal
& Joan Ruderman

Frog Oocyte Maturation Triggered by Progesterone



John Gerhart



1 mm

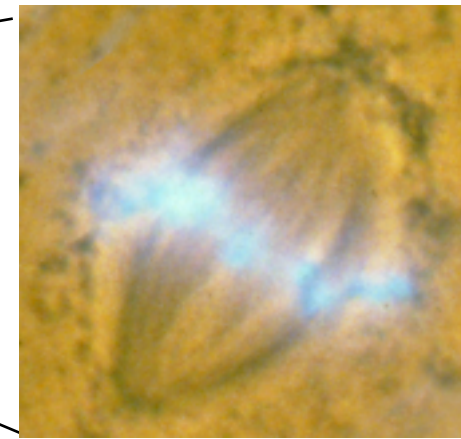
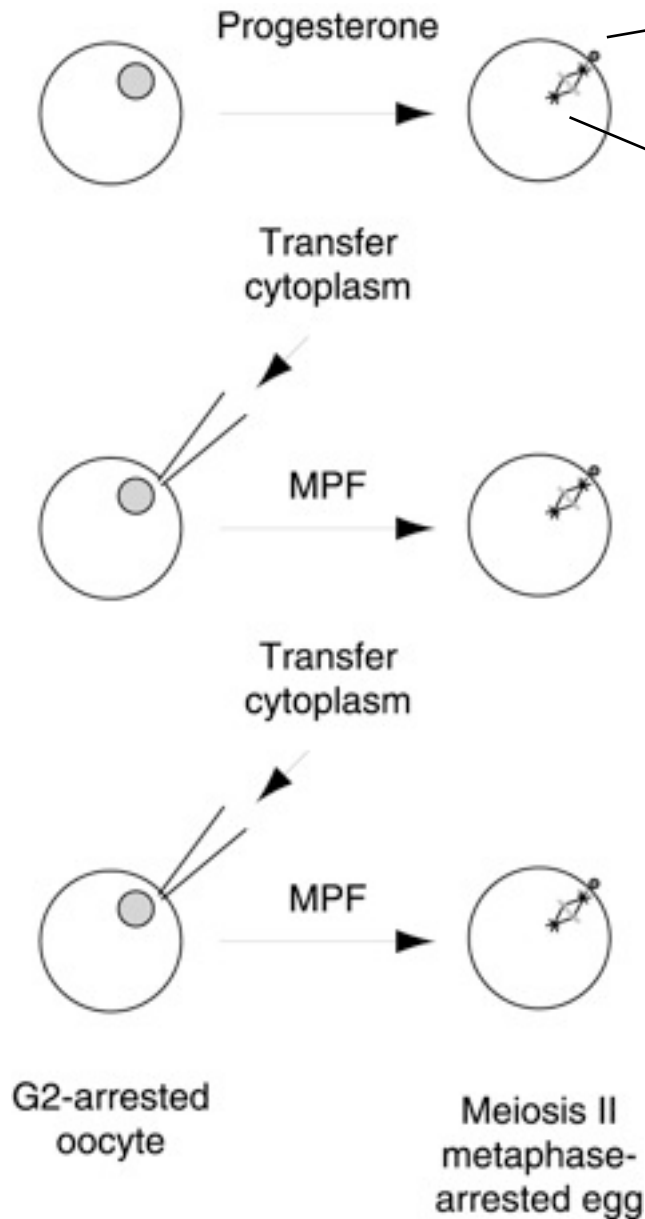
Frog Oocyte Maturation Triggered by Progesterone



John Gerhart



1 mm

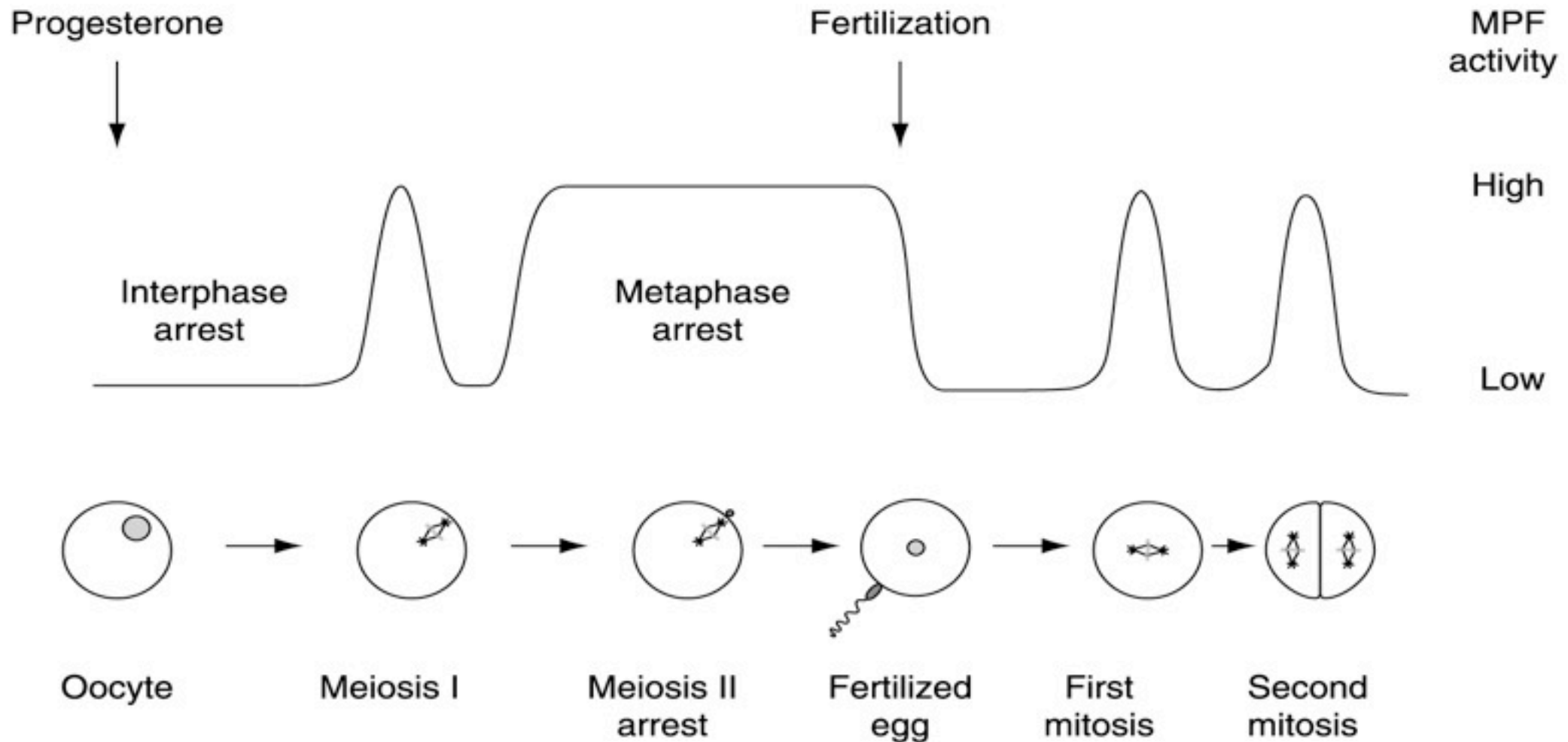


1971: Masui and Markert
Define MPF —
Maturation-Promoting Factor

An Enzyme that
 Catalyzes
 Cell Division!

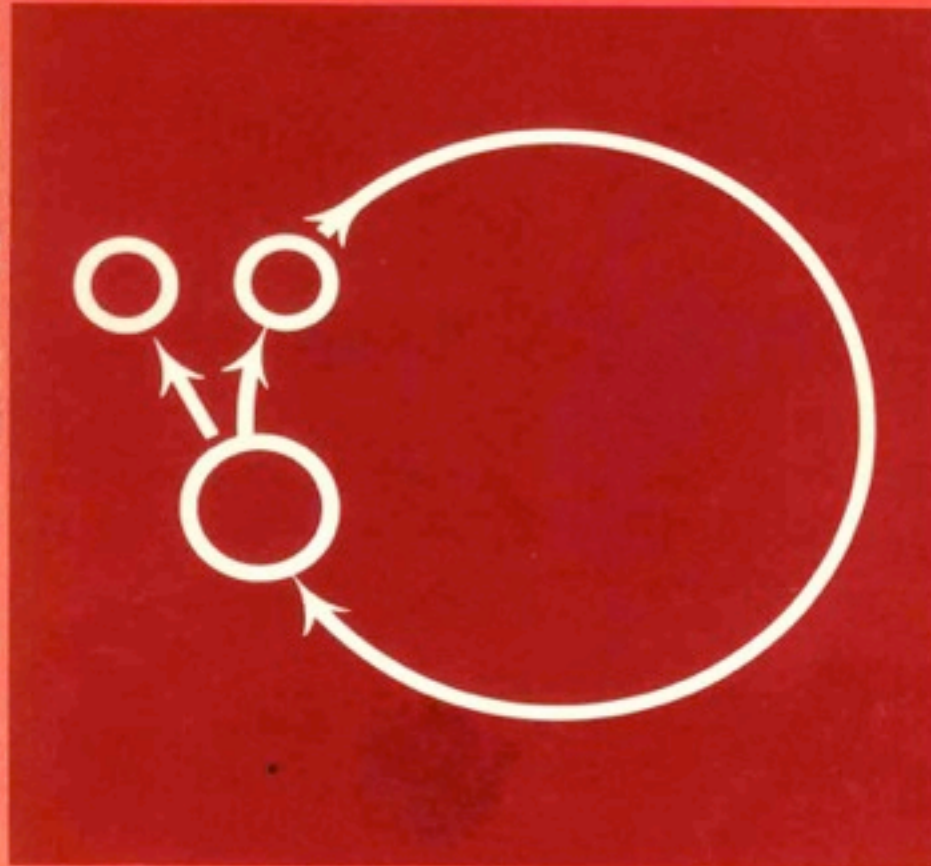
What a DELICIOUS problem!

1984: John GERHART, Mike WU & Marc KIRSCHNER—MPF OSCILLATES



J. M. MITCHISON

The Biology of the Cell Cycle



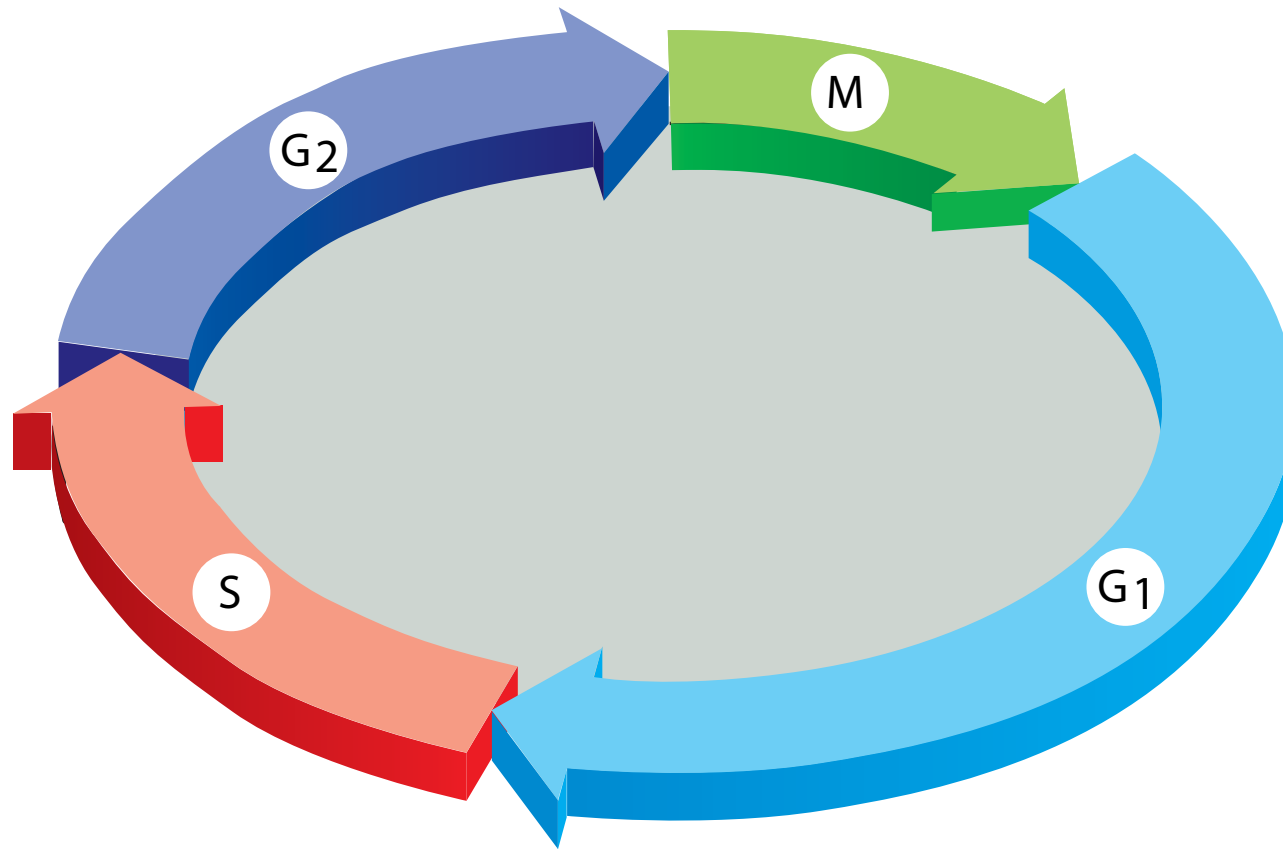
One Cell

Becomes
Two Cells

CAMBRIDGE UNIVERSITY PRESS

The Cell Cycle

Chromosome Segregation



DNA Replication

A Series of Events or Processes, S Alternates with M

10

Dan MAZIA, 1961

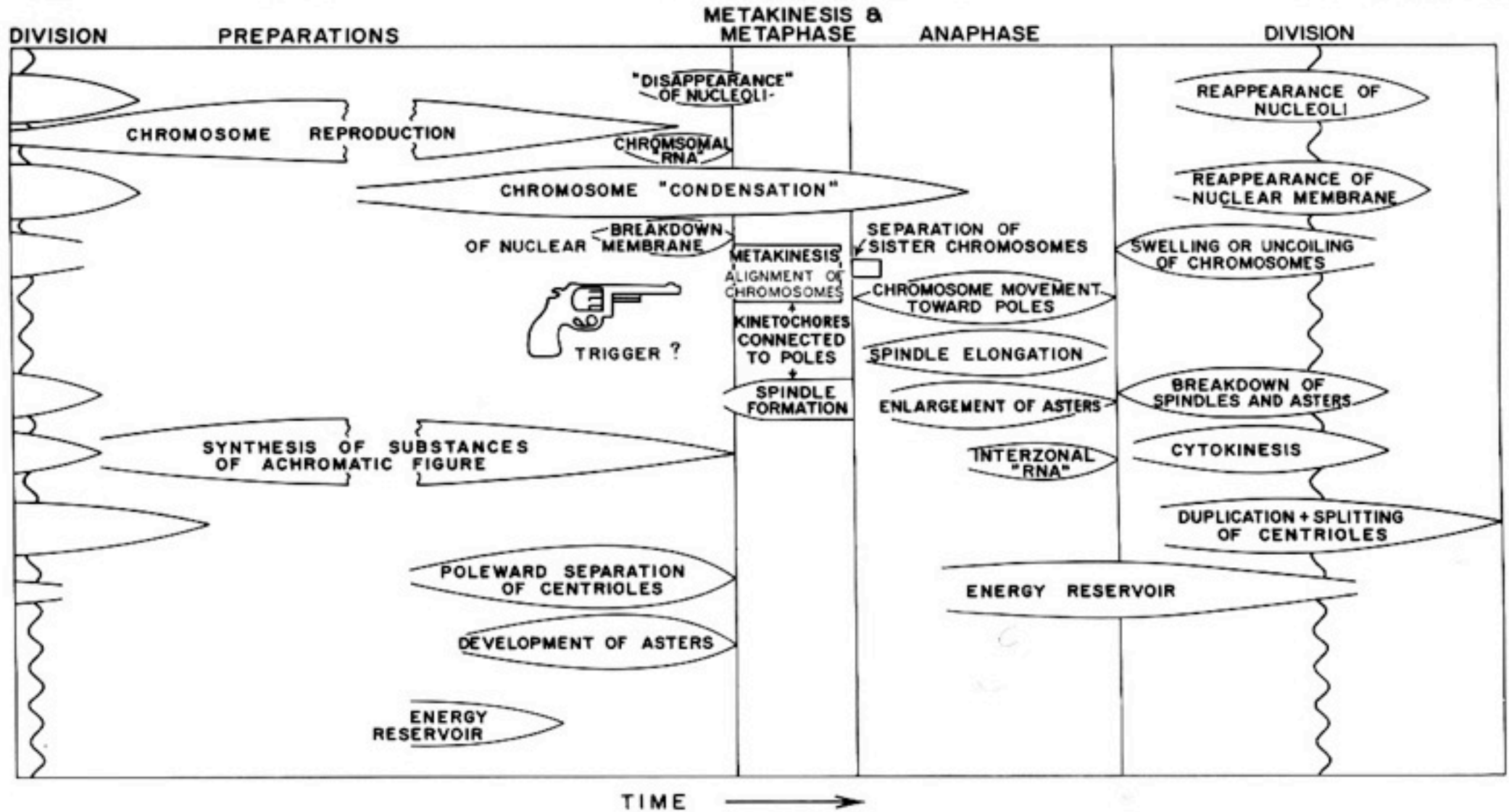
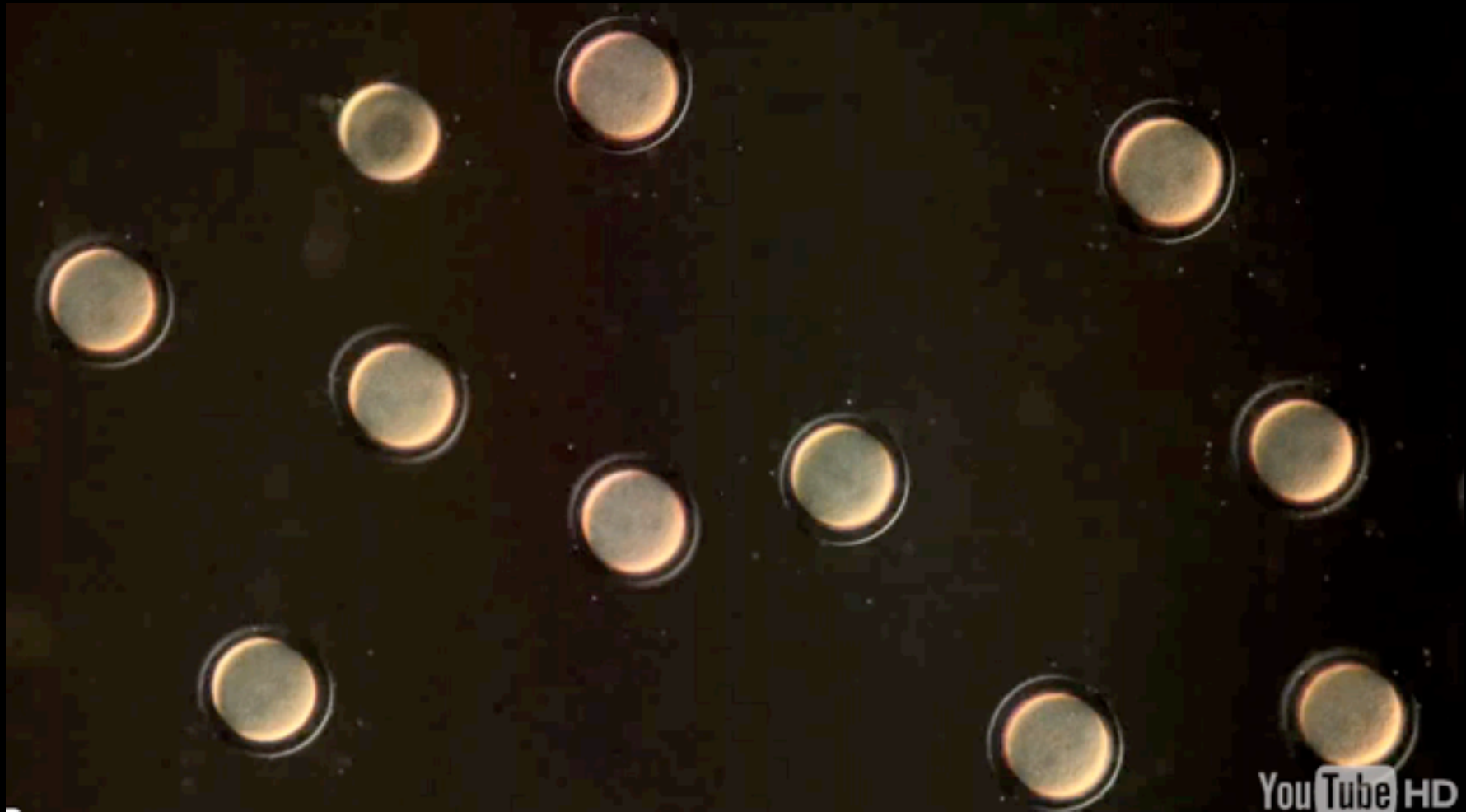


Figure 2. A generalized plan of the time flow of events in mitosis

The First 4 Divisions of Fertilized Sea Urchin Eggs

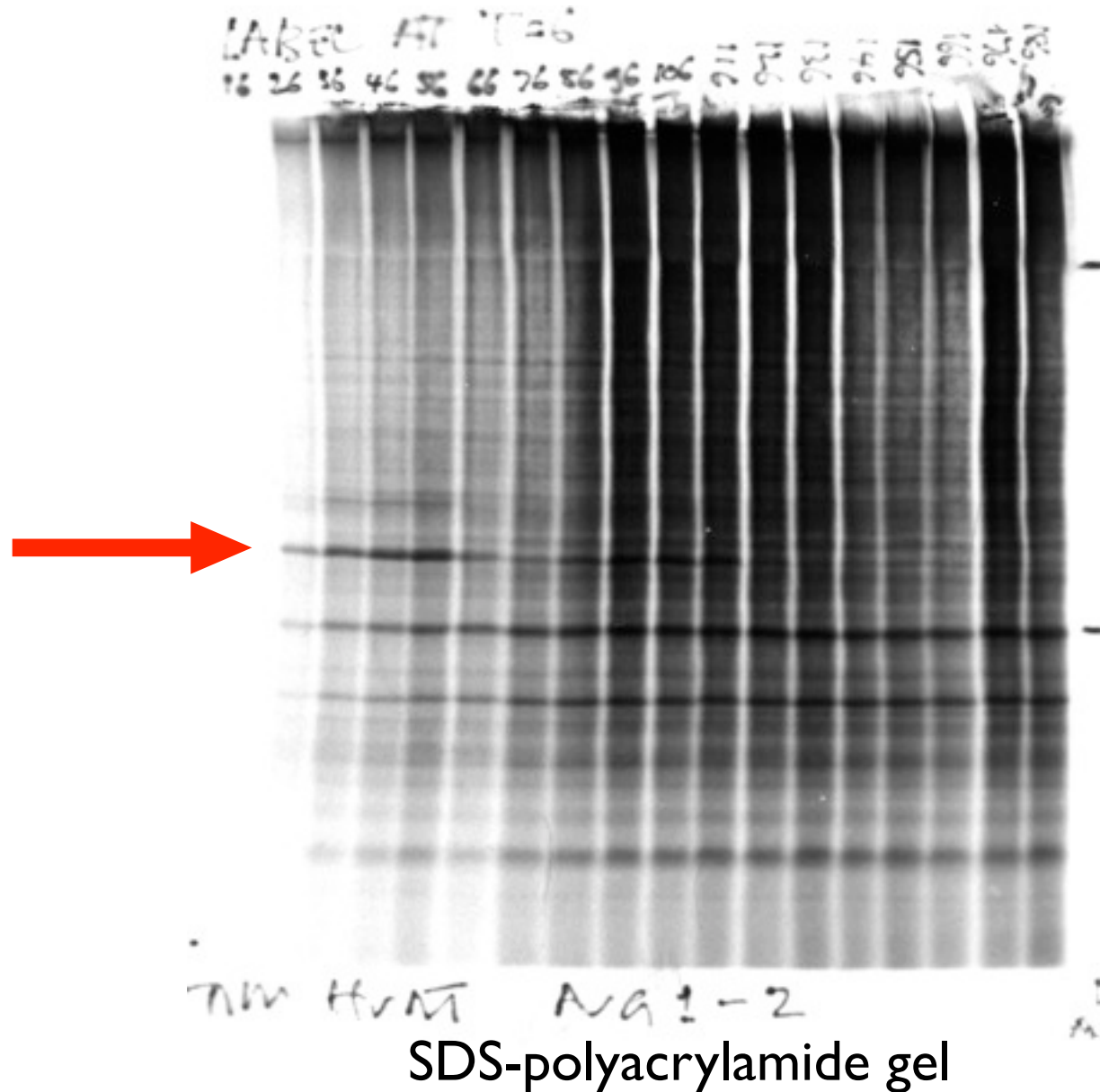
900X Speeded Up (by Christian Sardet)

The First 4 Divisions of Fertilized Sea Urchin Eggs

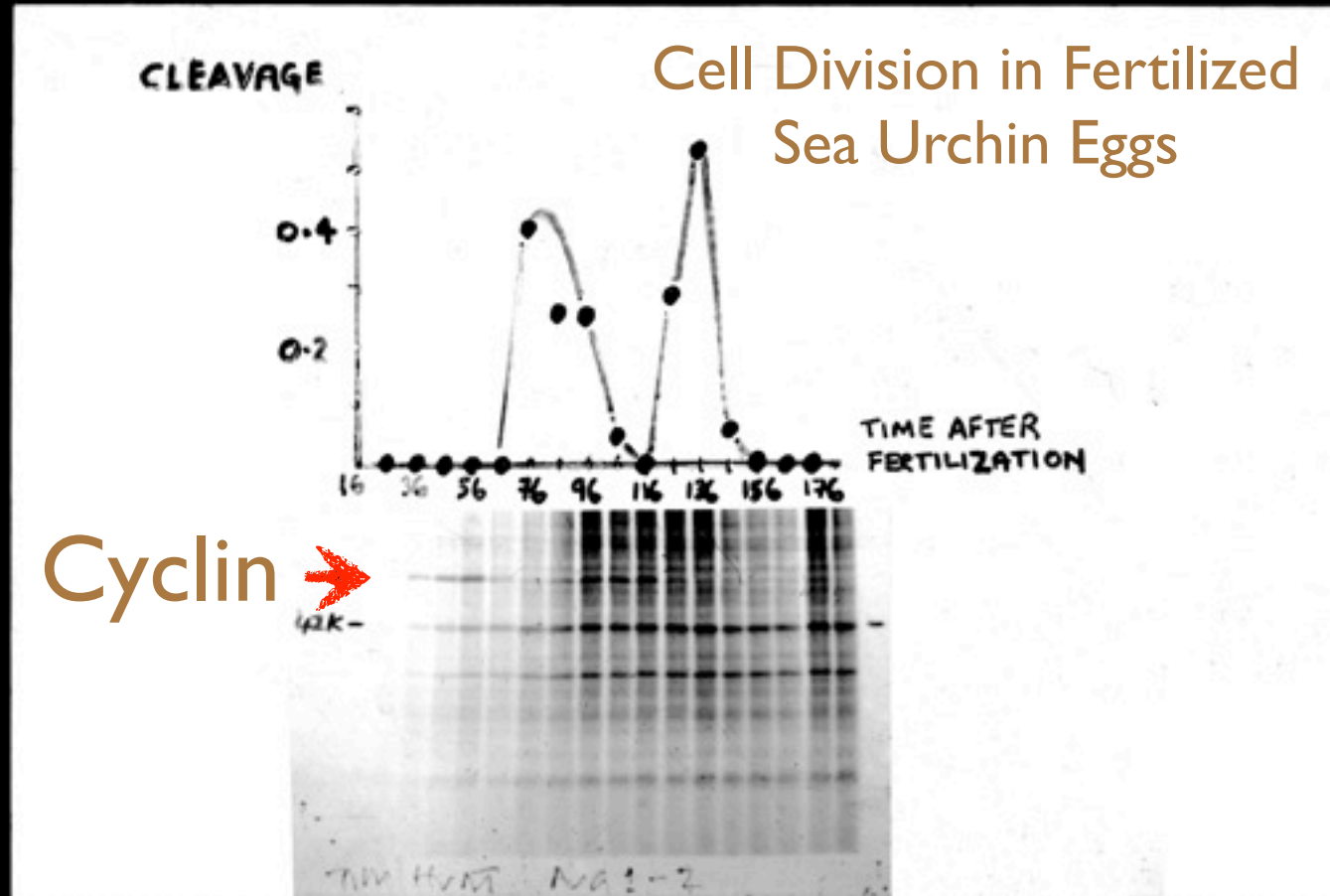


900X Speeded Up (by Christian Sardet)

CHANCE AND THE PREPARED MIND



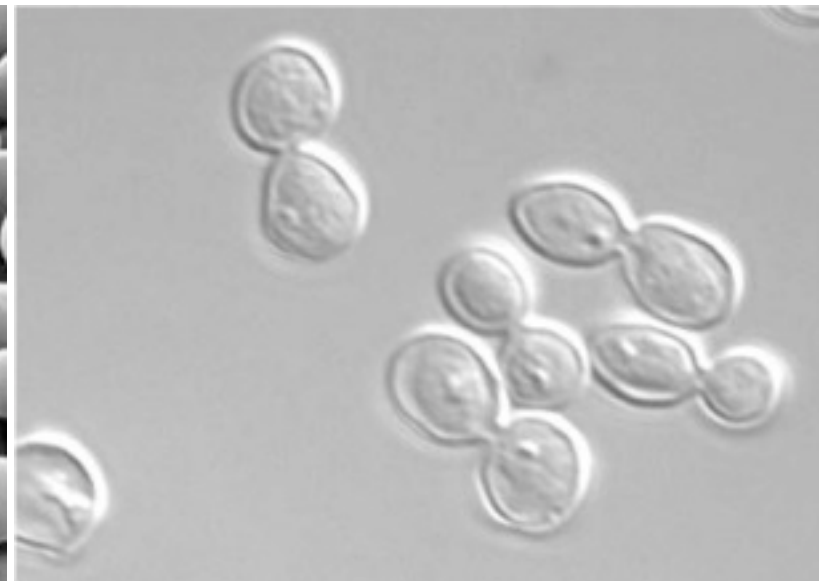
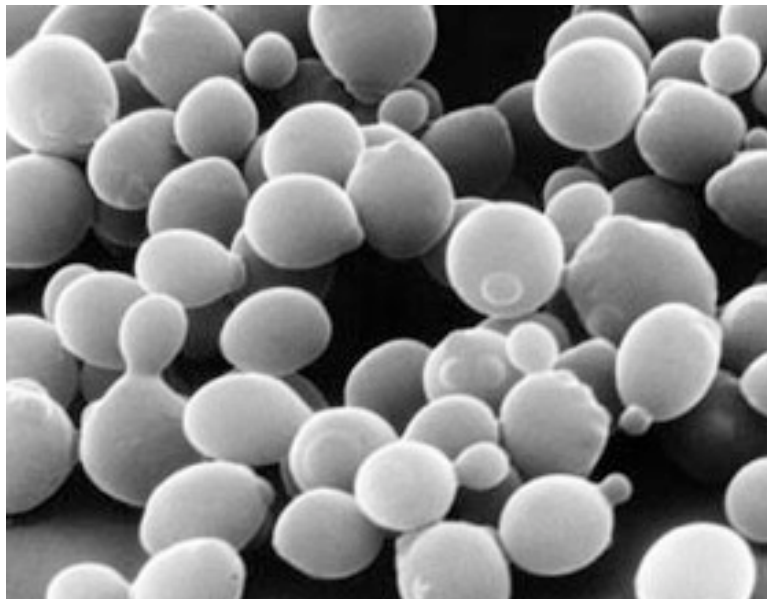
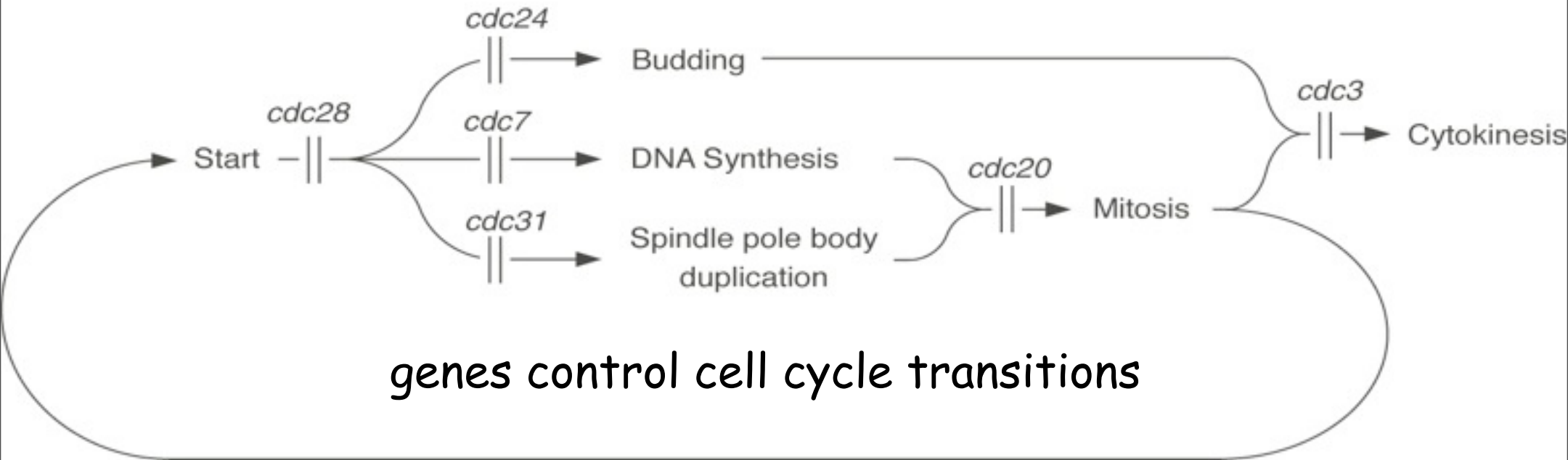
Now you see it, now you don't



NEW HORIZONS, NEW FRIENDS

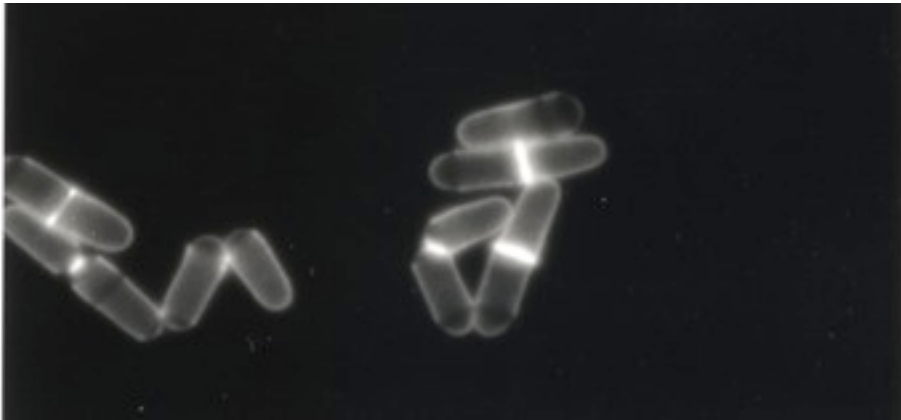
What is the cell cycle, and how is it controlled?

1970: Lee HARTWELL'S CDC STRAINS

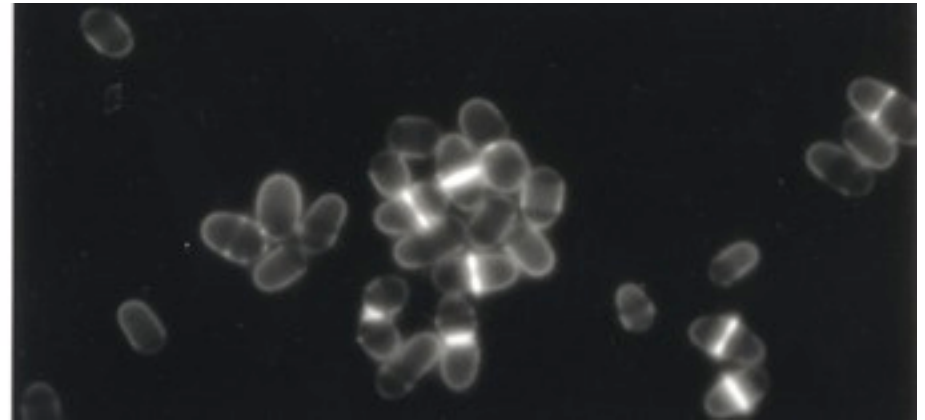




1975: Paul NURSE GETS GOING

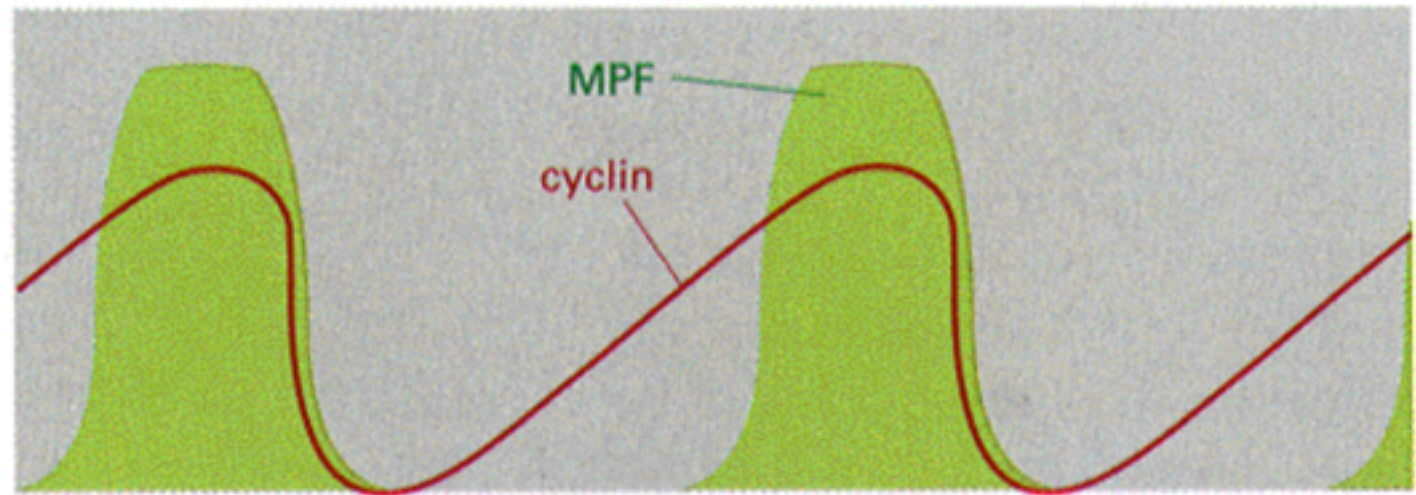
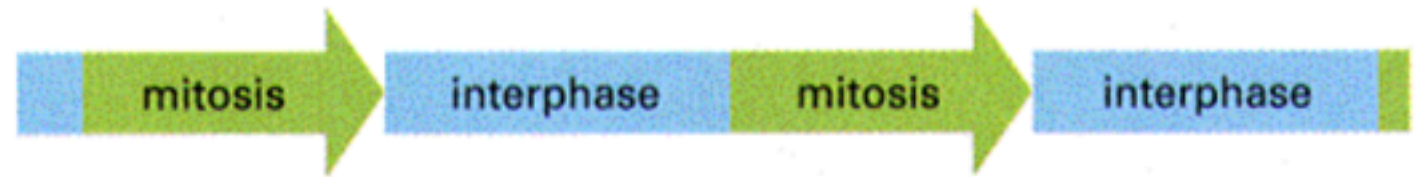


wild-type



wee1

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



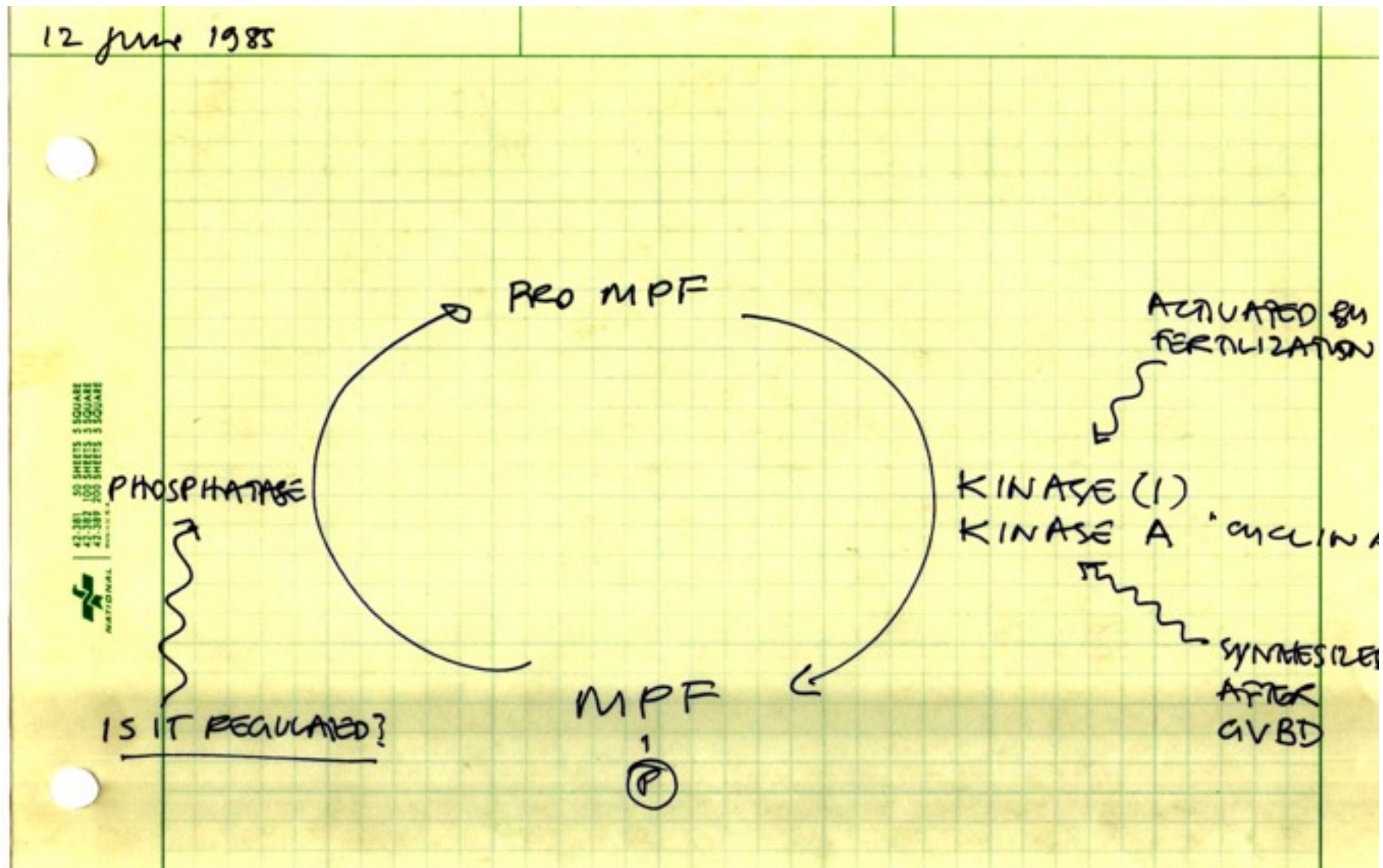
Concentrations

Cyclin A

Cyclin B

Ribonucleotide
reductase

DON'T TRY TO BE TOO CLEVER



Attract great STUDENTS, make good FRIENDS

Jeremy
Minshull



Jon
Pines

Paul Nurse

A photograph of a man with curly brown hair and glasses, wearing a red sweater over a blue collared shirt. He is smiling and holding a young child with blonde hair and blue eyes. The child is wearing a dark blue patterned shirt. The background is a light blue wall with white trim.

Andrew and Phoebe Murray

Tuesday, 22 January 13

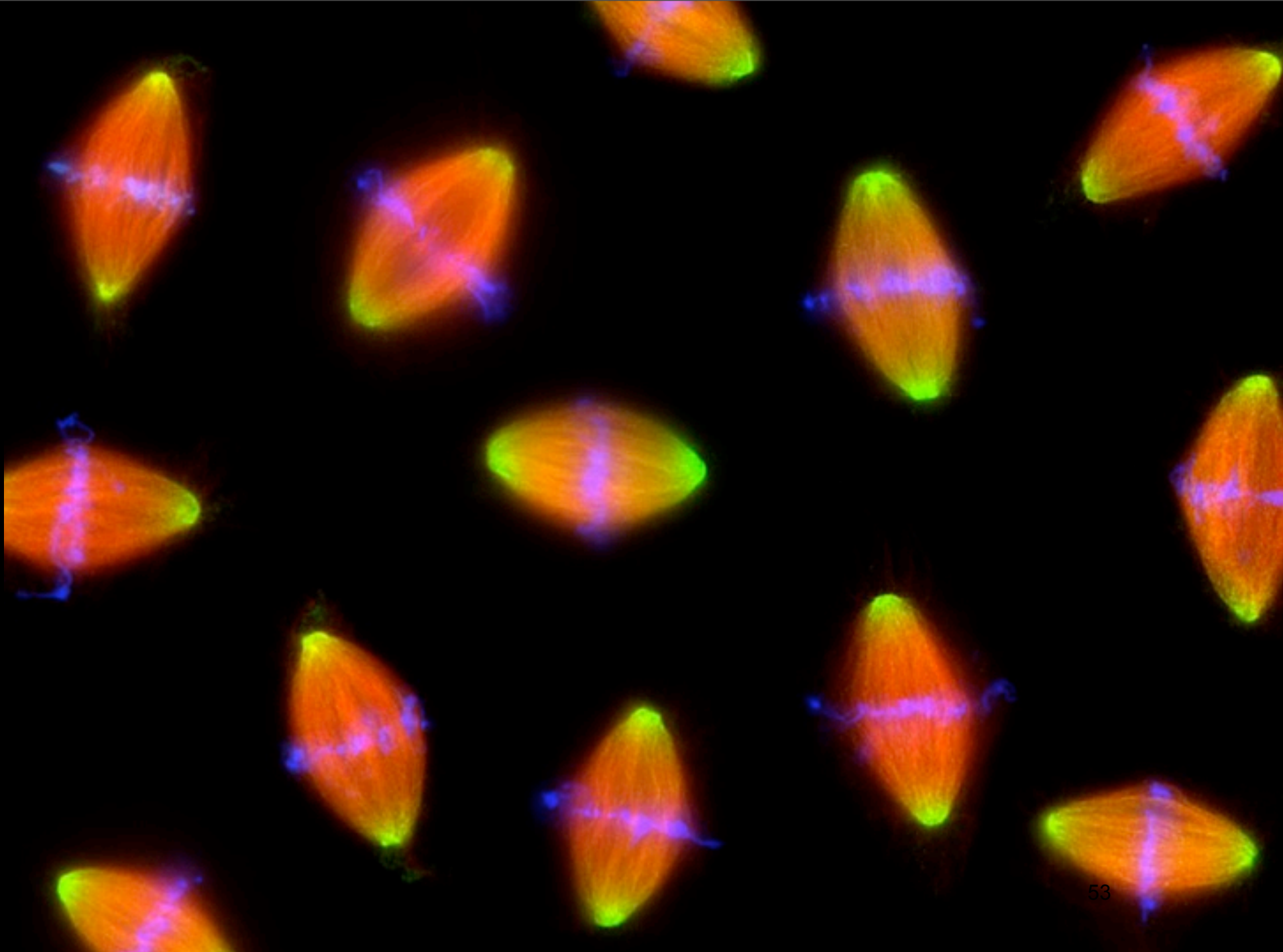
Frog Egg Extract: Pure Cytoplasm

Spin

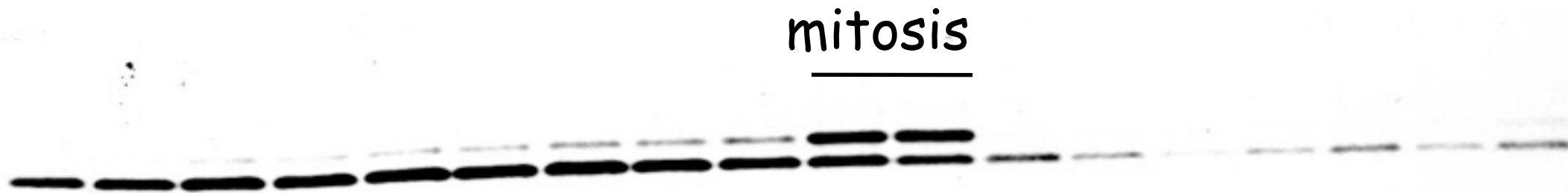
Lohka & Maller

Murray

Ohsumi

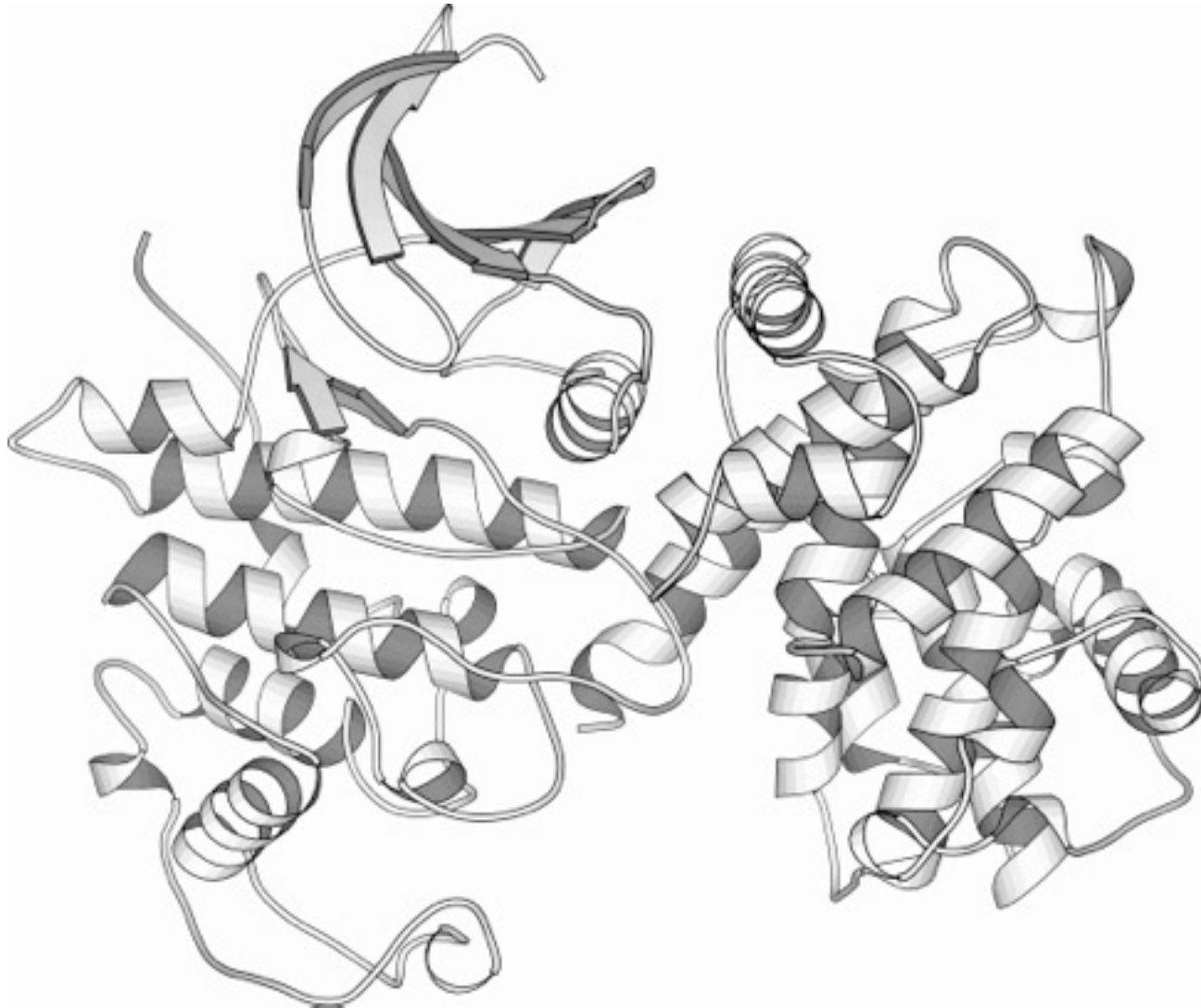


1988: “FAITES SIMPLE” — Andrew MURRAY & Marc KIRSCHNER



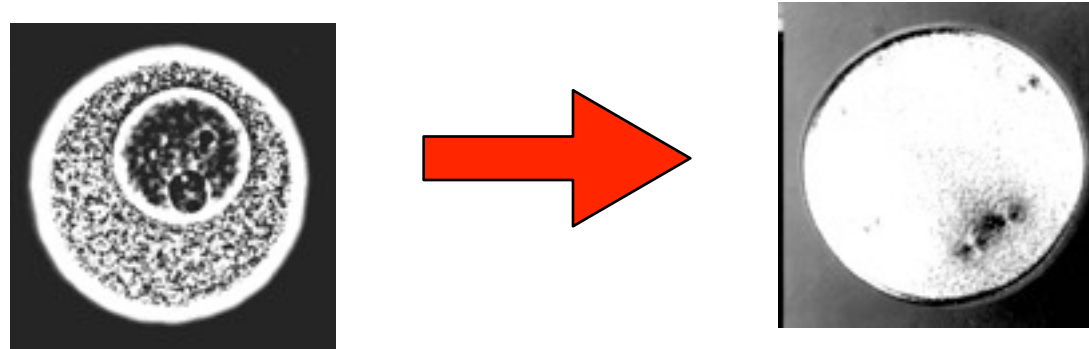
Cyclin synthesis drives the cell cycle

CDC2 + CYCLIN = MPF

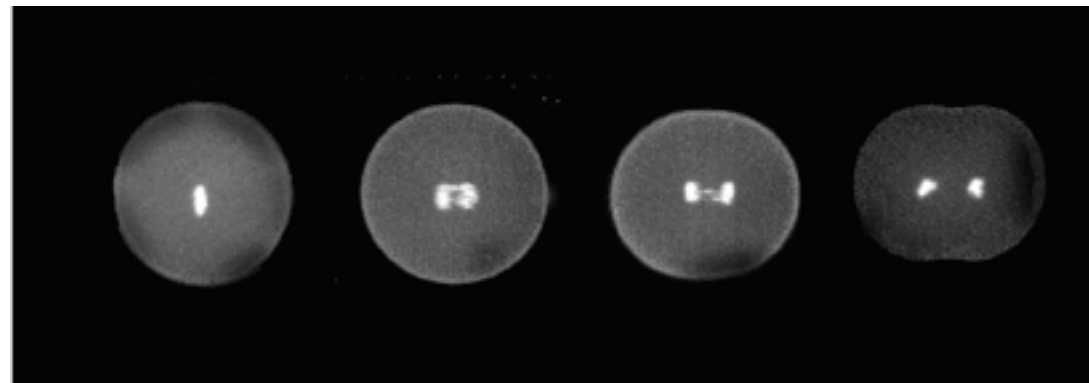


SIMPLE WHEN YOU UNDERSTAND!

Cyclin Accumulates, CDK I Turns On,
Cell Enters Mitosis



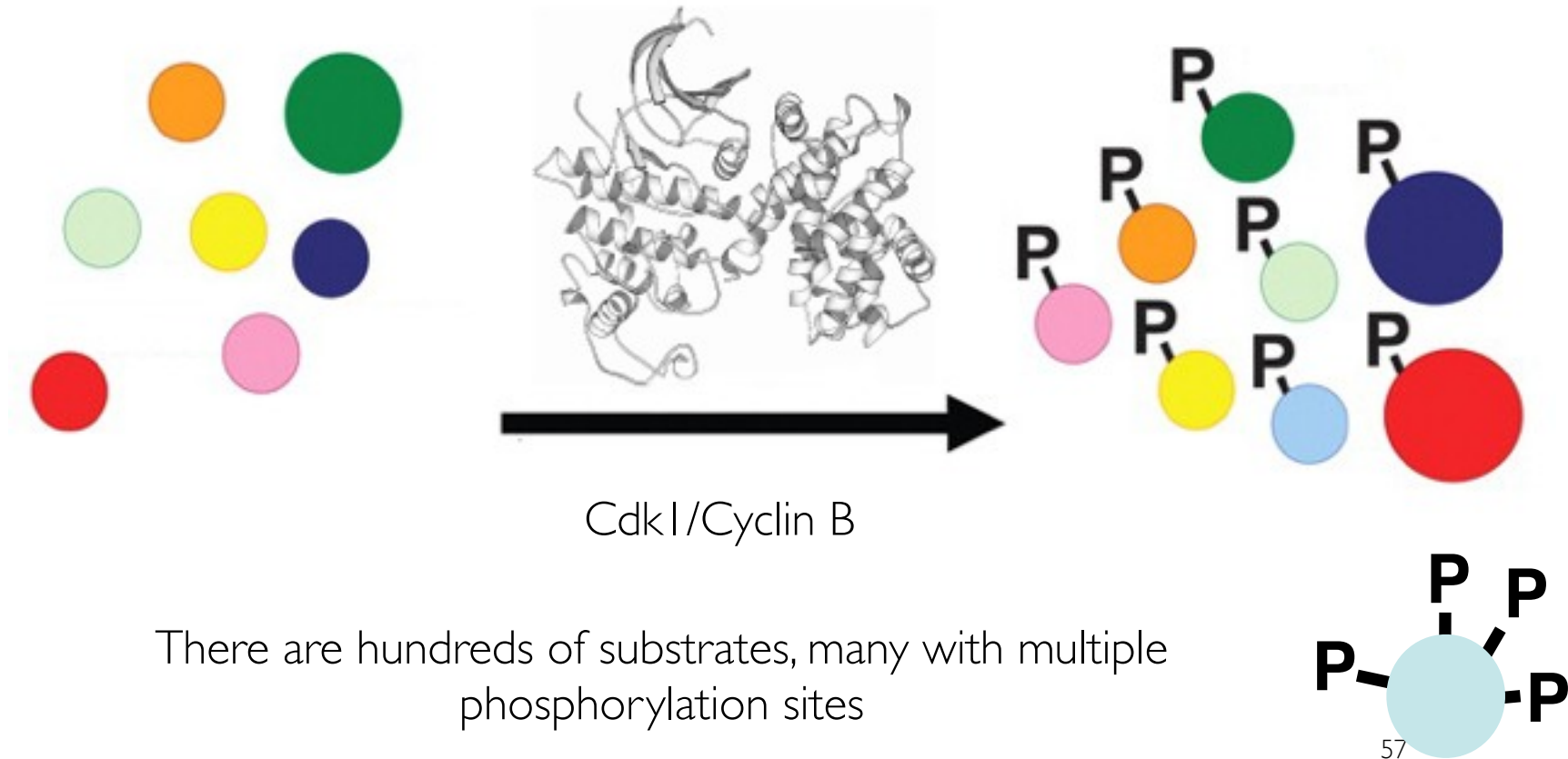
Cyclin is Destroyed, CDK I Turns Off,
Cell Exits Mitosis



How Does It Actually Work?

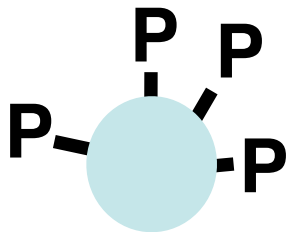
Interphase

Mitosis



How Do You Get Out Of Mitosis?

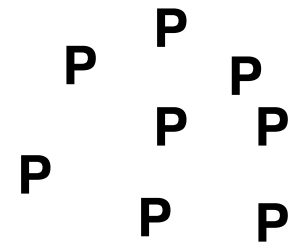
Mitosis



??



Interphase



But that's another story...
where will the road lead?



THINGS BEST AVOIDED:

- Initiatives
- Networks
- Strategy

ABOVE ALL—Don't Be Scared!

