

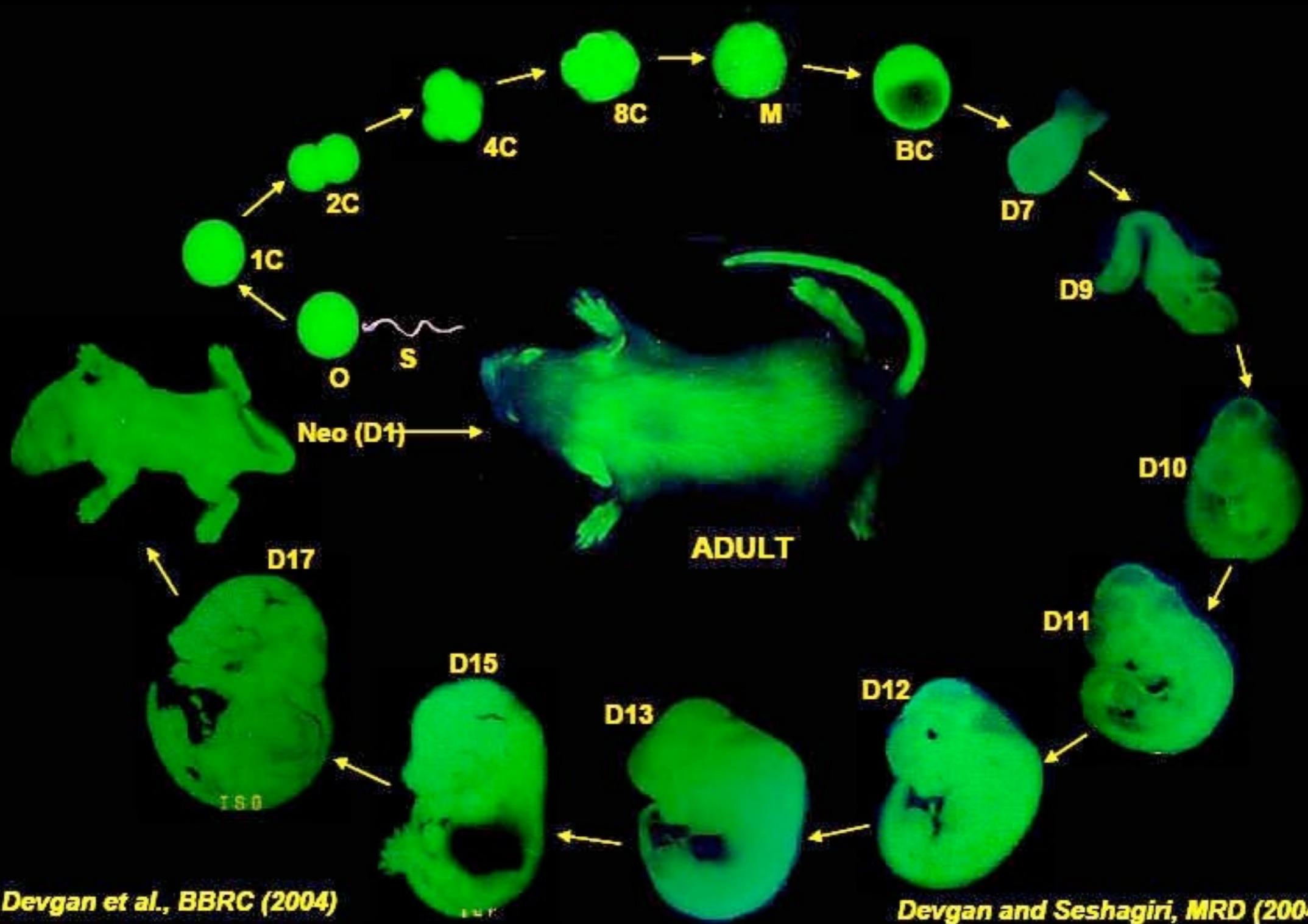
Biological dynamical systems

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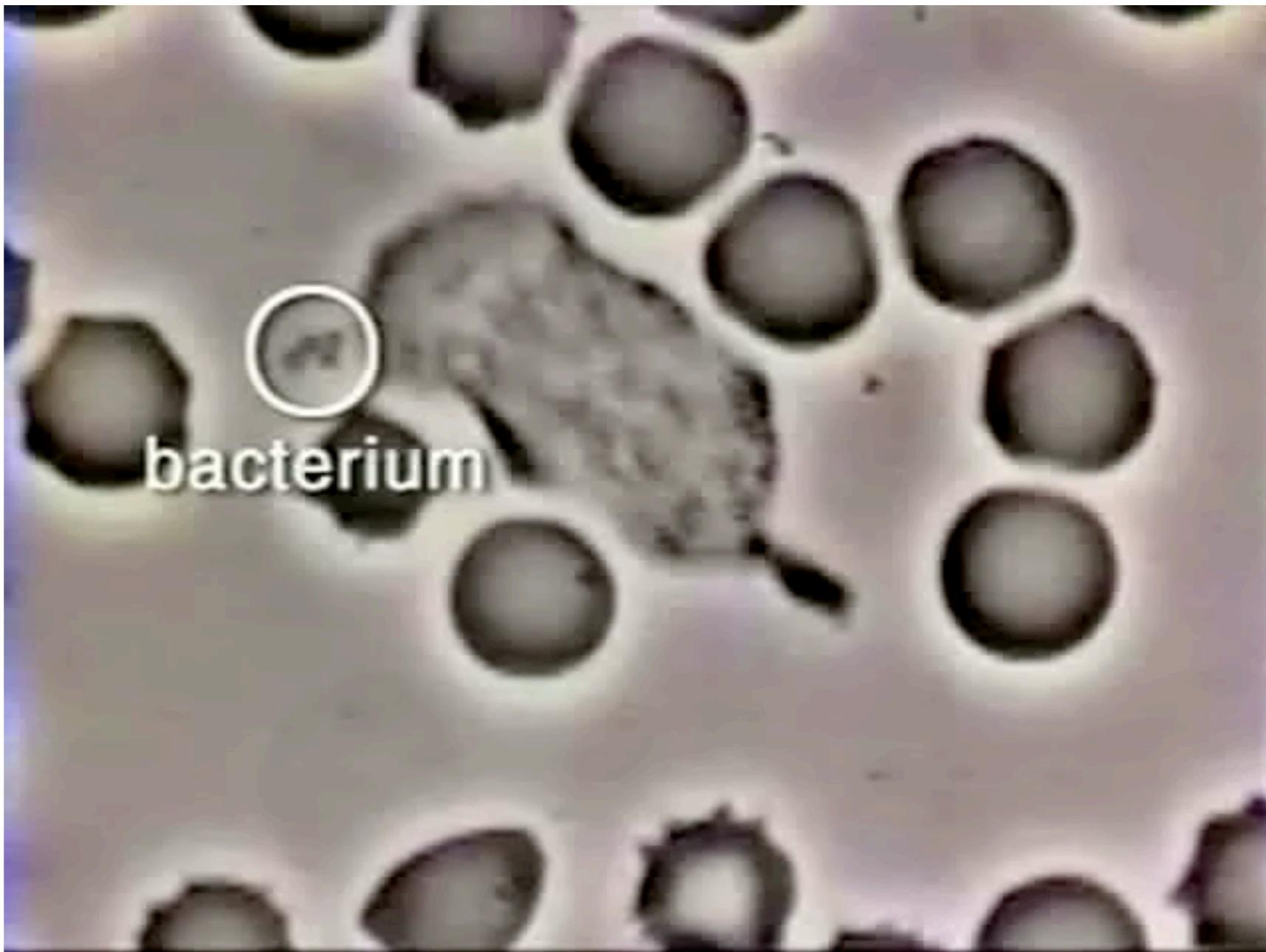
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Cells are adaptive

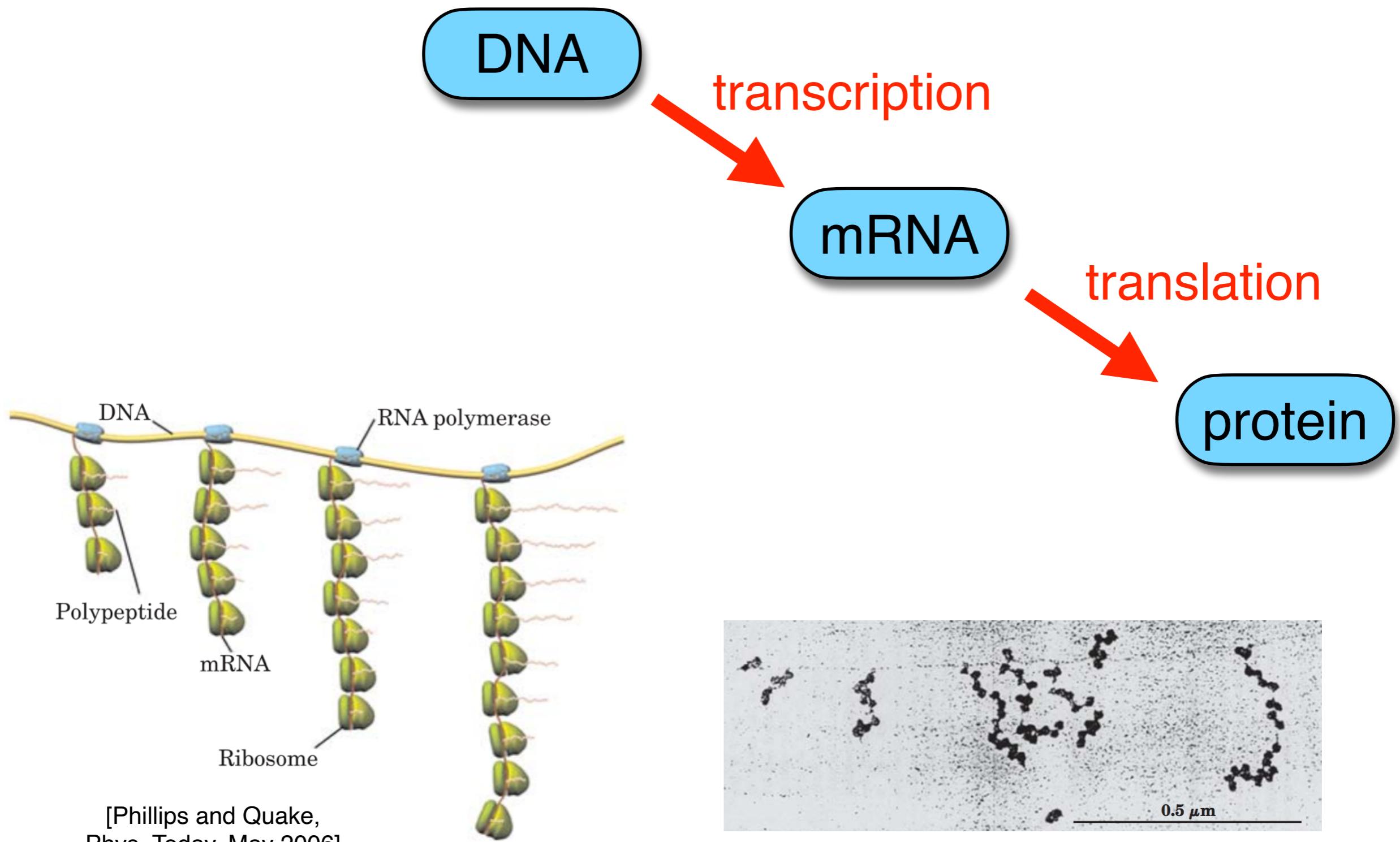
A blood neutrophil chasing a bacterium



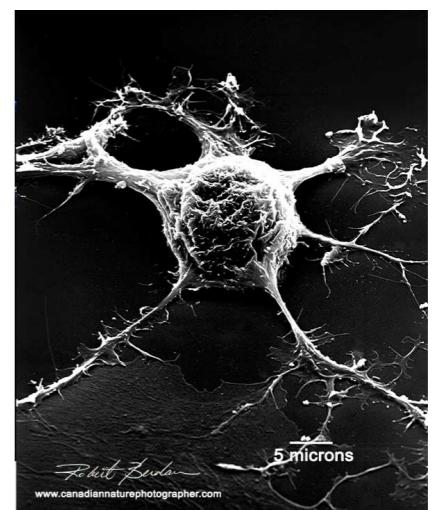
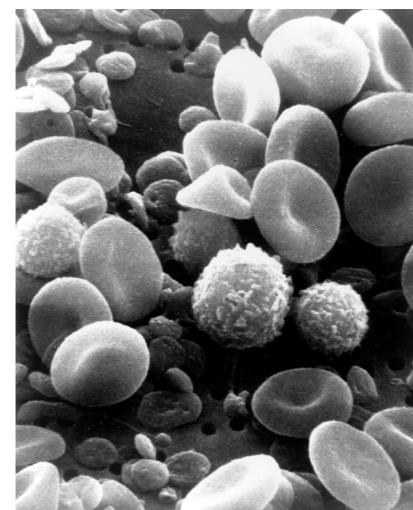
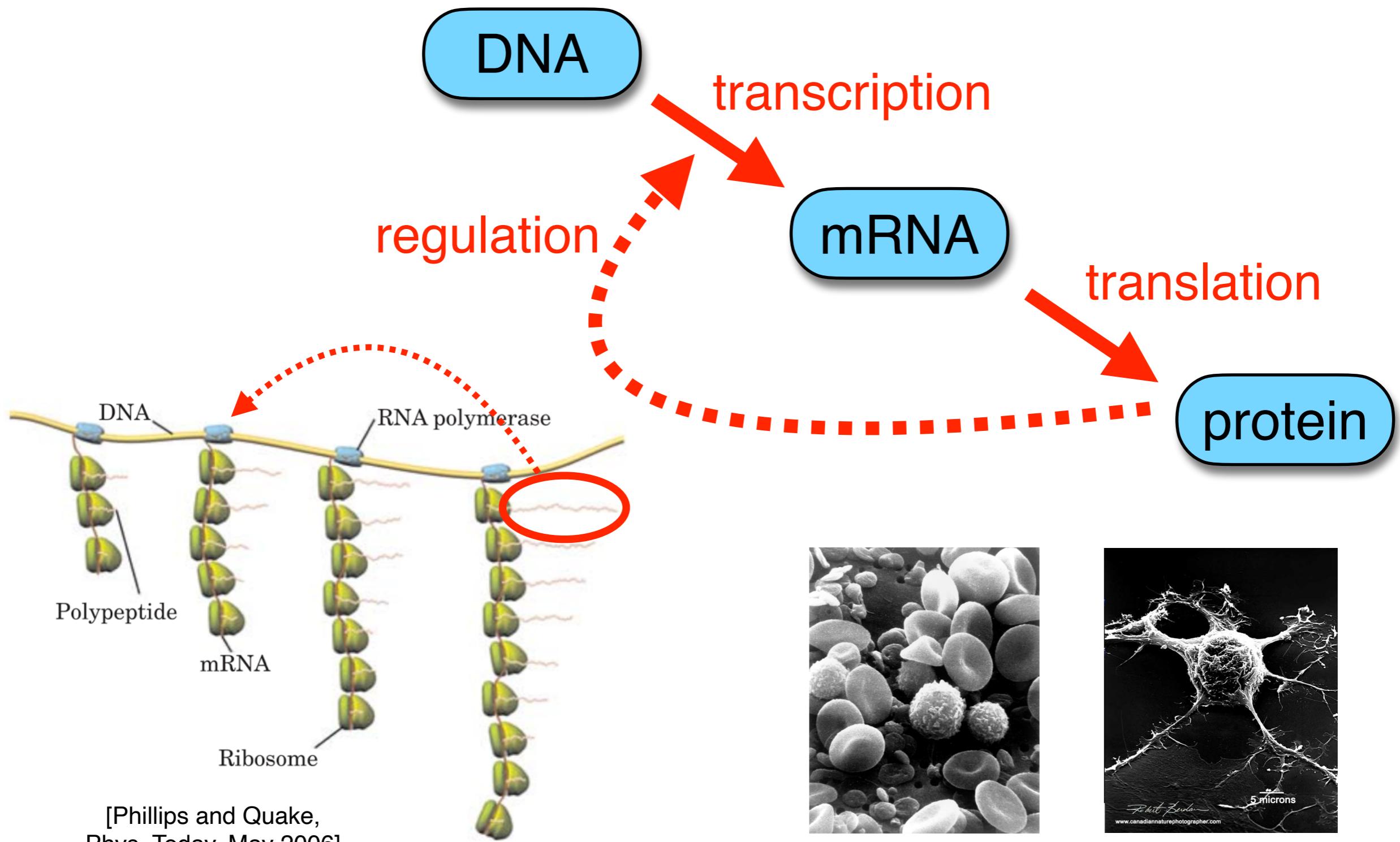
David Roger (Vanderbilt Univ.)
http://www.youtube.com/watch?v=OWUmXx5V_wE

Most cellular functions are performed by proteins

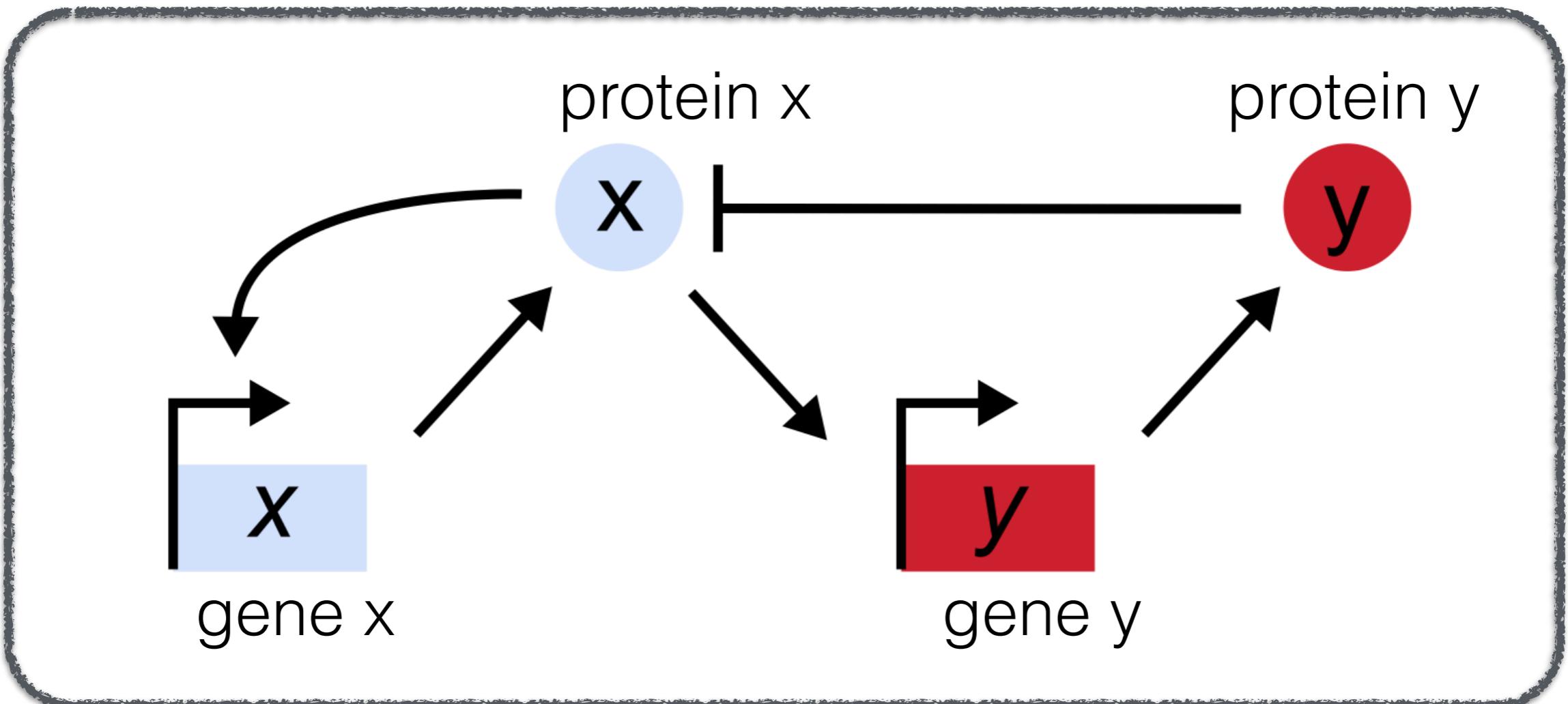
The flow of genetic information (gene expression)



The flow of genetic information (gene expression)



Gene circuits



→ activation

→ repression

Dynamics of gene regulatory circuits

1. Gene circuit dynamics
2. Dissecting a genetic circuit
3. Noise in genetic circuits

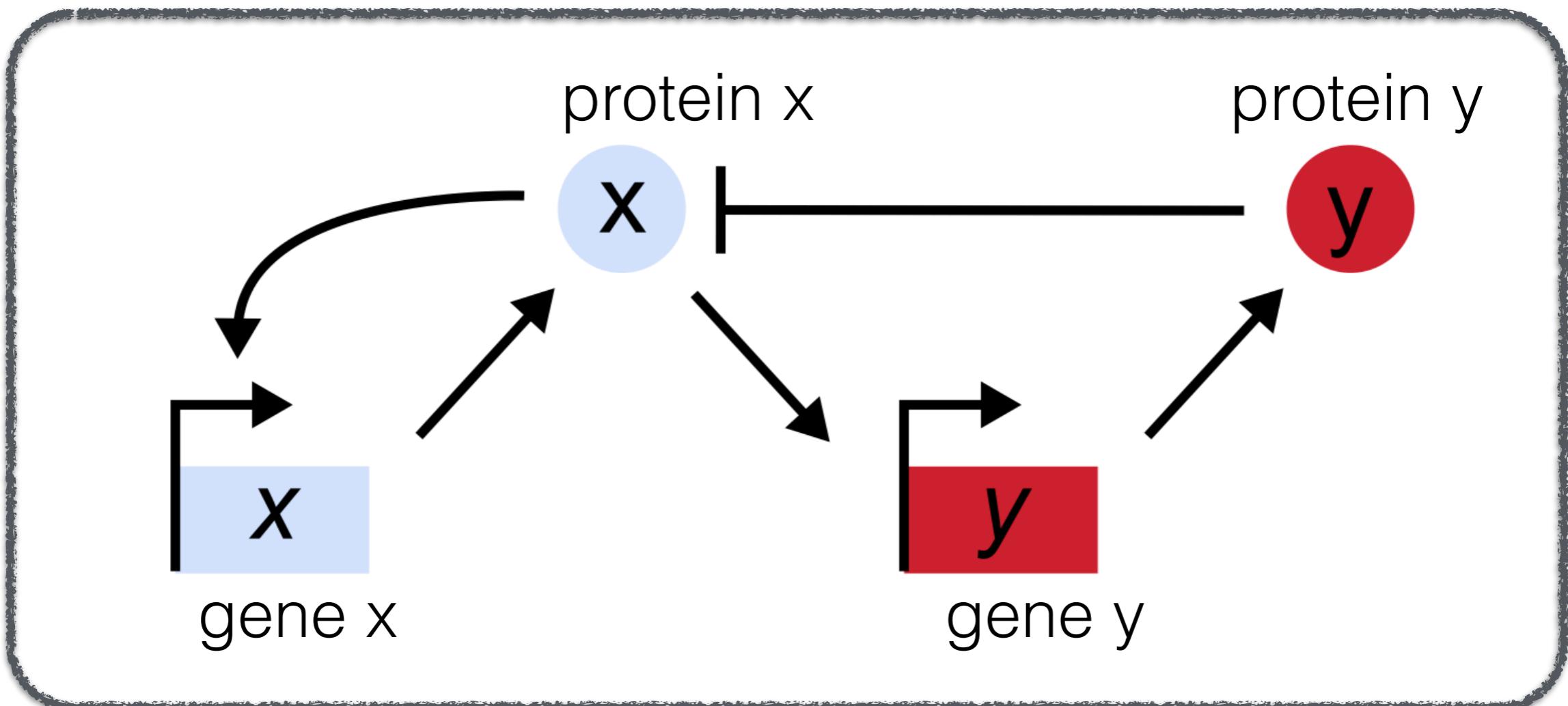
Course material at
<https://github.com/jgojalvo/CRMcourse>



Dynamics of gene regulatory circuits

1. Gene circuit dynamics
2. Dissecting a genetic circuit
3. Noise in genetic circuits

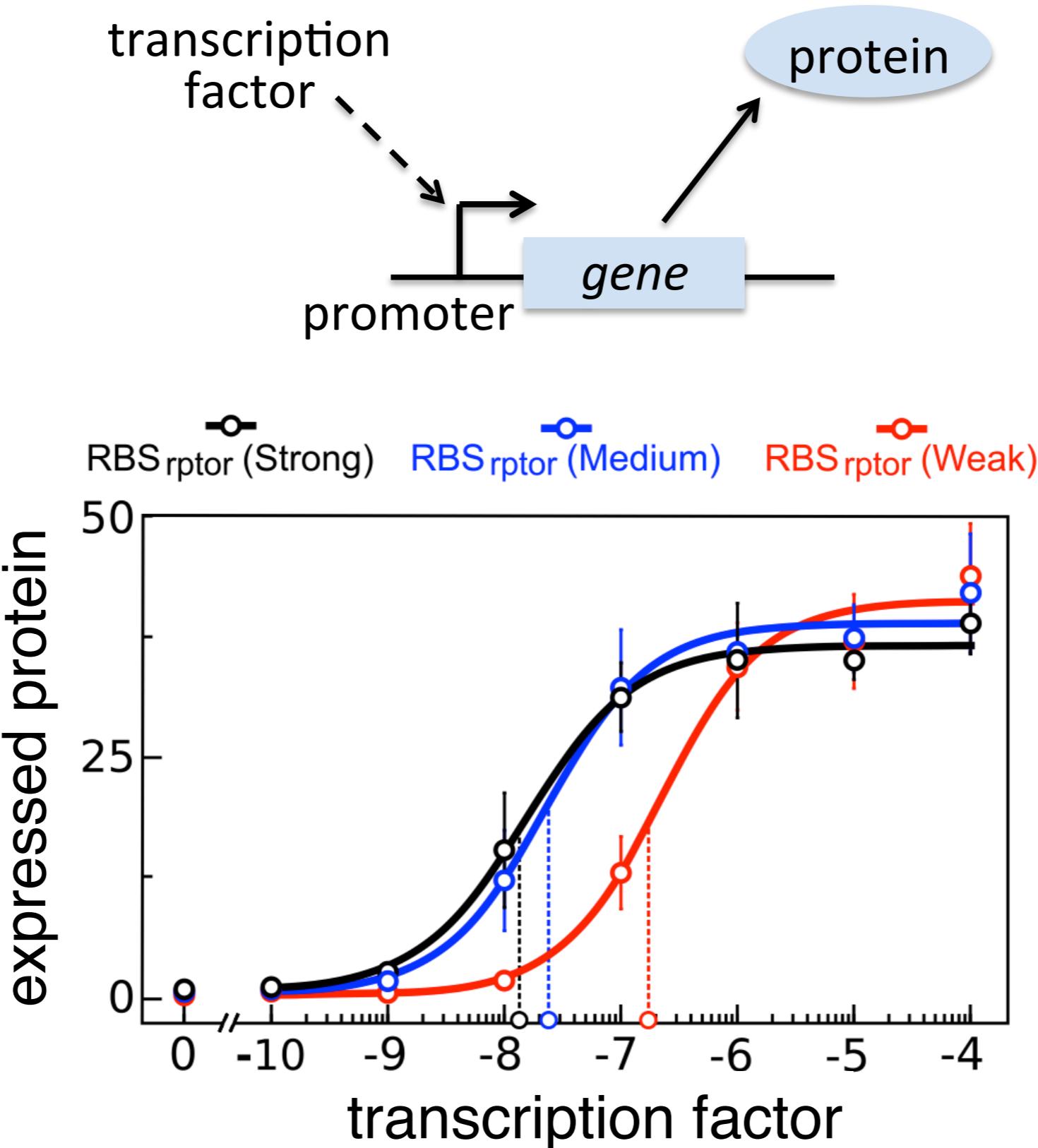
Gene circuits



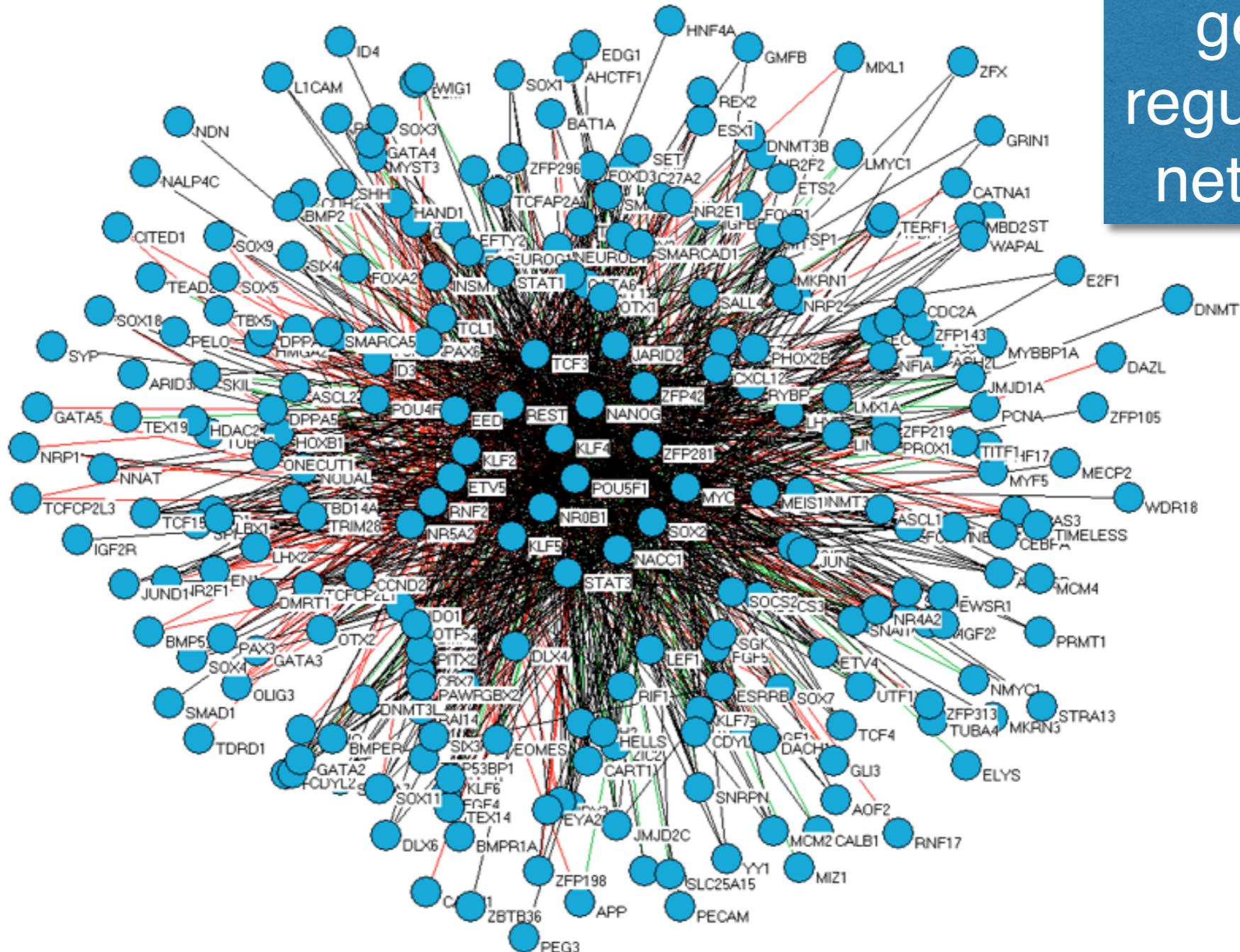
→ activation

→ repression

Challenge #1: Genetic interactions are frequently nonlinear

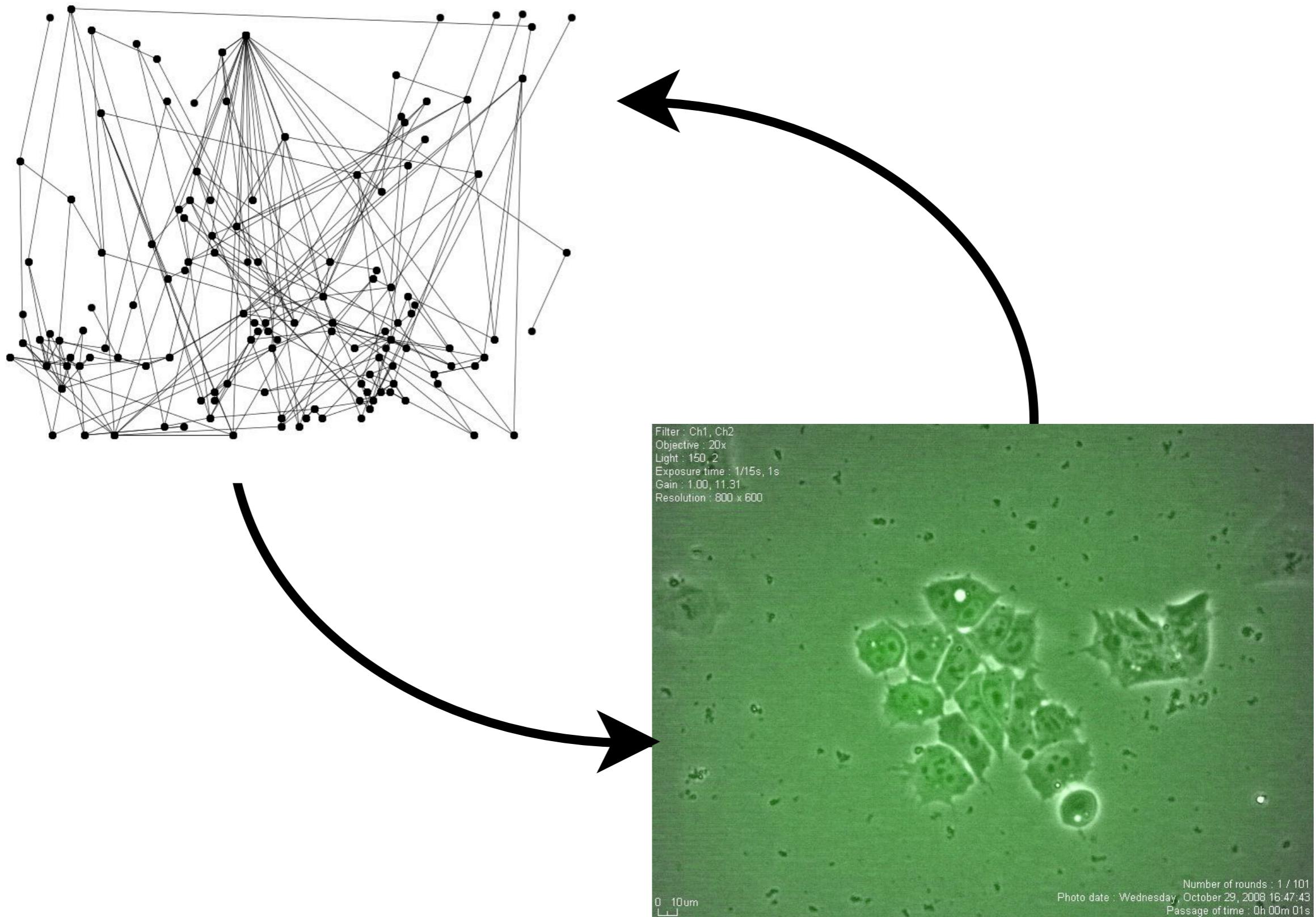


Challenge #2: Genes and proteins are intricately connected

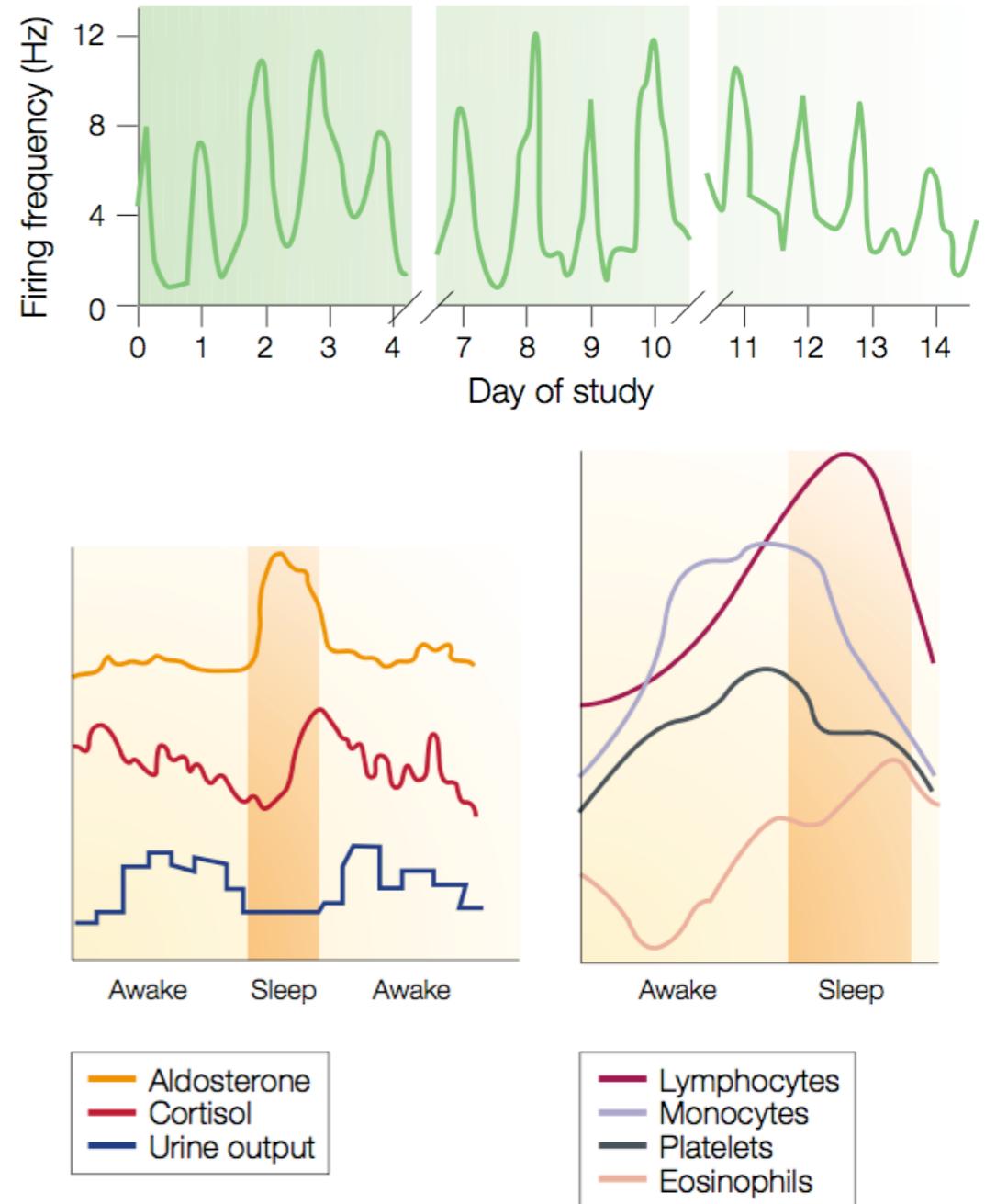
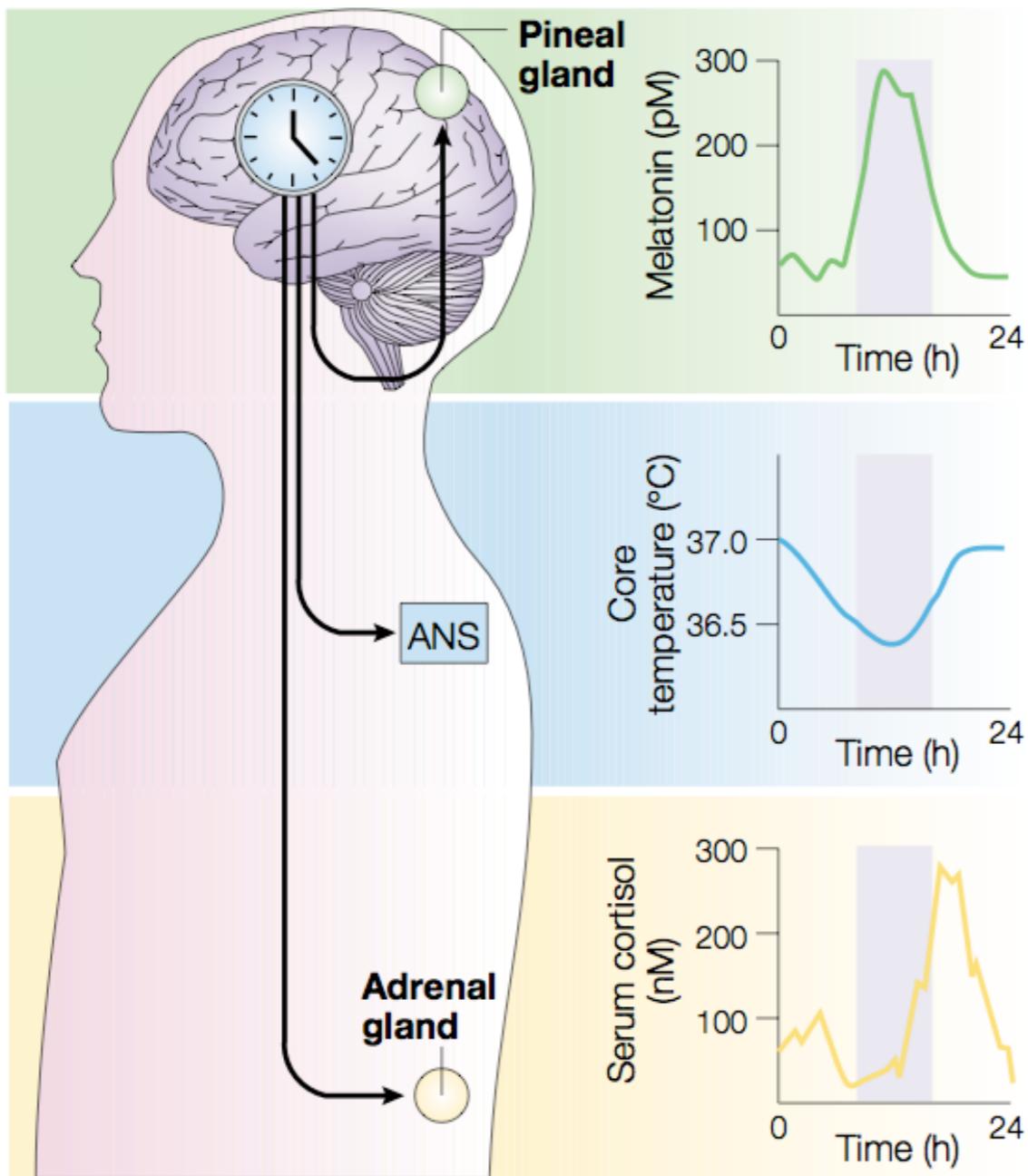


Gene regulatory network for pluripotency
[Integrated Stem Cell Molecular Interaction Database]

Challenge #3: Living processes are usually dynamical



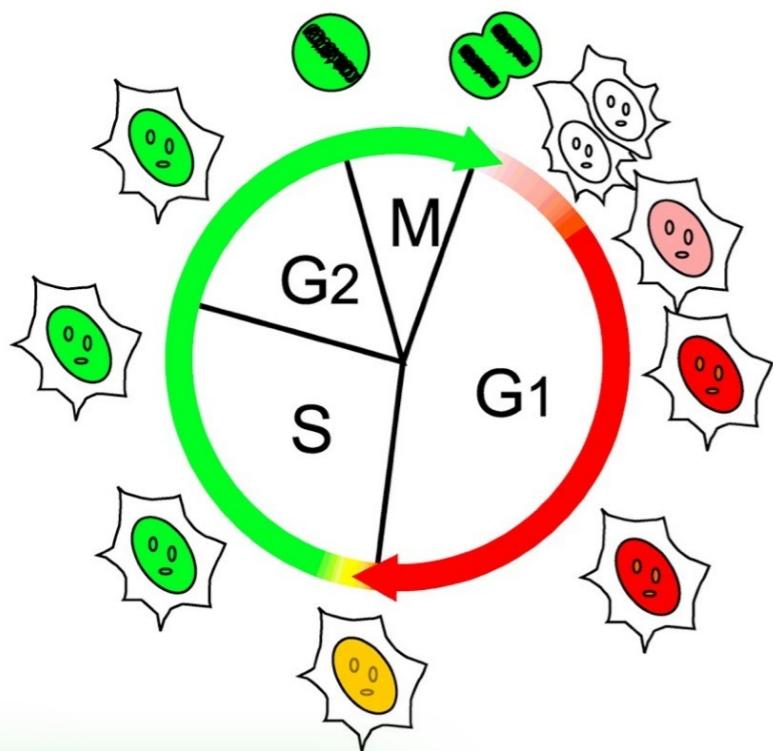
The circadian clock



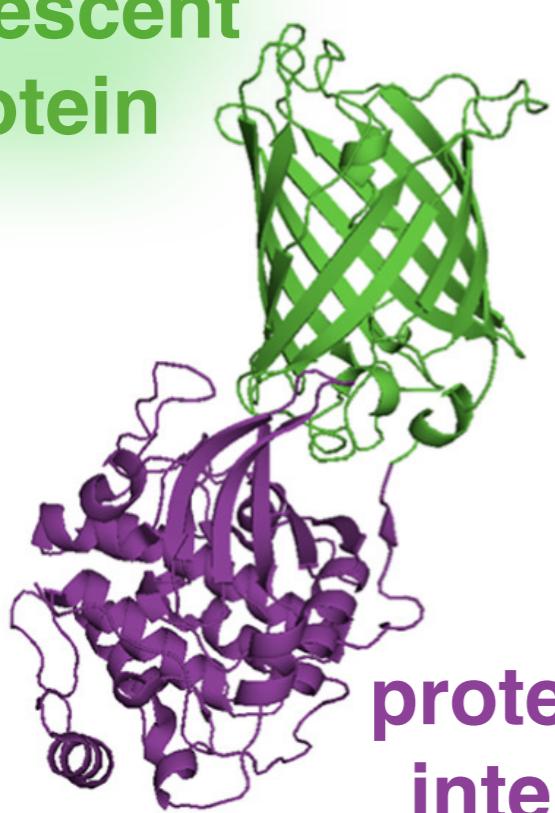
[Hastings, Reddy & Maywood, Nature Rev. Neurosci. 4, 649 (2003)]

[Fu & Lee, Nature Rev. Cancer 3, 350 (2003)]

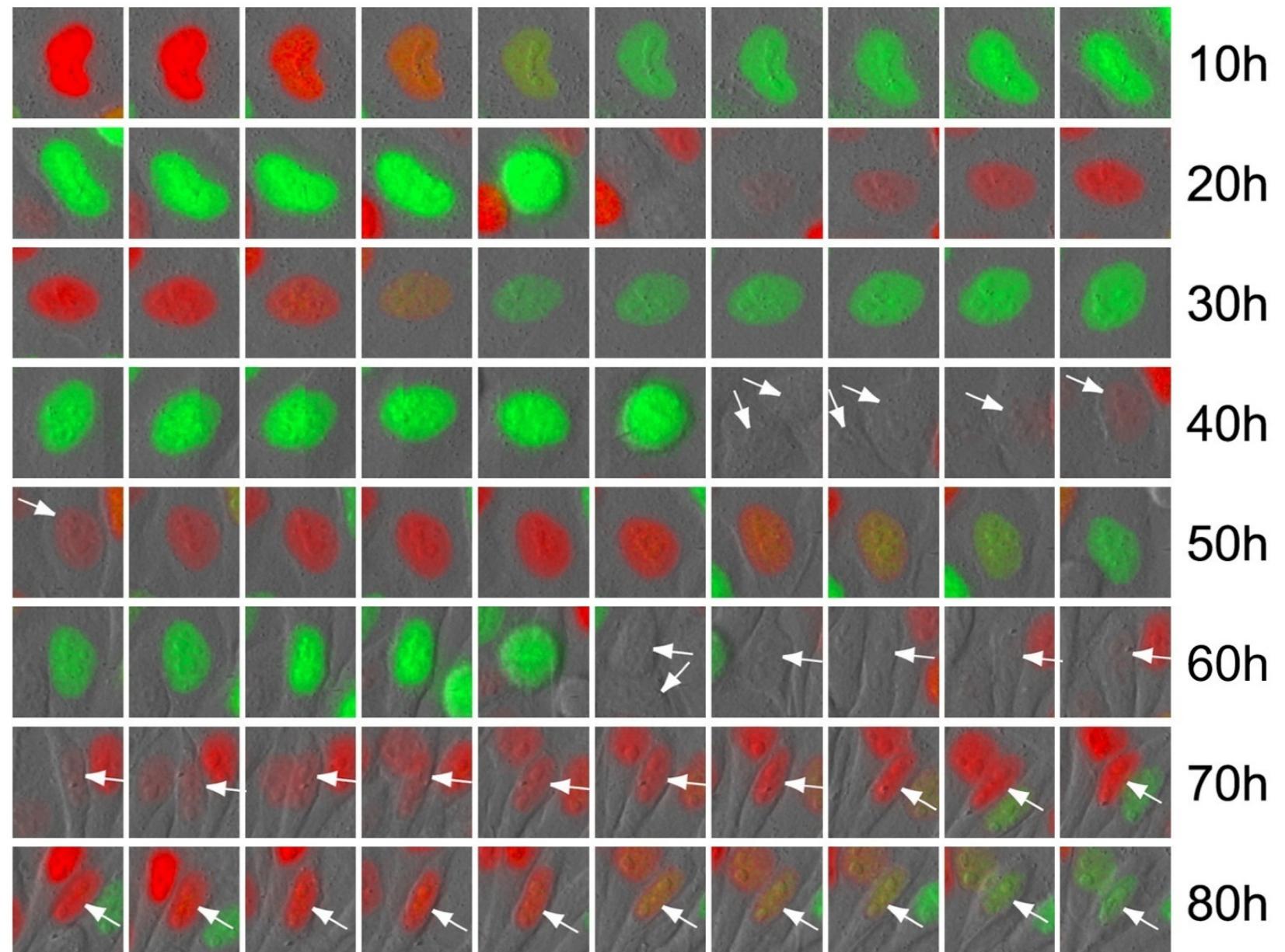
The cell cycle



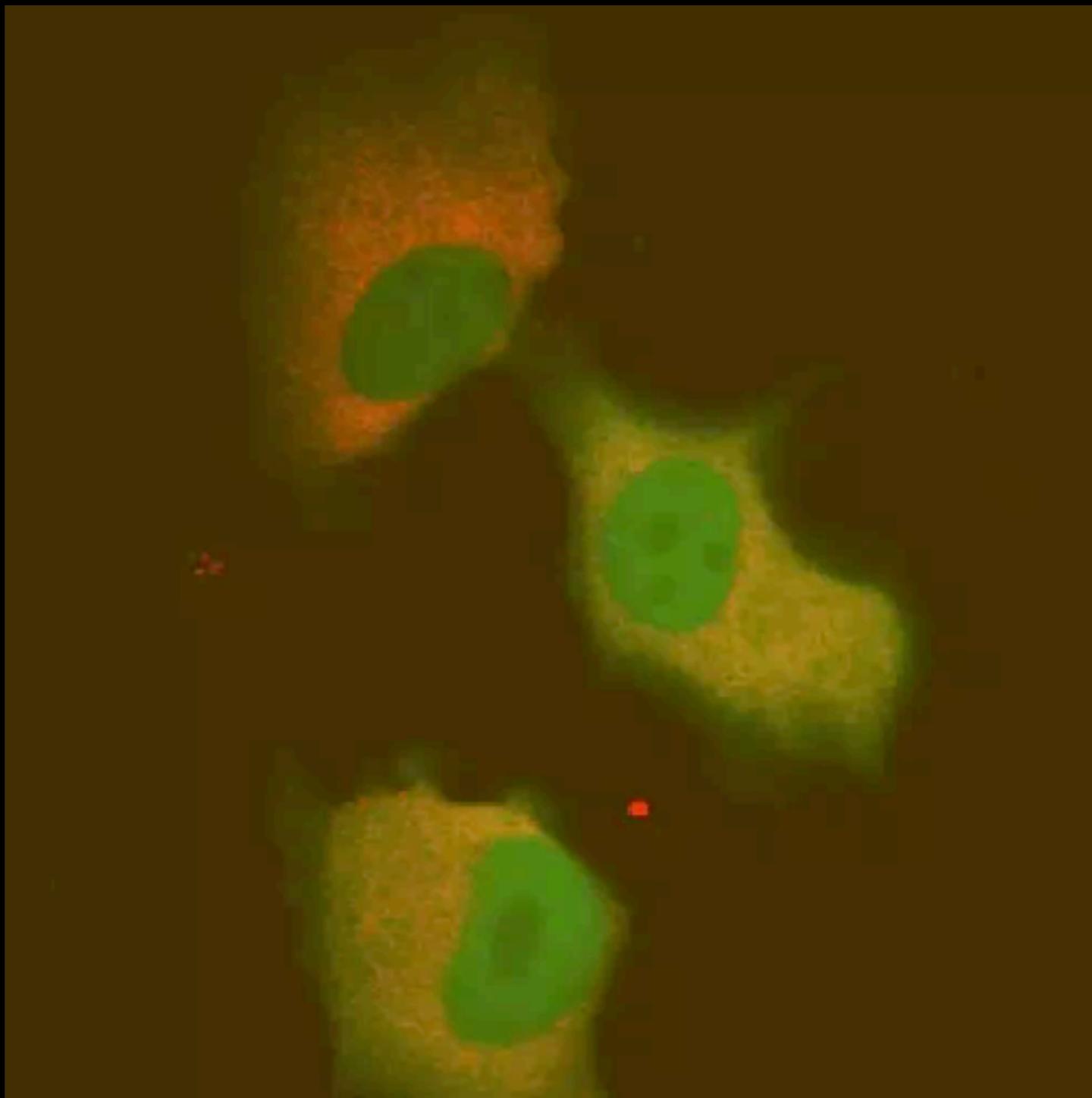
fluorescent
protein



protein of
interest



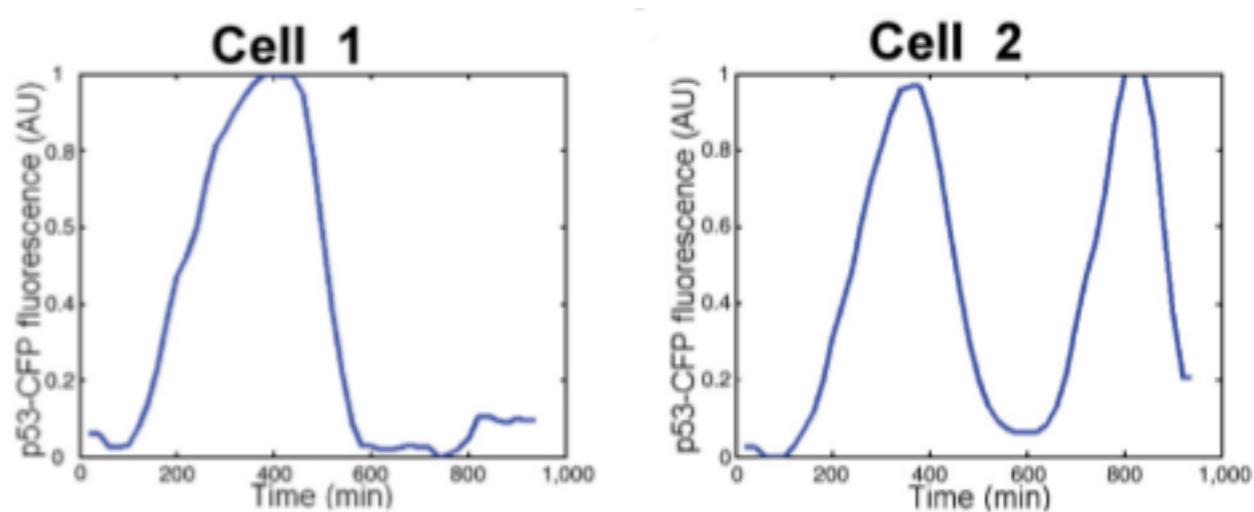
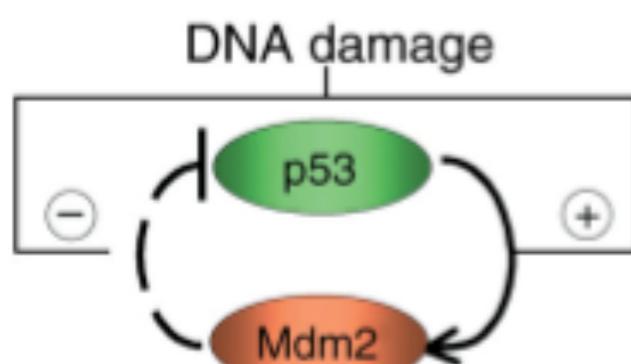
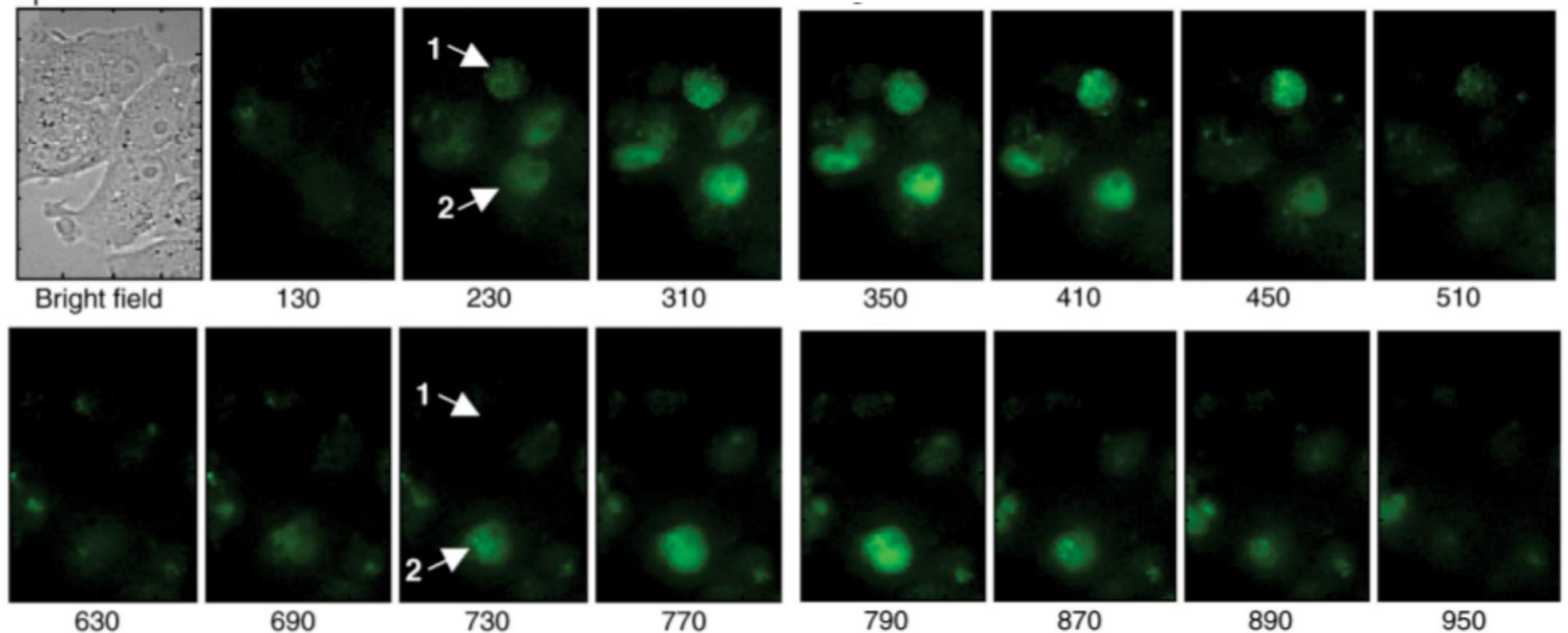
Oscillations in NF-κB activity in response to TNF-α signaling



[Nelson *et al*, Science 306, 704 (2004)]

Dynamics of the p53-Mdm2 feedback loop
in individual cells

Galit Lahav¹, Nitzan Rosenfeld¹, Alex Sigal¹, Naama Geva-Zatorsky¹, Arnold J Levine², Michael B Elowitz³ & Uri Alon¹



Oscillations in cell regulation

Period (seconds)

10

10^2

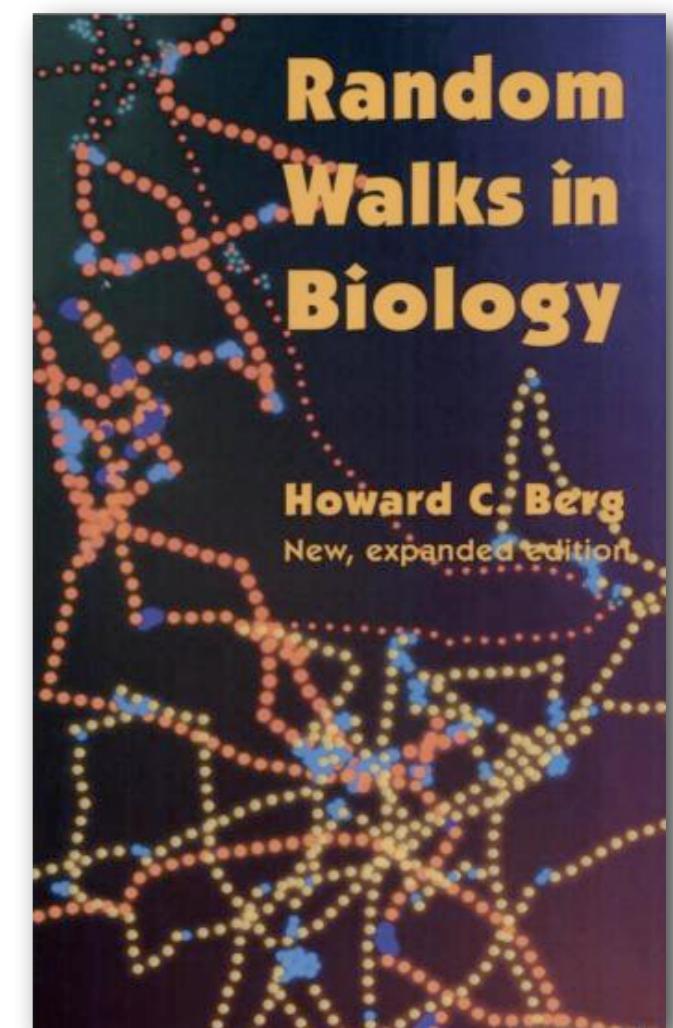
10^3

10^4

10^5

10^7

- Calcium signaling
- Crz1 nuclear localization
- cAMP signaling
- Glycolysis
- ERK nuclear localization
- Transcription cycles
- Cell cycle
- NF- κ B signaling
- Segmentation
- p53 response to DNA damage
- Circadian rhythmicity
- Seasonal rhythmicity

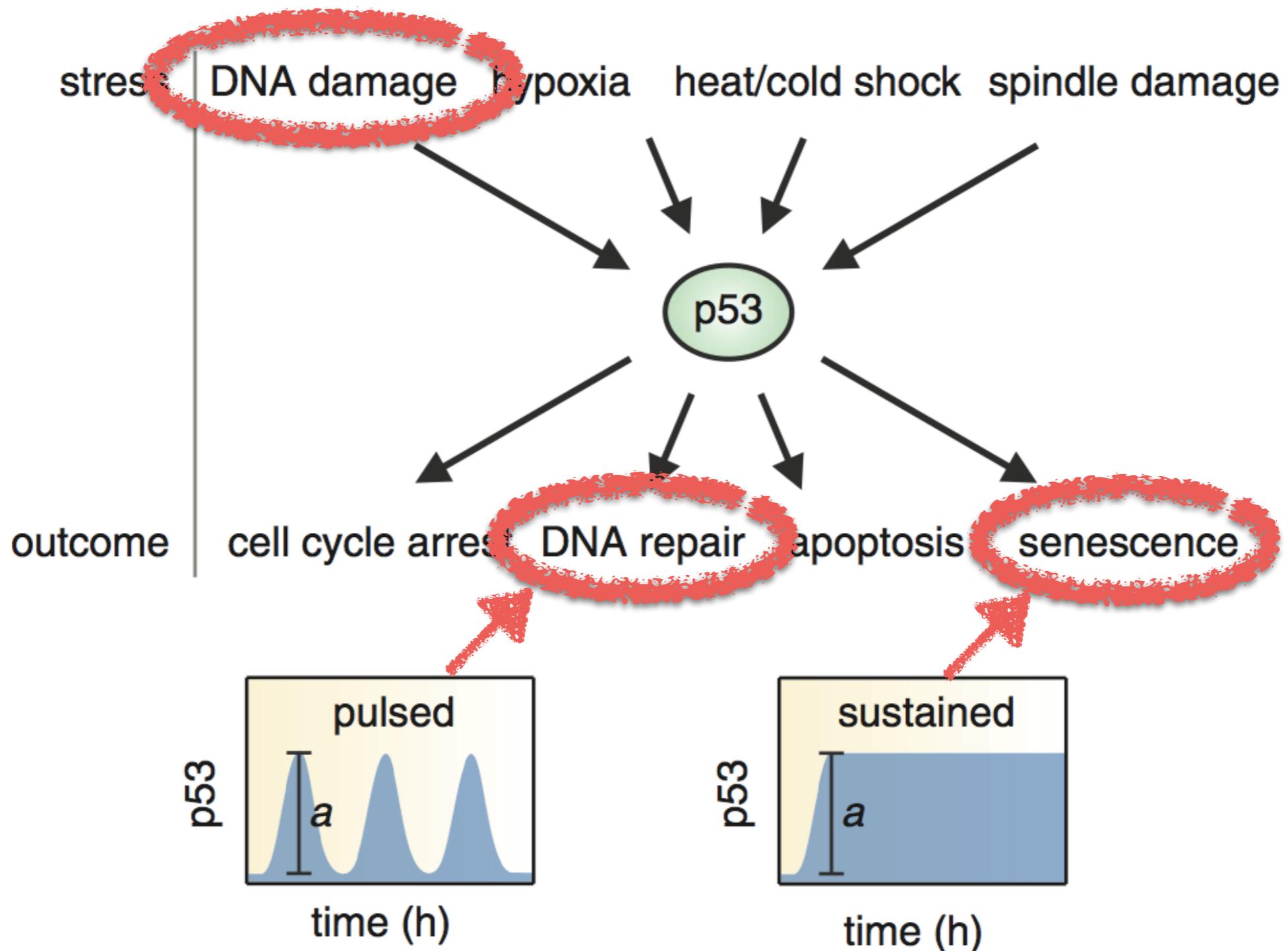


“Biology is wet and dynamic”
[Howard Berg, 1993]

Dynamical phenomena
have biological relevance
(i.e. a function)

p53 Dynamics Control Cell Fate

Jeremy E. Purvis, Kyle W. Karhohs, Caroline Mock, Eric Batchelor,*
Alexander Loewer,† Galit Lahav‡



The challenges of systems biology

- The interactions are usually nonlinear
- There are many interactions
- Cells are highly dynamic

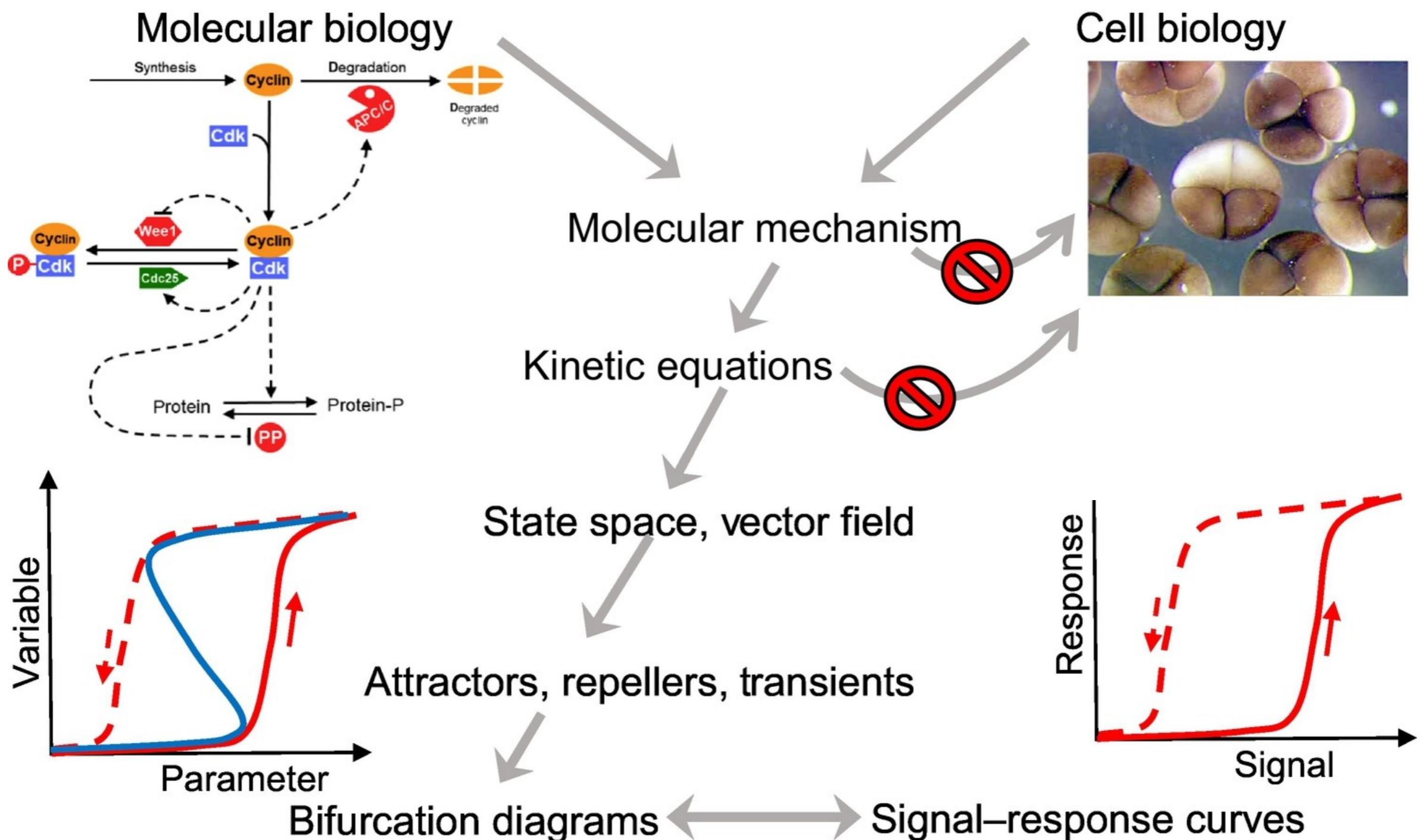
Mathematical modelling helps addressing these challenges

On the use of mathematical modeling

“The situation is something like finding a jumble of jigsaw puzzle pieces in a paper bag. Our job is to put the puzzle together but we do not have the picture on the front of the box nor any assurance that all the pieces are in the bag, nor a table to lay out the parts that seem to fit together. Mathematical modeling provides the table.”

John Tyson

A dynamical paradigm for molecular cell biology



Trends in Cell Biology

Tyson and Novak, "A dynamical paradigm for molecular cell biology"
Trends in Cell Biology, vol. 30, p. 504 (2020)