量化/系統生物學的 why, when and what

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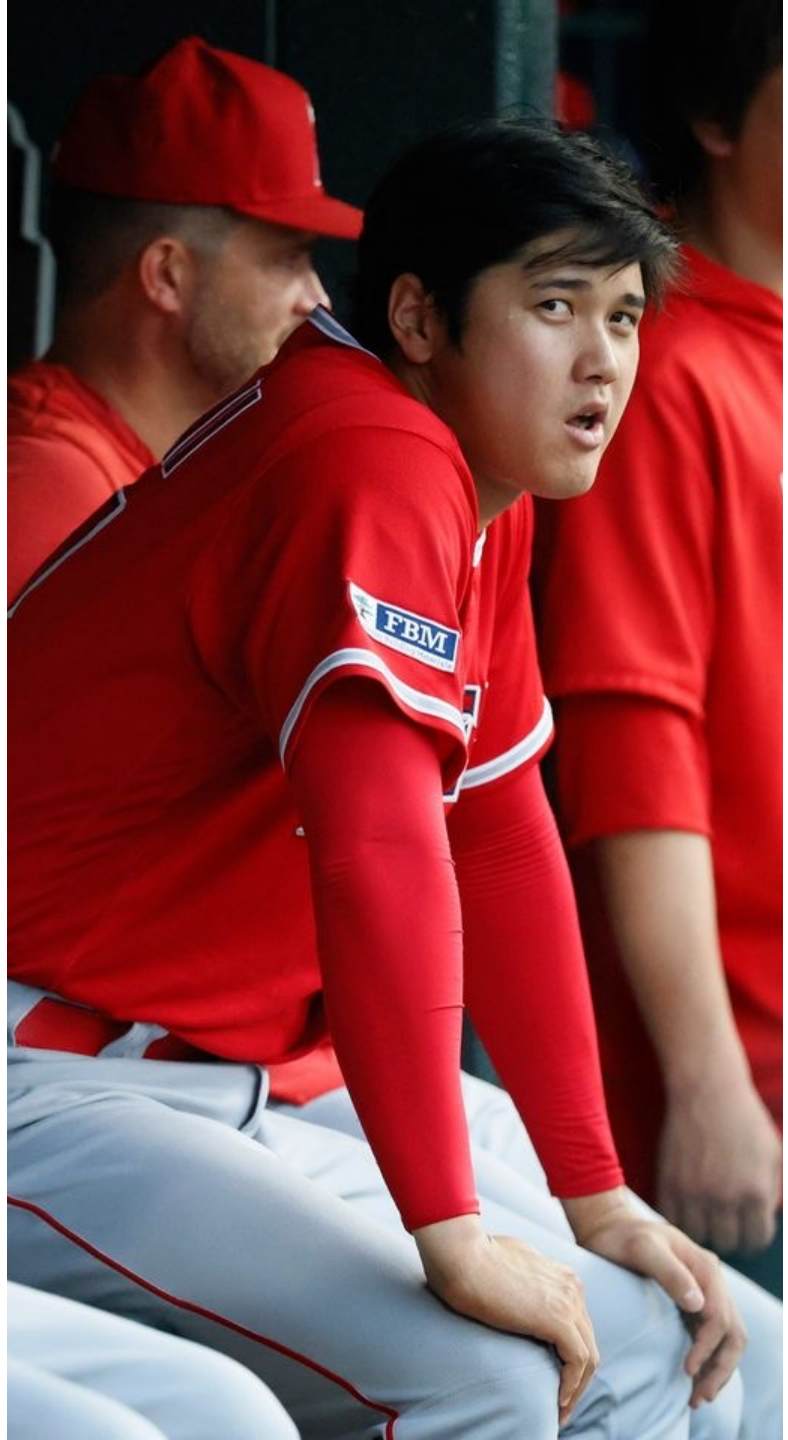
高中生命科學研究人才培育計畫, April/13/2024

SHARING
IS
CARING

Lab for Cell Dynamics

Uncover rhythm of lives for curing human diseases


FBM

這是棒球史上單一選手最偉大的一天 ！

史上唯一一位在一日雙重賽一場丟出完封勝，另一場敲出全壘打（兩隻）的球員！

『要做就做別人做不到的事。』

『我覺得自己沒什麼才能，真要說的話，那我只有為了自己喜愛的事物全力以赴的才能。因為我找不到比棒球更有趣的事物，一心只想著棒球。』

成為世界第一的棒球選手！

— 大谷翔平, 2012, 09, 12

A life-long decision

A reminder
for all of you,
high school students!

成為世界第一的

X X X

咖啡達人？

科學家？

計程車司機？

2024年
4月
13號

Q1: Do you REALLY like a subject or are you REALLY good at something?

Ask yourself in the next ~10 mins

Where are we in biology?

Swarm of death

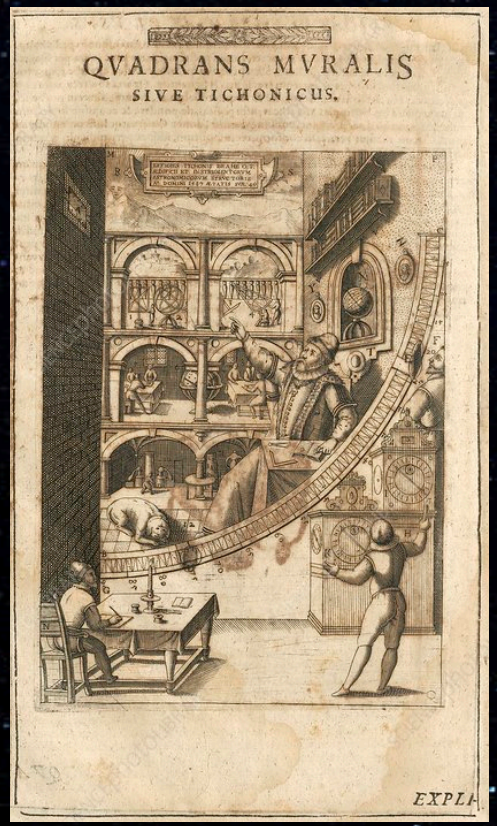
"The Triumph of Death," by Pieter Bruegel the Elder

The spread of COVID-19 across the globe

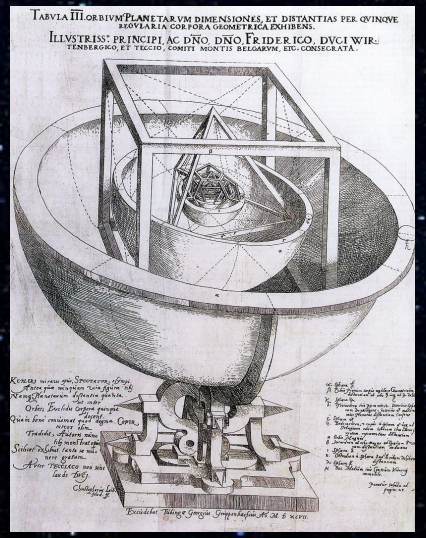
Why quantitative biology?

Where were we in astronomy?

High-quality quantitative dataset



Tycho Brahe
1546-1601



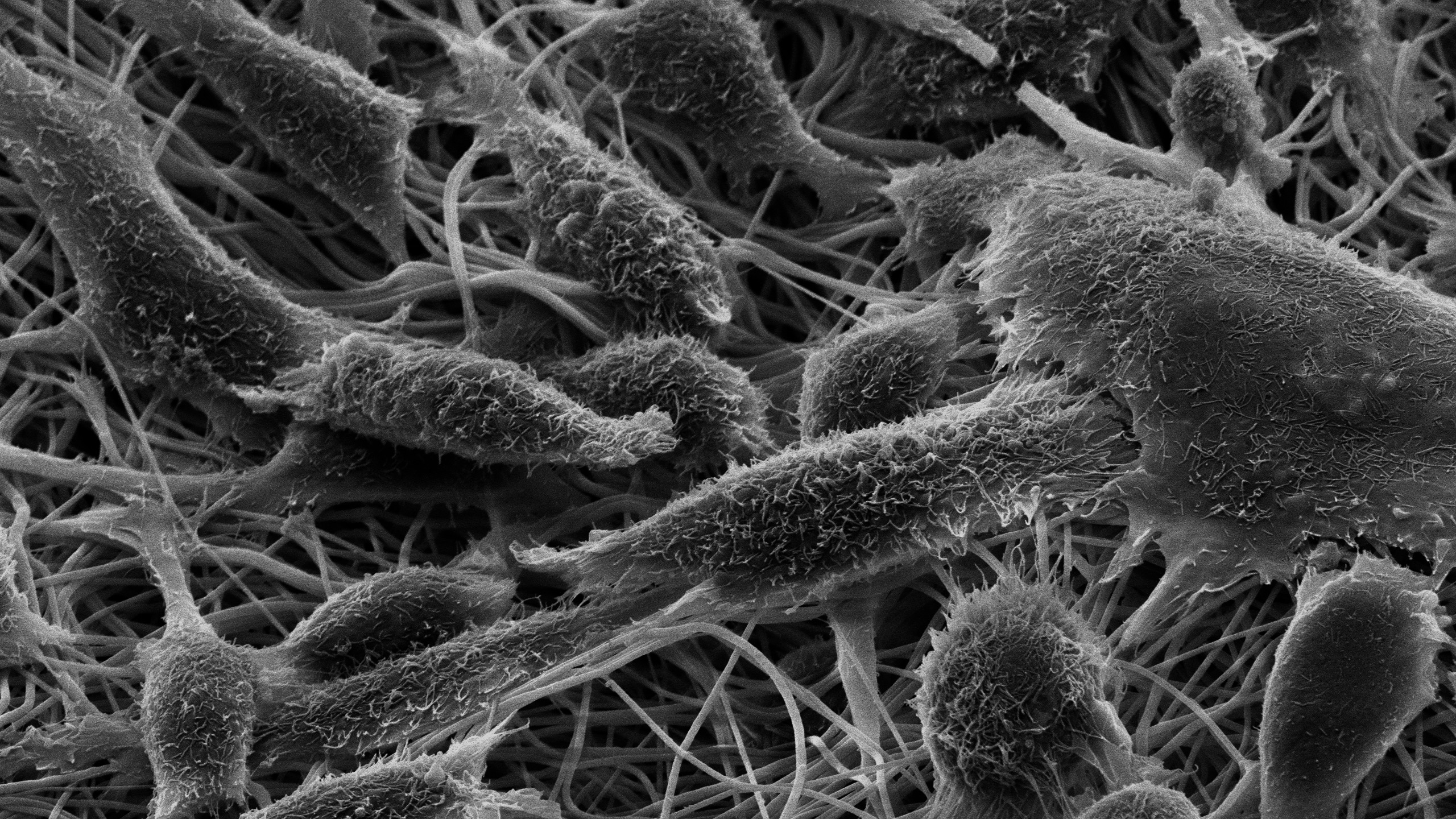
Simplifying theory

Johannes Kepler
1571-1630

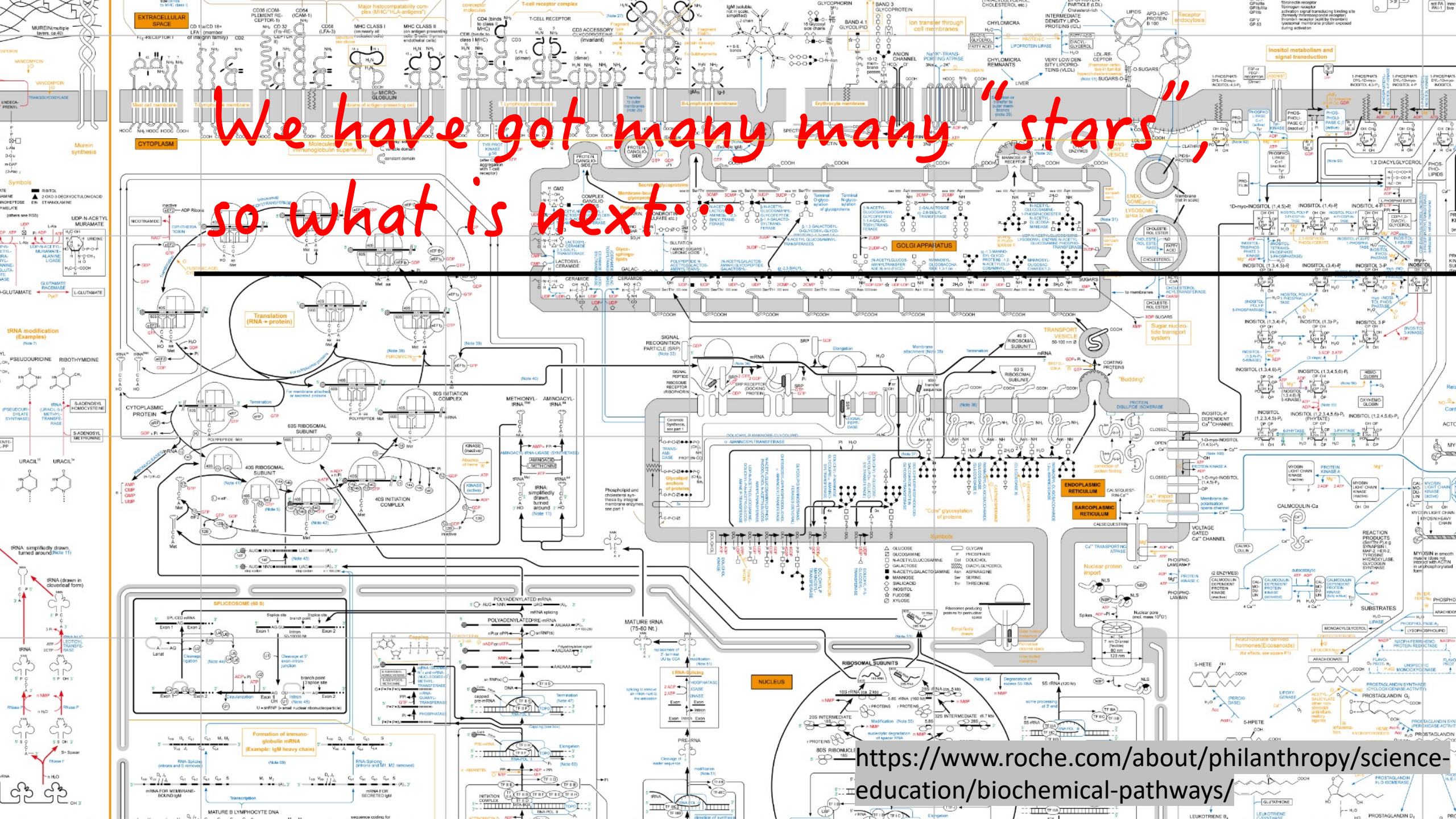
Deeper simplifying theory

Isaac Newton
1642-1727

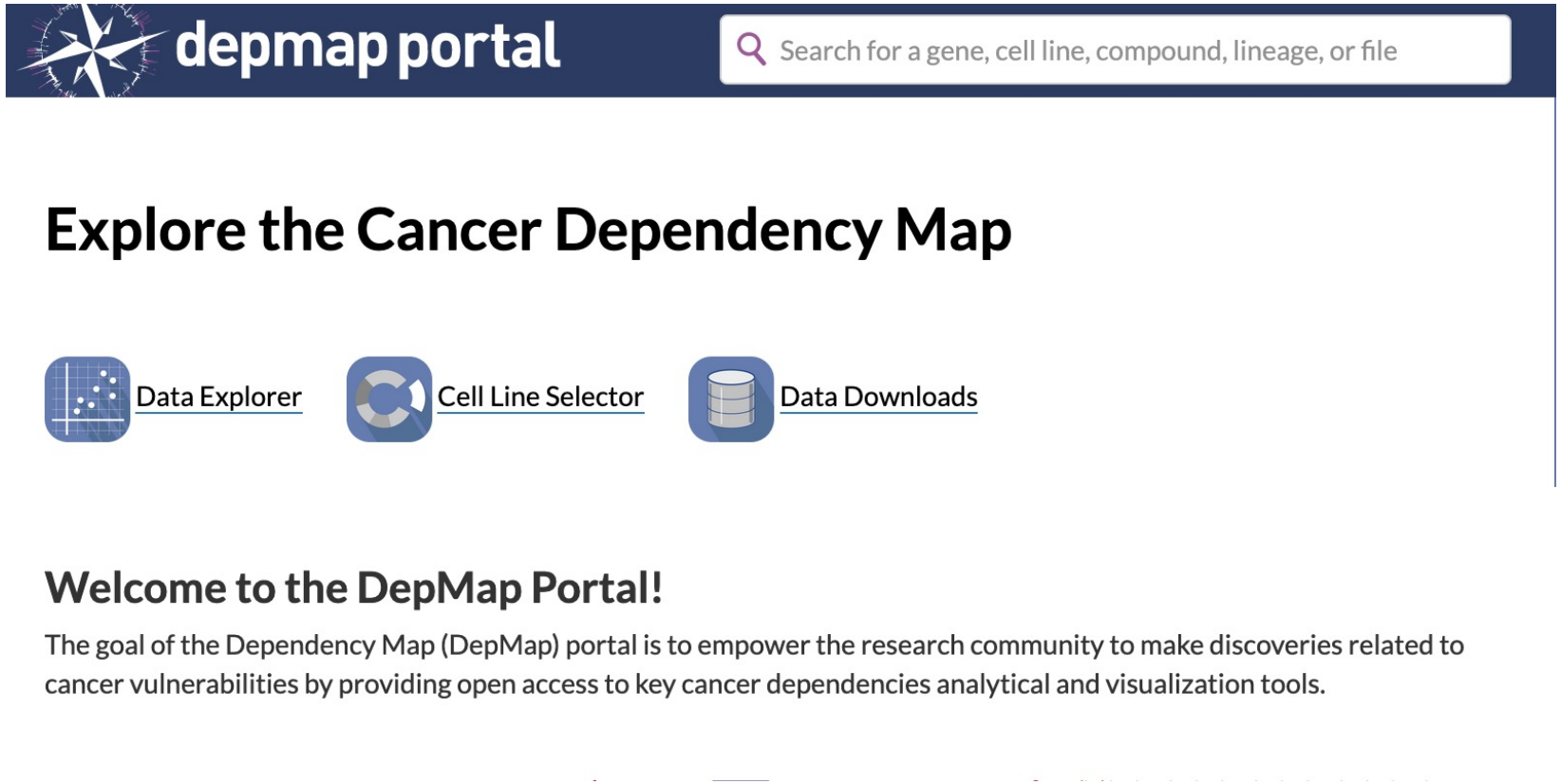
$$F = G\frac{m_1 m_2}{r^2}$$



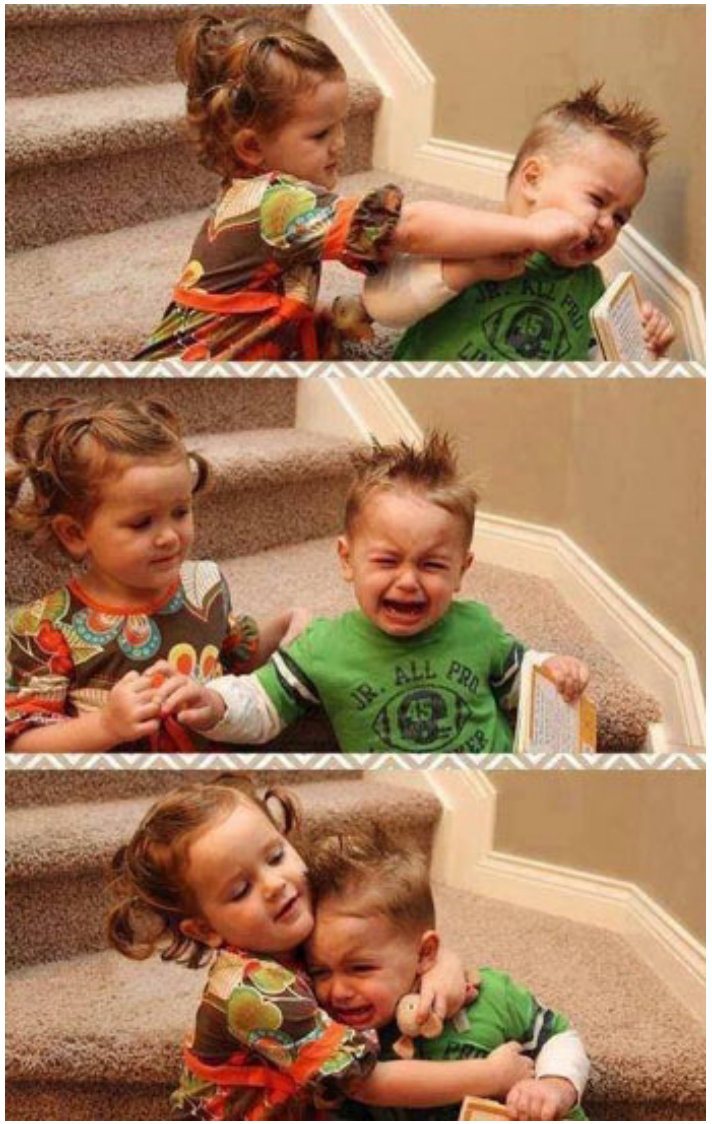
High-quality quantitative dataset
Simplifying theory
Deeper simplifying theory
Where are we in biology?


We have got many many "stars",
so what is next...
https://www.roche.com/about/philanthropy/science-education/biochemical-pathways/

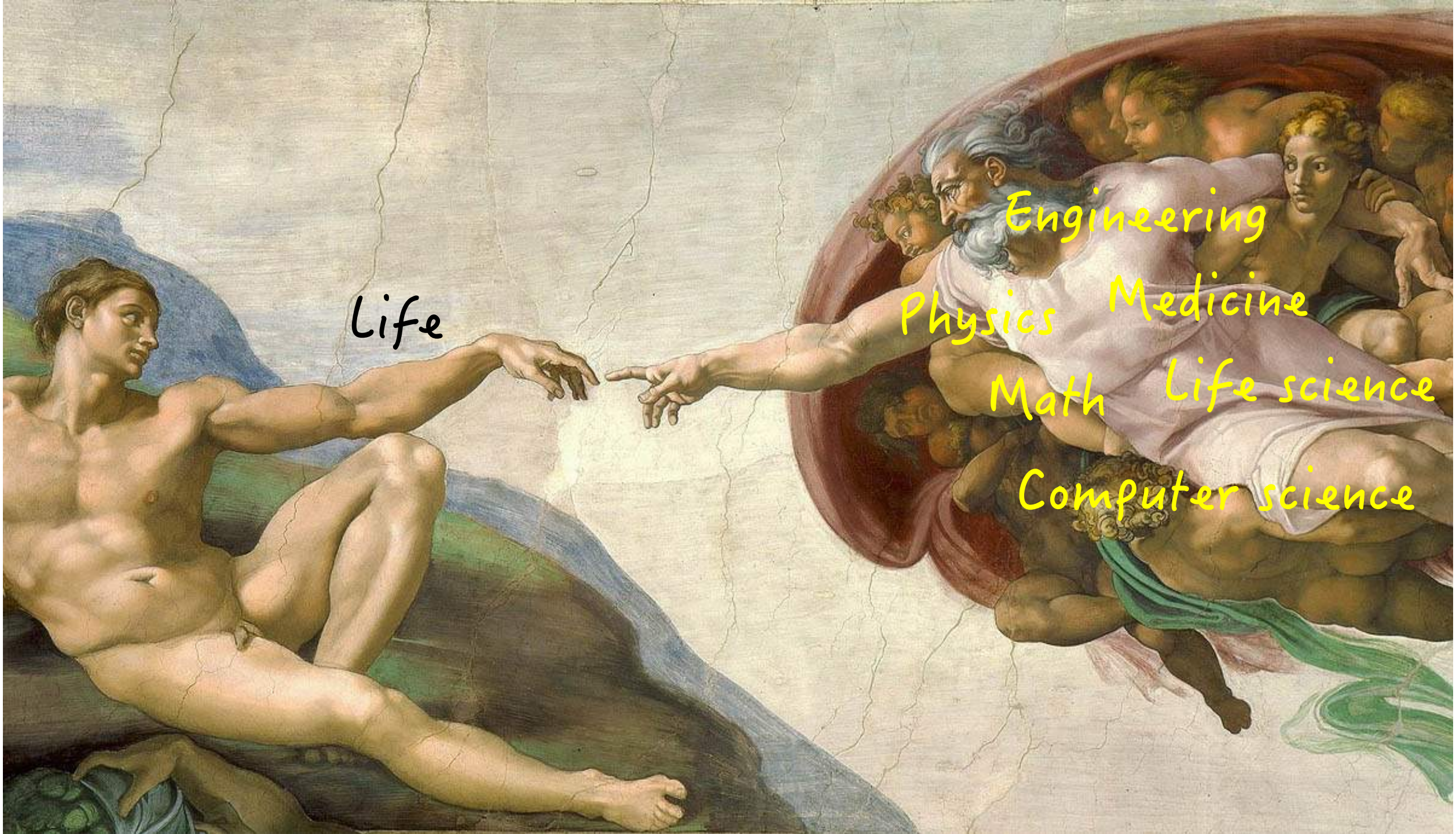
We have got many many "stars", so what is next…



Dynamics are important!



time


Life
Engineering
Physics
Medicine
Math
Life science
Computer science

Acknowledgements

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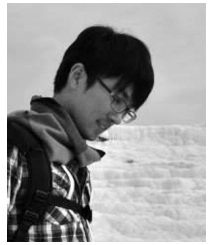
Mogens Høgh Jensen, PhD, University of Copenhagen

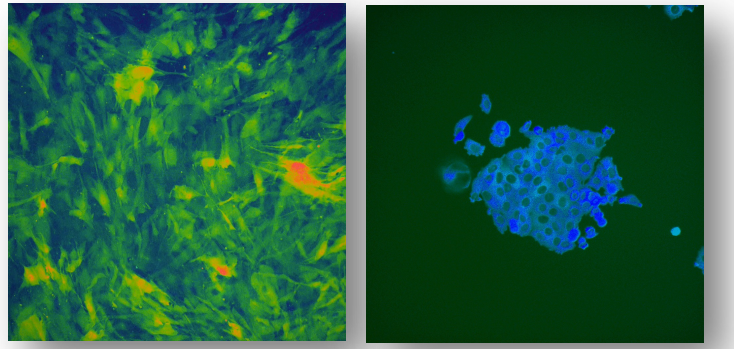
Hannah Co

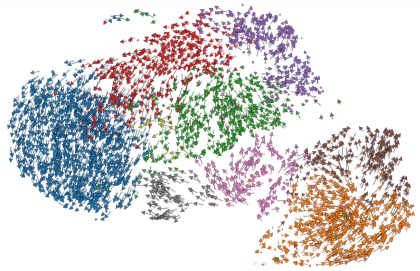
Chia-Chou Wu

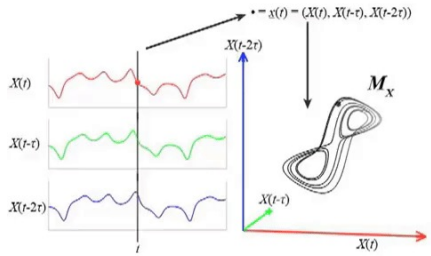
Hao-Kuen Lin

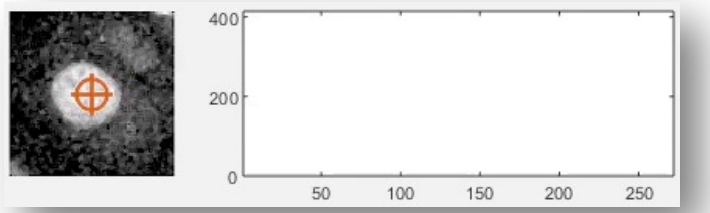


Jen-Hao Cheng









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Duy Pham
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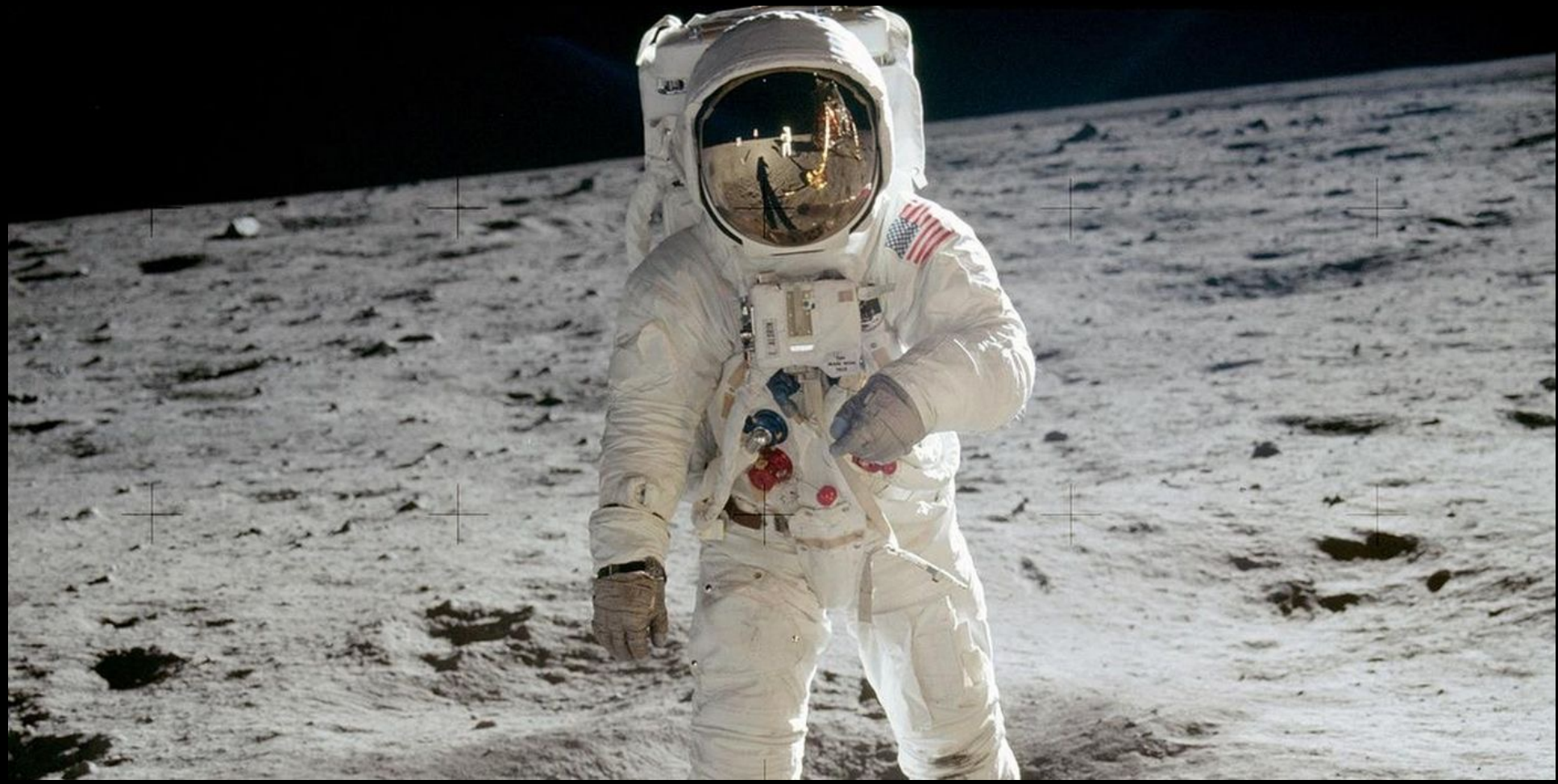
Physics Division 國家理論科學研究中心 物理組

From quantitative biology
To design principles in biology
To the human-based design and control of biology



Q1: Do you REALLY like a subject or are you REALLY good at something?

Any thought?

Q2: What kind of people you want to become?

Ask yourself in the next ~10 mins

When quantitative biology?

Technology development has made great impacts on quantitative biology in the past two decades

- Chemistry
- Engineering
- Imaging
- Computation

Technology development has made great impacts on quantitative biology in the past two decades

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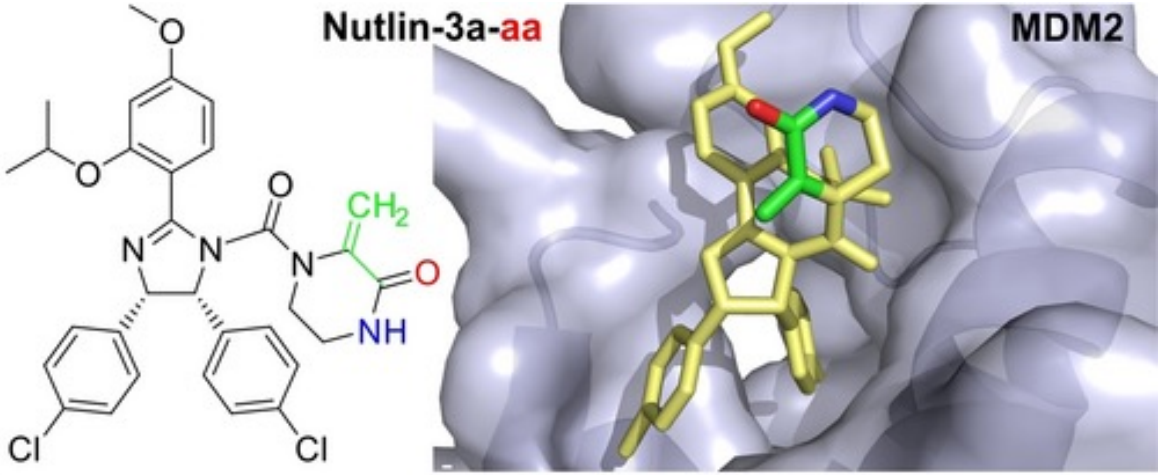
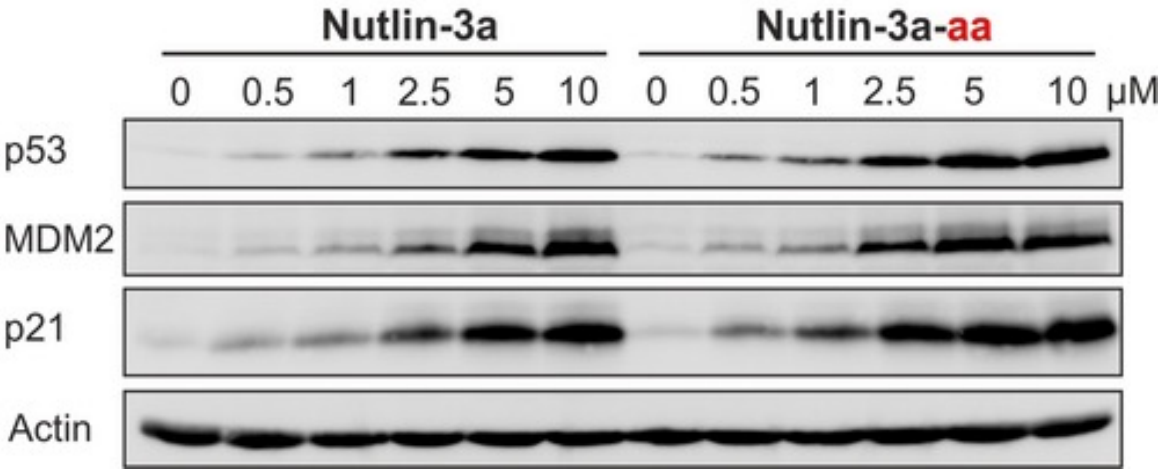
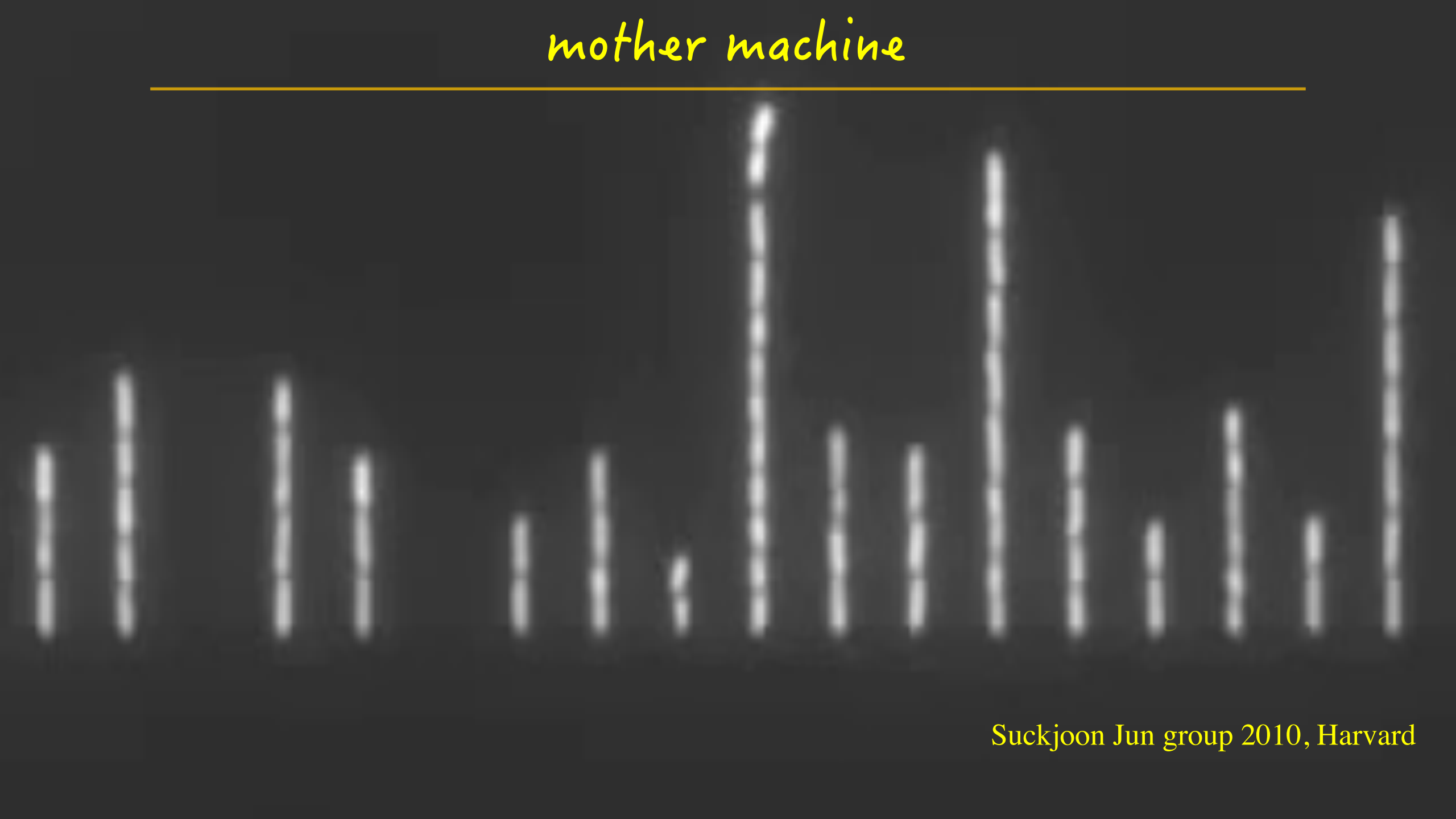




Technology development has made great impacts on quantitative biology in the past two decades

- Chemistry
- Engineering
- Imaging
- Computation

mother machine

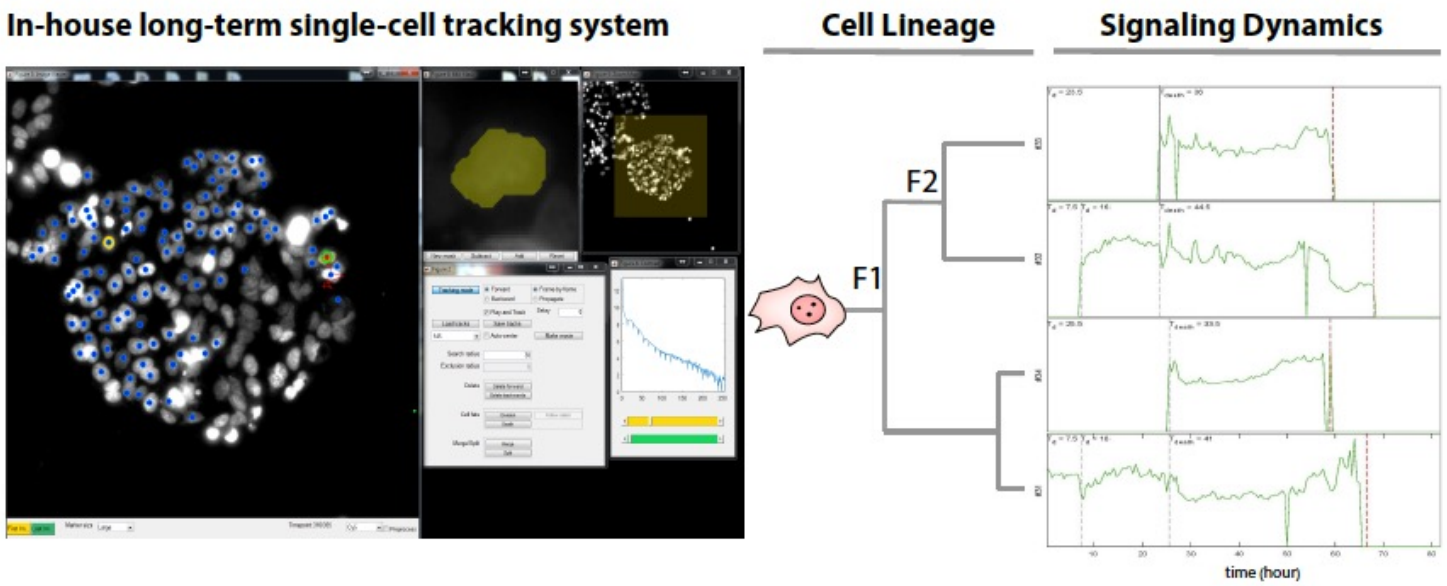


Suckjoon Jun group 2010, Harvard

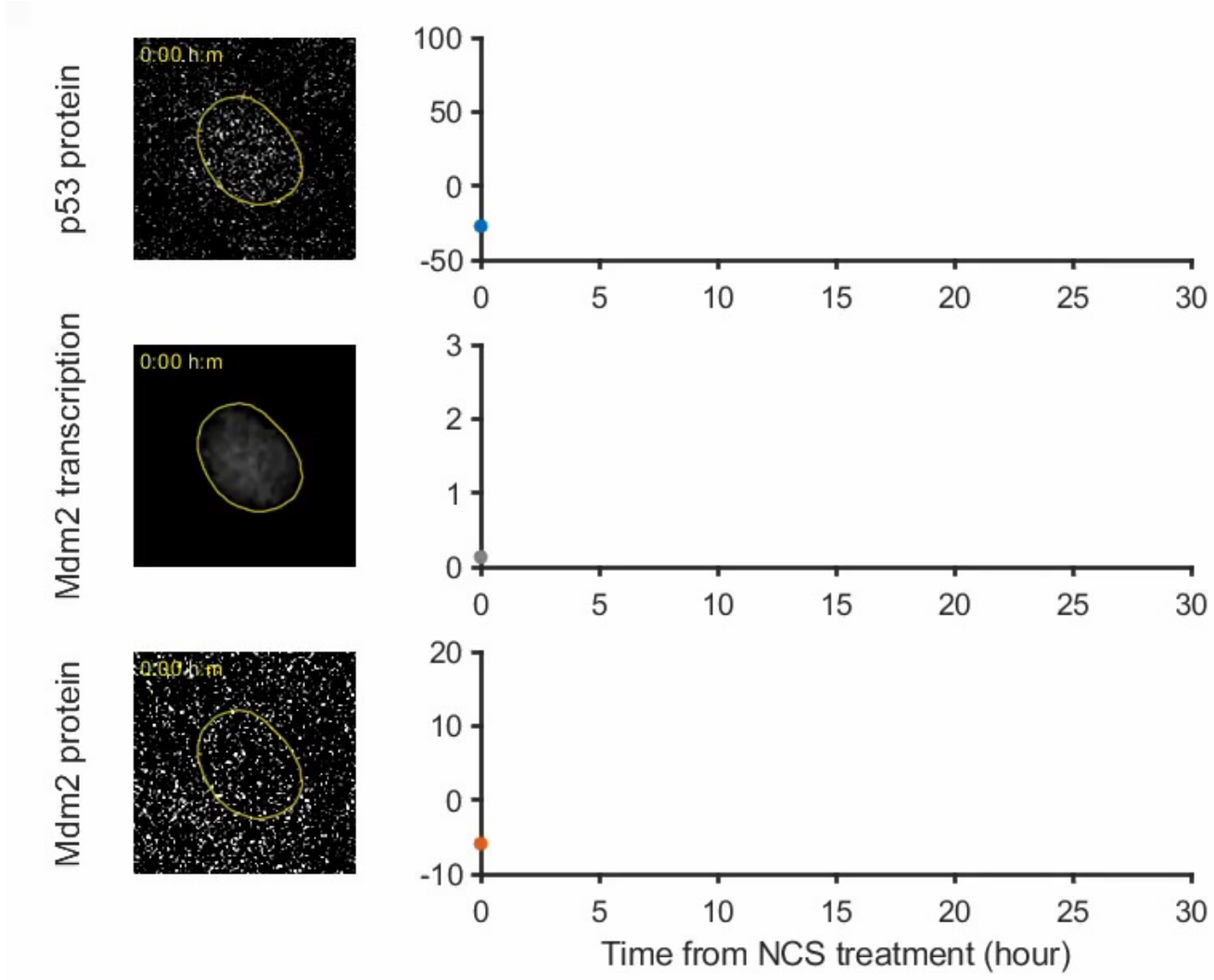
Technology development has made great impacts on quantitative biology in the past two decades

- Chemistry
- Engineering
- Imaging
- Computation

Quantify biological dynamics using the state-of-the-art experimental techniques



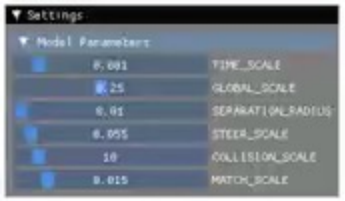
Tool development has made great impacts on quantitative biology in the past decades

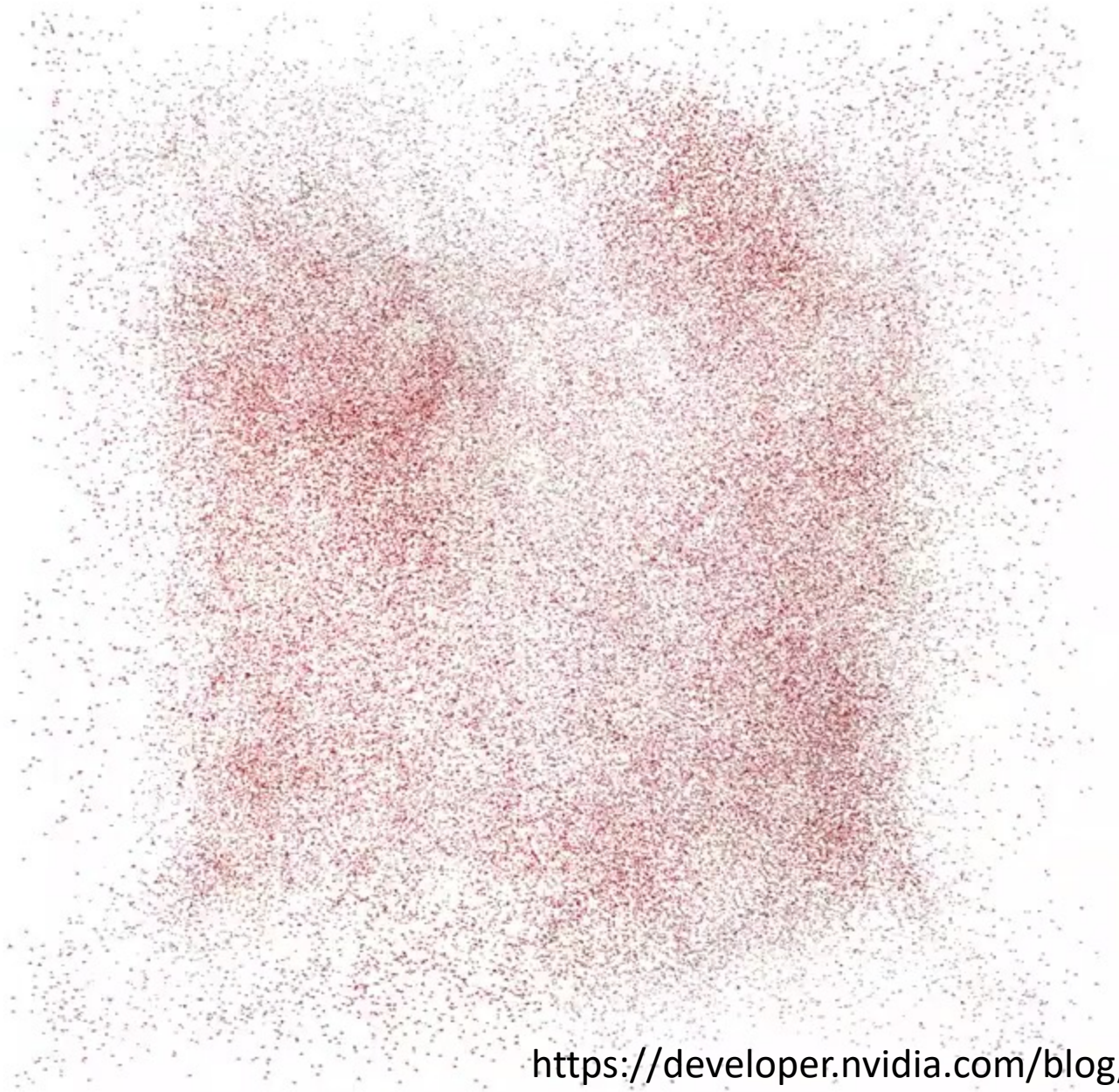


Technology development has made great impacts on quantitative biology in the past two decades

- Chemistry
- Engineering
- Imaging
- Computation

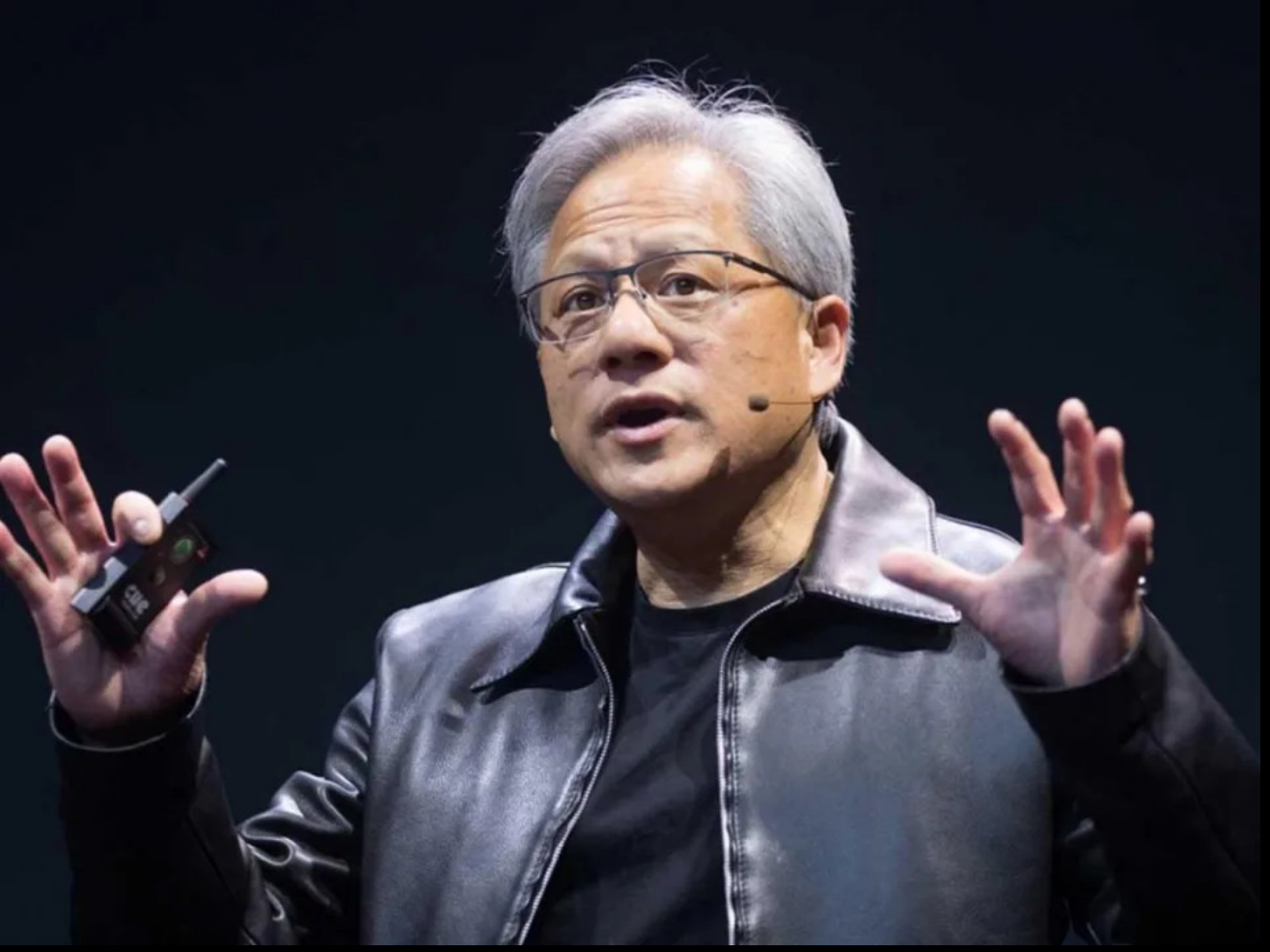
BBC





https://developer.nvidia.com/blog/fast-large-scale-agent-based-simulations-on-nvidia-gpus-with-flame-gpu/

政發生
SGT iNEWS
畫面來源:X平台
近期OPEN AI
在研發新技術，只要使用者
簡述一行字就能根據描述編
寫一分鐘的動態動畫，在網
路上也出現許多玩家實測分
享



“我們的工作是創造計算技術，讓所有人都不需要編程，現在世界上每個人都是程式設計師，這就是奇蹟—人工智慧的奇蹟。我們首次縮小了程式設計的技術鴻溝，現在正是讓大家意識到技術鴻溝已經彌合的絕佳時機。”

阿聯酋人工智慧部長詢問黃仁勳，「若自己要選擇一門攻讀學位的專業，會給出什麼建議？」黃仁勳則談到生命科學，他認為，若重新選擇，會體認人類生物學才是科學裡最複雜的領域之一。它不僅是複雜的，如此難以理解，同時也具有難以置信的影響力。

黃仁勳表示，每年我們的電腦科學、軟體都勝過以往，晶片、基礎設施也都勝過前一年，然而在生命科學上的進展寥寥。如果給他一次重新選擇的機會，他將意識到，將生命科學工程化的學科，「生命工程」即將到來。

黃仁勳 --- 2024年世界政府峰會

Q2: What kind of people you want to become?

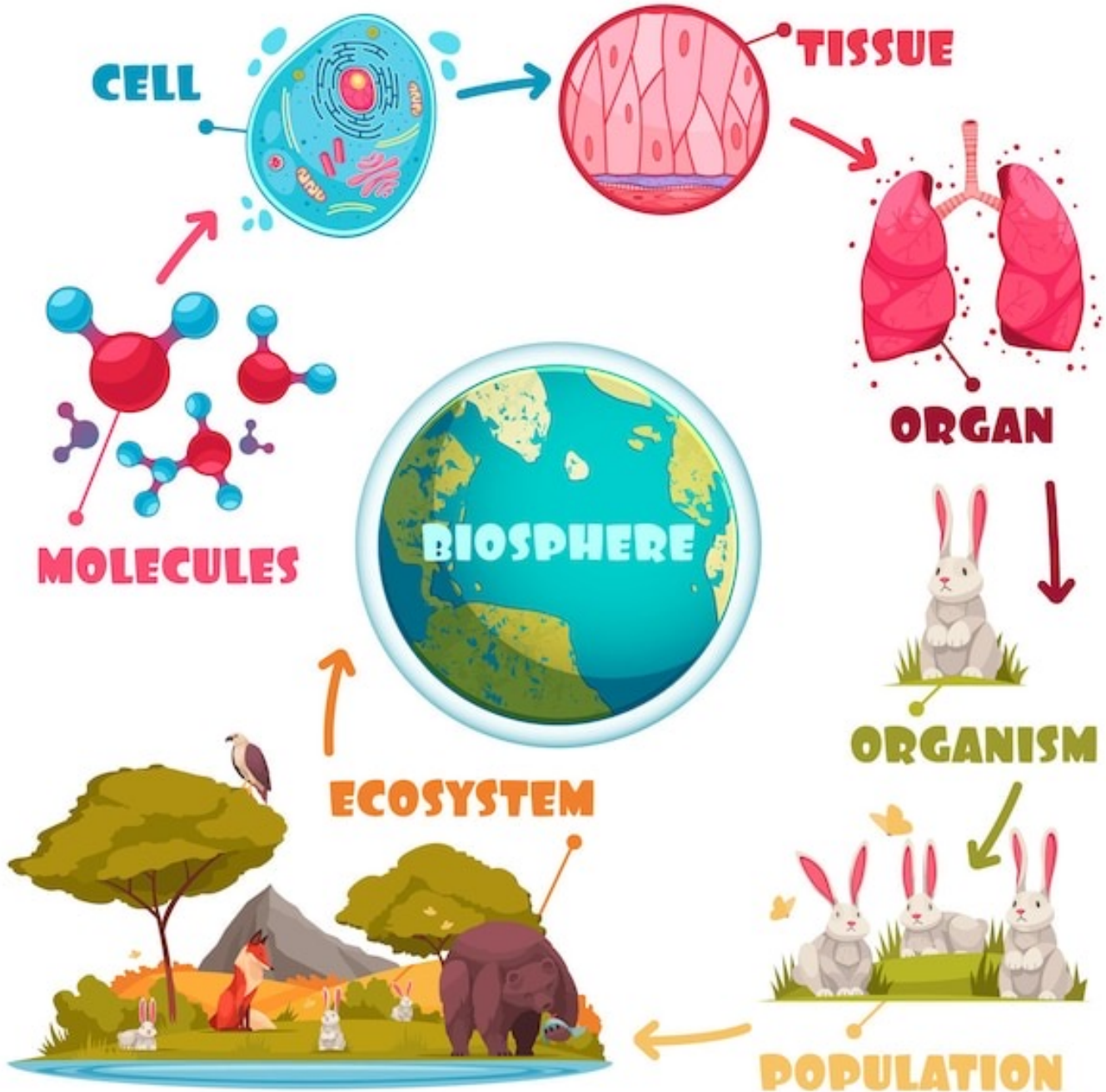
Any idea?

Q3: Do you have any question for my presentation so far?

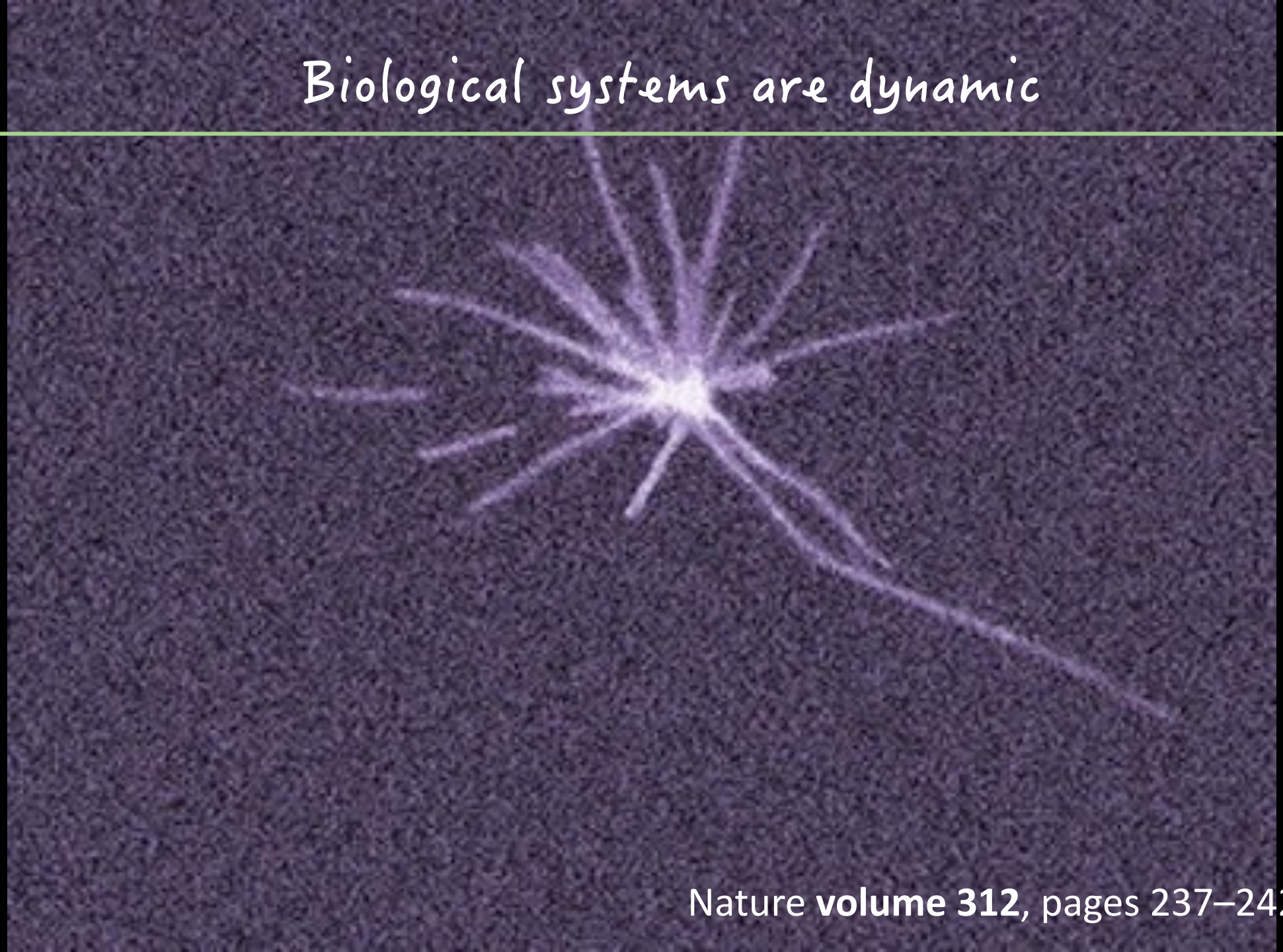
Ask yourself in the next ~15 mins

What quantitative biology?

Biological systems are dynamic

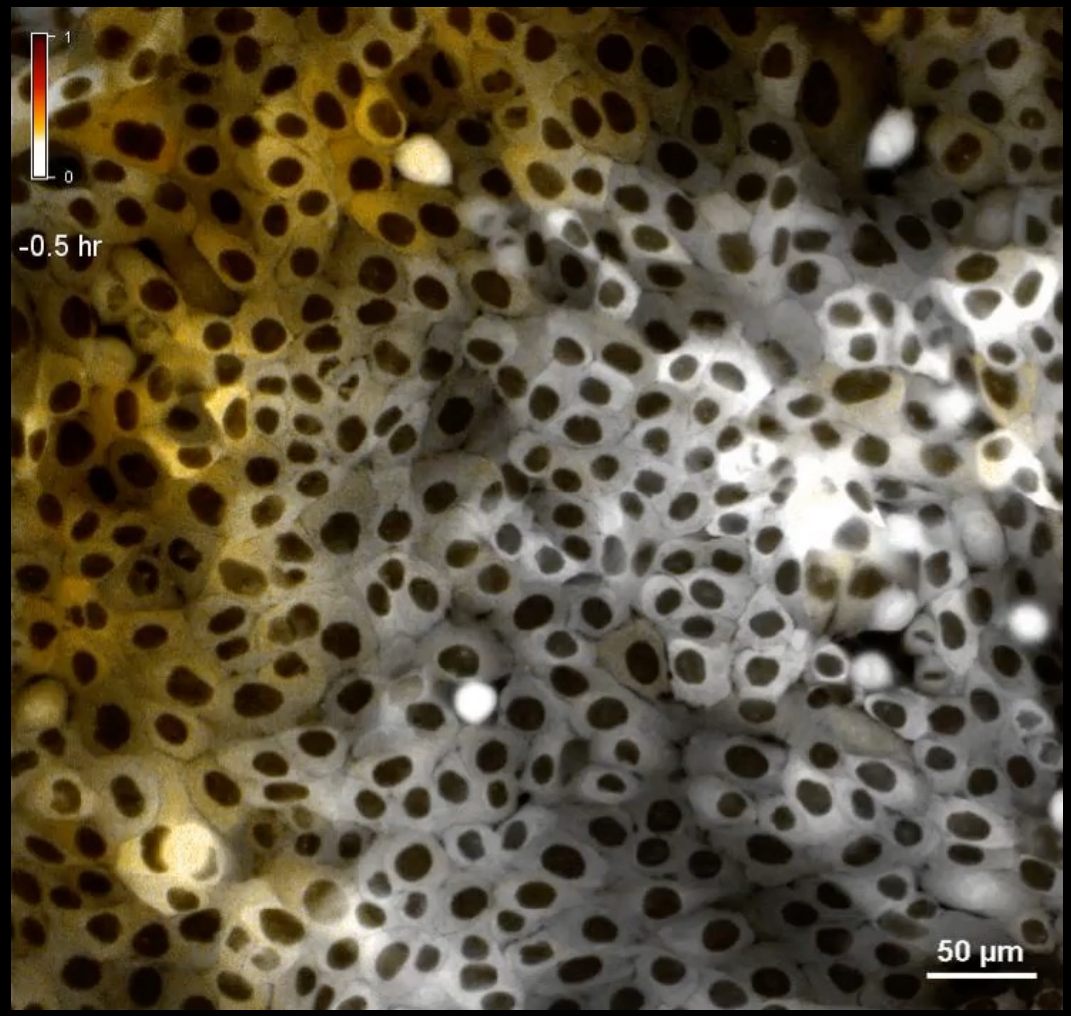

CELL
TISSUE
ORGAN
MOLECULES
BIOSPHERE
ORGANISM
ECOSYSTEM
POPULATION

Biological systems are dynamic

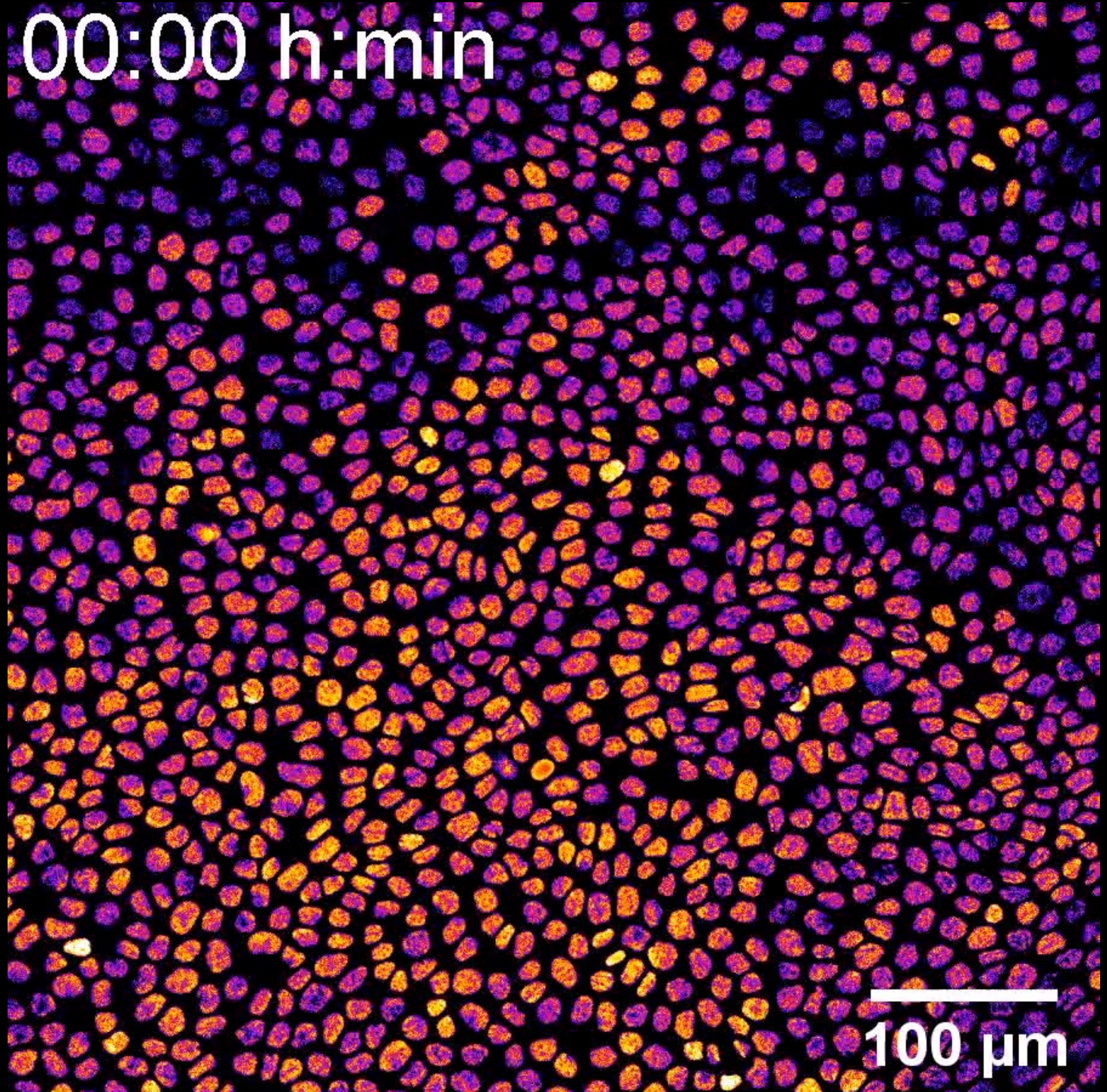


Nature **volume 312**, pages 237–242 (1984)

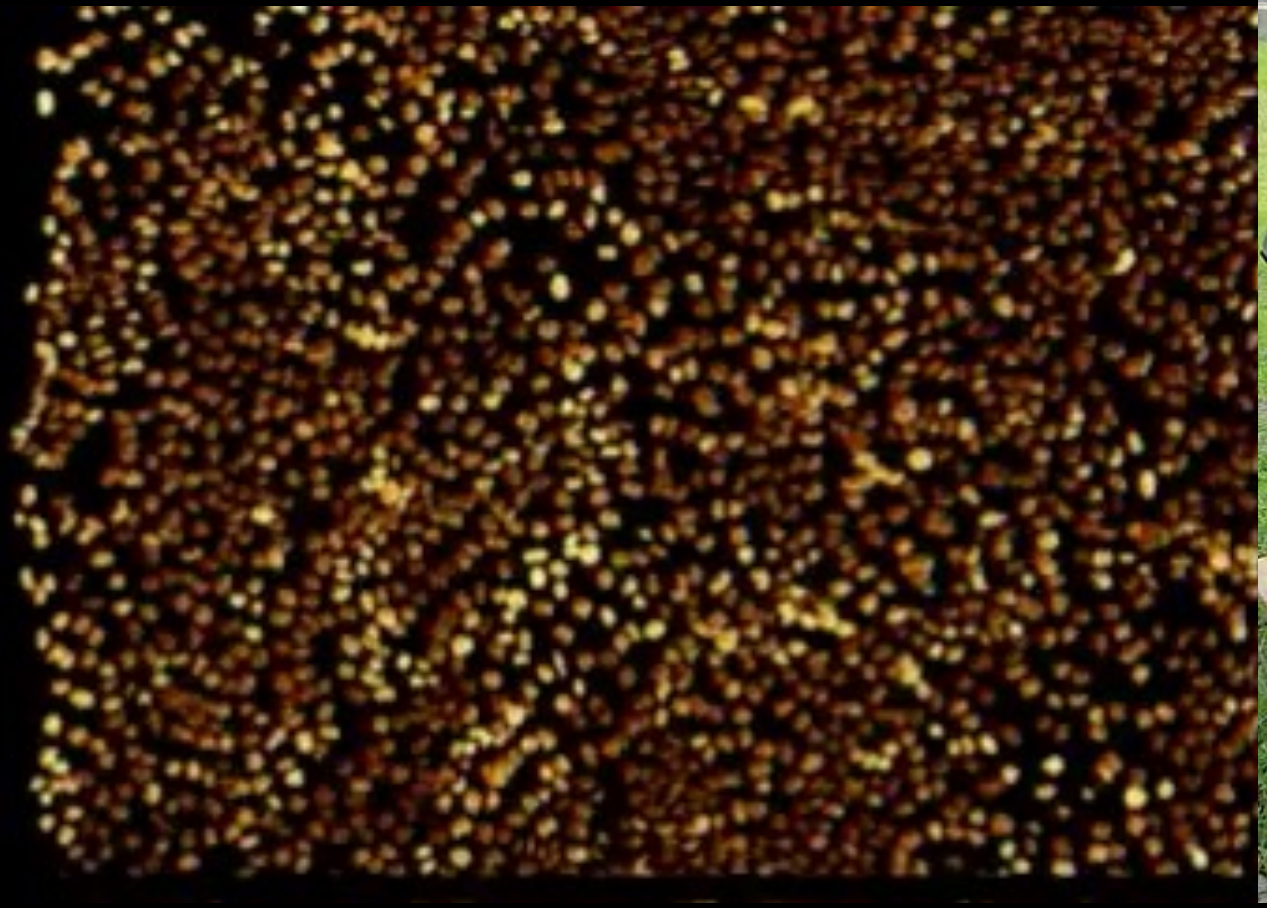
AMPK oscillations after suppressing glycolysis



Hung *et al*. eLife 2017;6:e27293.

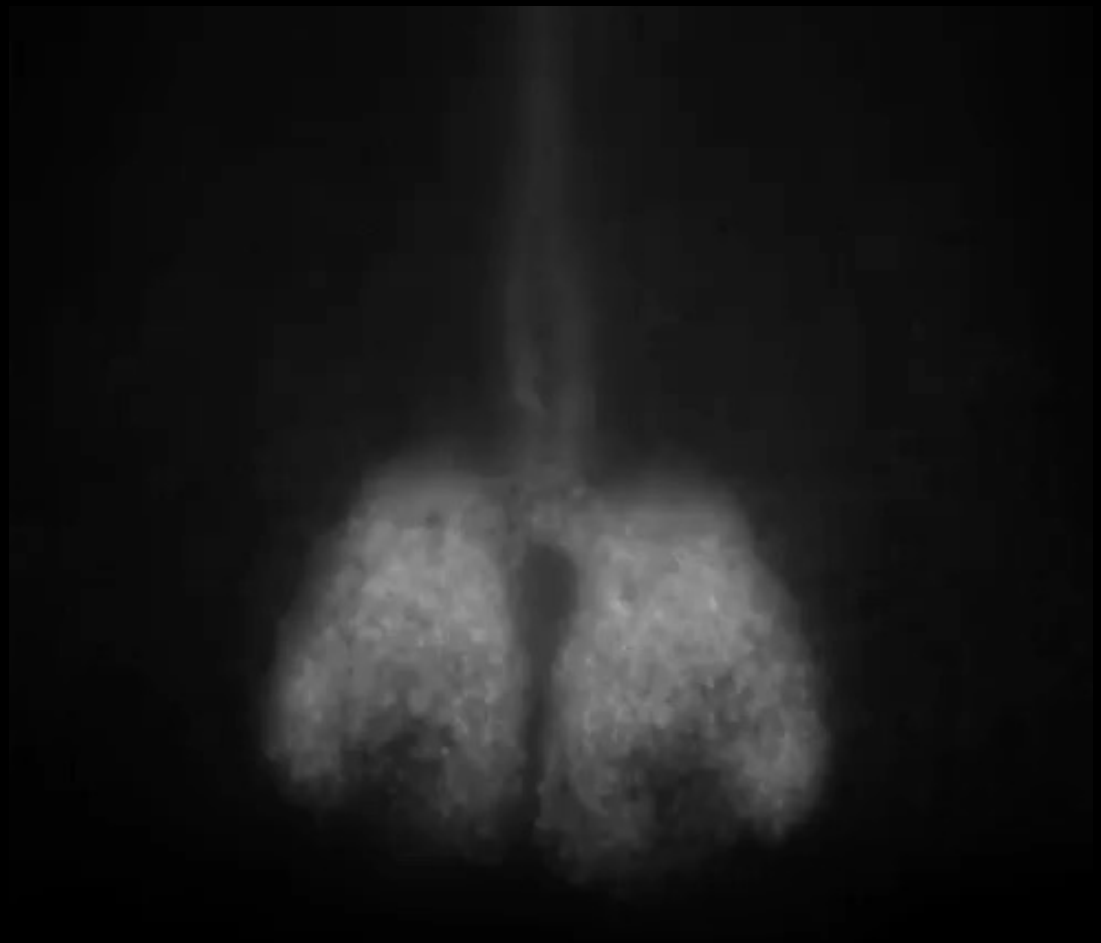


Olivier Pertz group, University of Bern, Switzerland, 2021



Developmental Cell *53*, 646–660, June 22, 2020

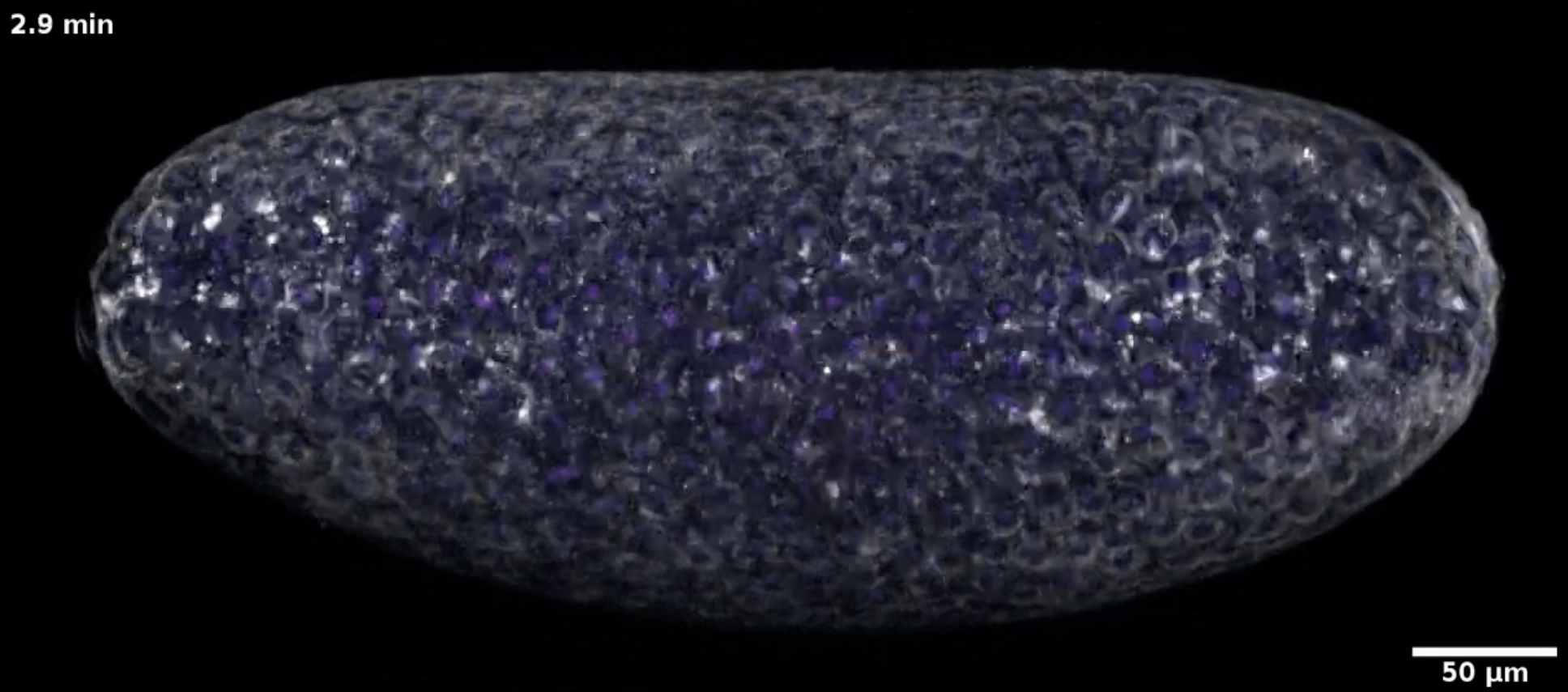
Circadian clock



SupraChiasmatic Nucleus (SCN)

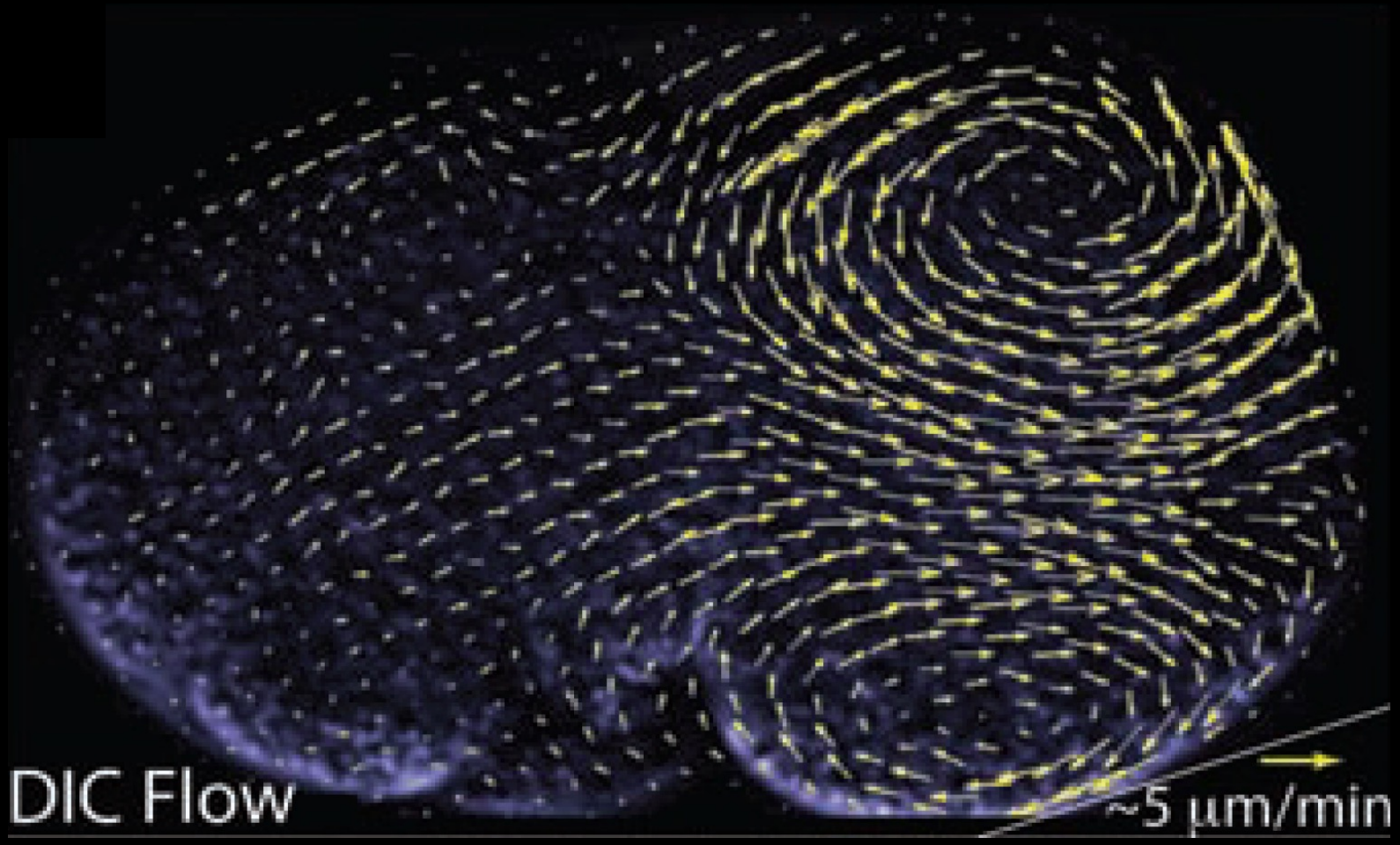
Steve Kay, UCSD

Biological waves in fly embryo



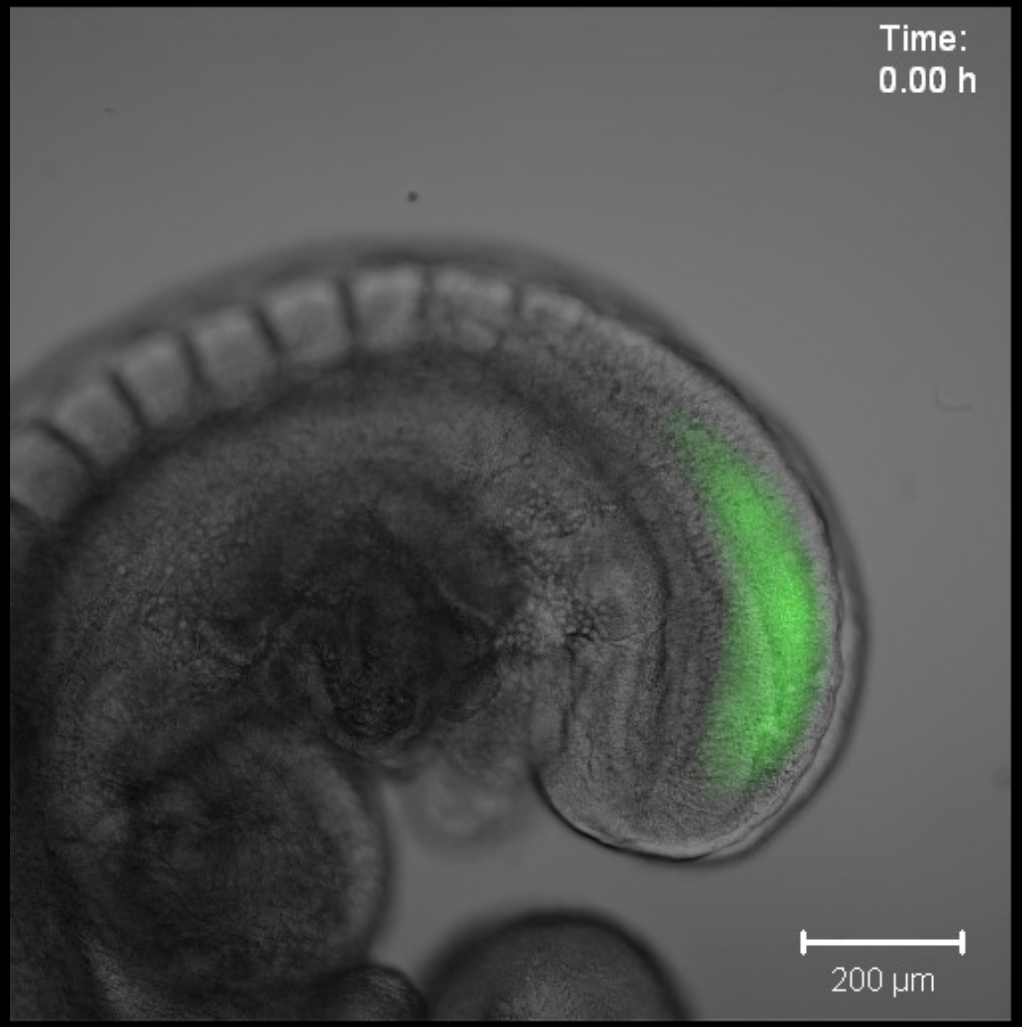
Deneke et al., 2019, Cell *177*, 925–941

P granules in C. elegance



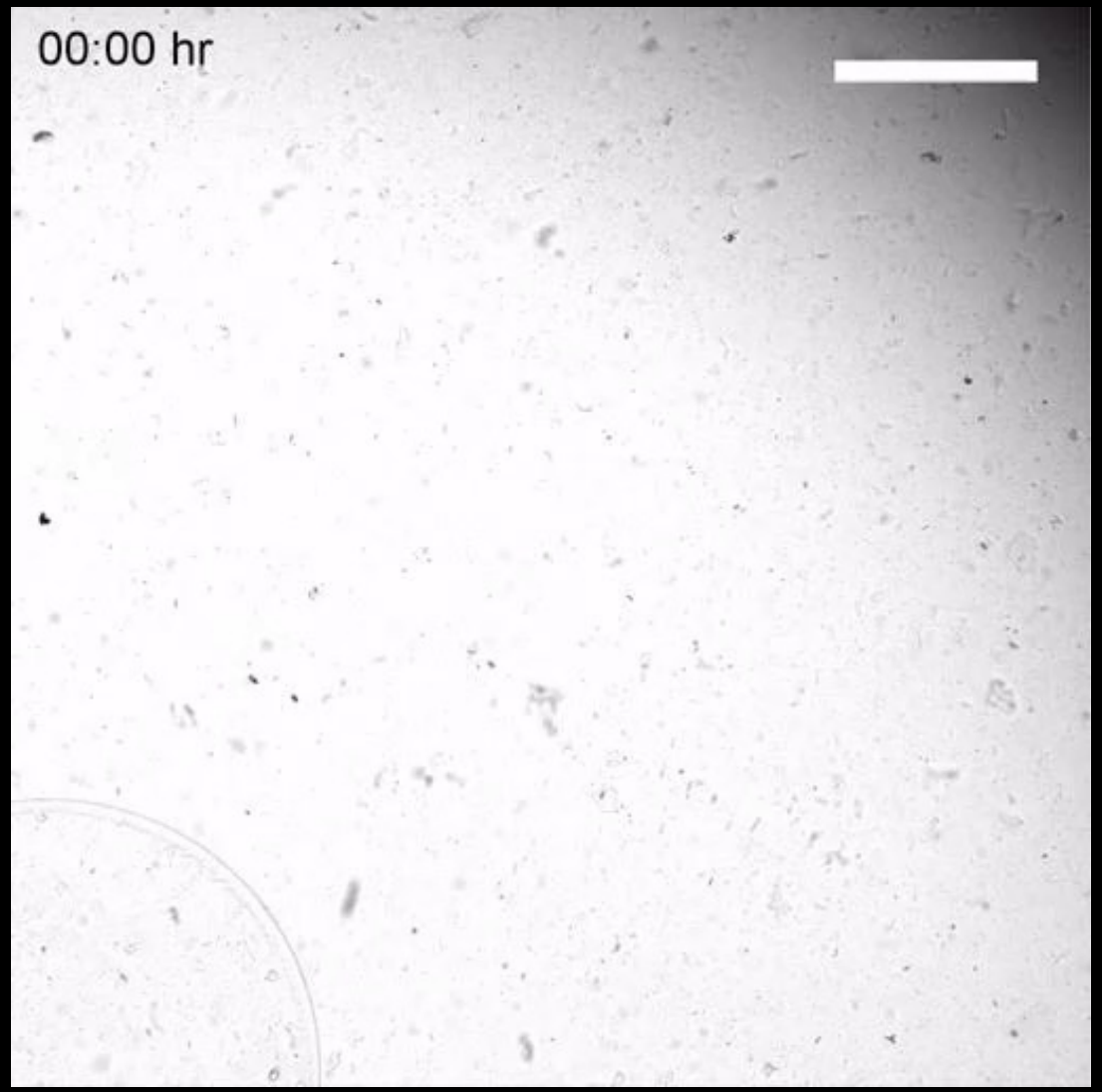
SCIENCE VOL 324 26 JUNE 2009

Oscillations and segmentation



NATURE CELL BIOLOGY VOLUME 10 | NUMBER 2 | FEBRUARY 2008

Nitrogen starvation in biofilm



Cell *185*, 145–157, January 6, 2022

Q3: Do you have any question for my presentation so far?

Any question?

Q4: Do you have a dream?

Ask yourself in the next ~15 mins

What is quantitative biology looking for?

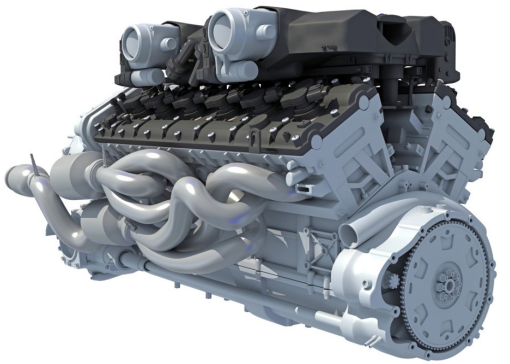
High-quality quantitative dataset
Simplifying theory
Deeper simplifying theory
Where are we in biology?

General principles in biology

What are the principles in car-ology?

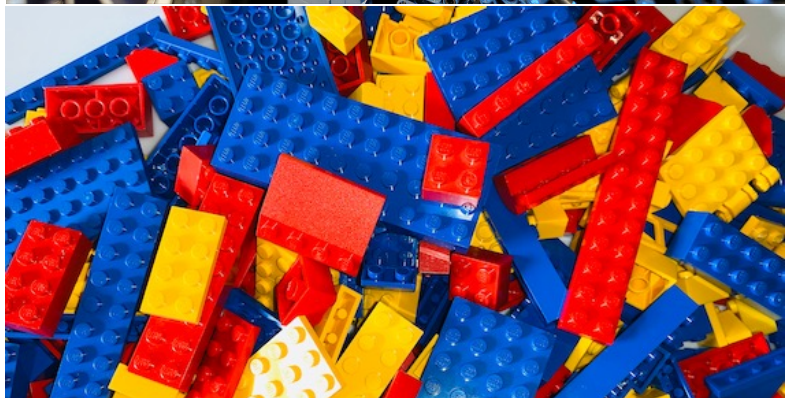
Design principles in car-ology

- What is a car?
- What makes a car?
- What are the functions of a car?



Emergent properties

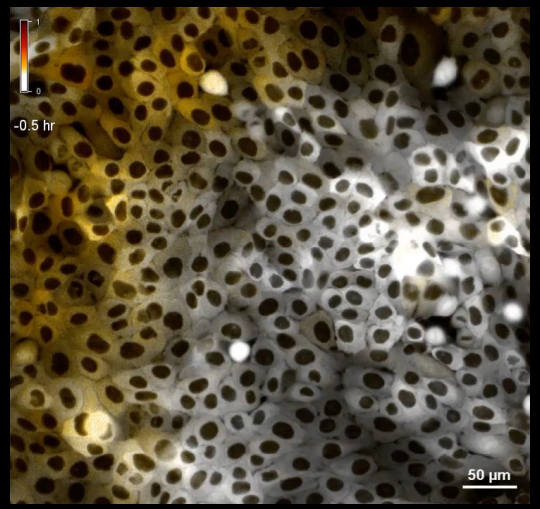
Design principles

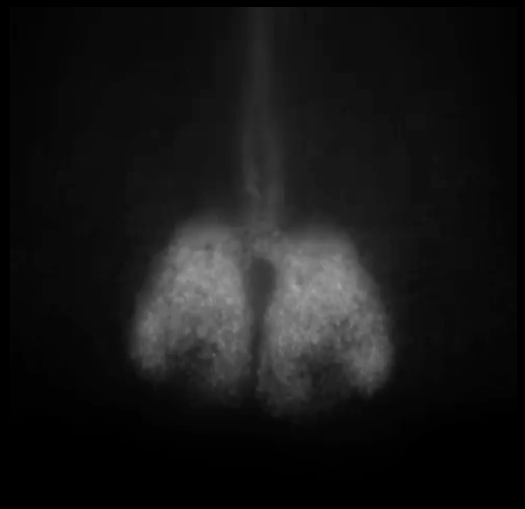


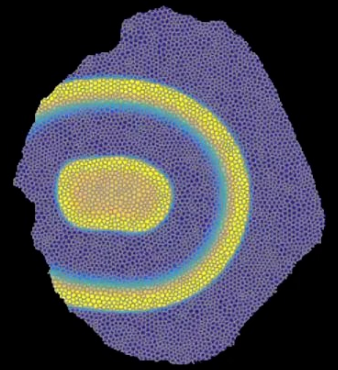
Individual components

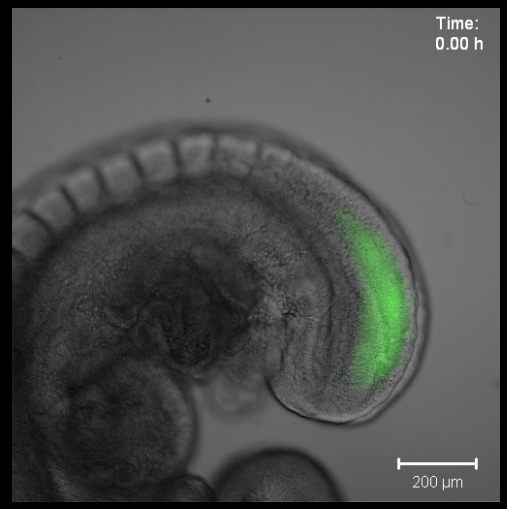
What are the design principles in biology?

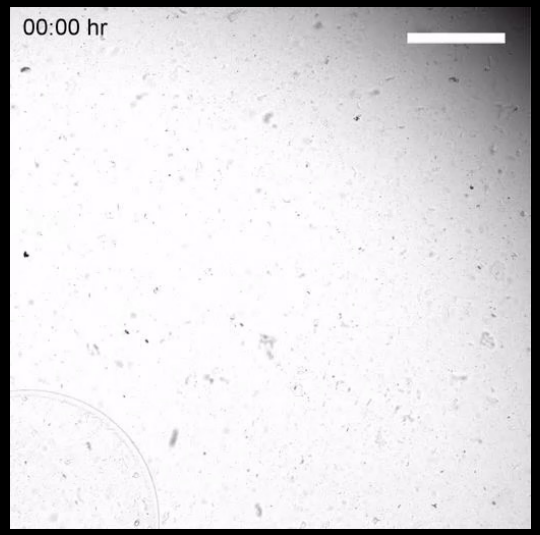
"General principles" underlying biological dynamics

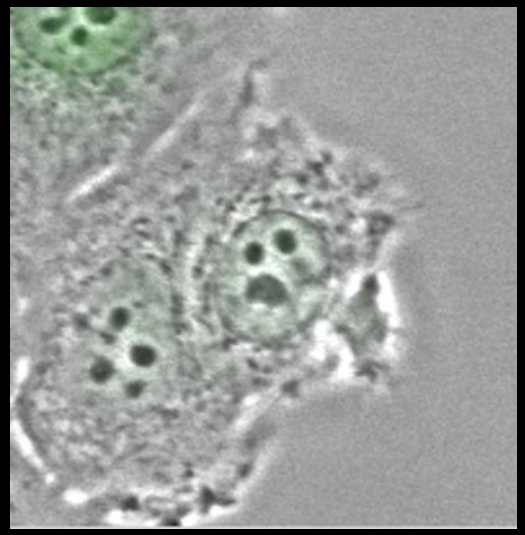




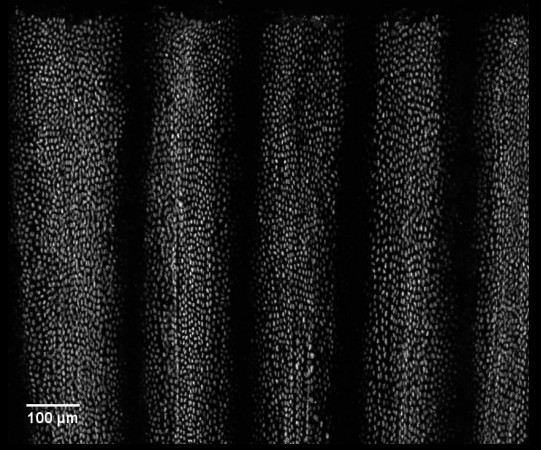


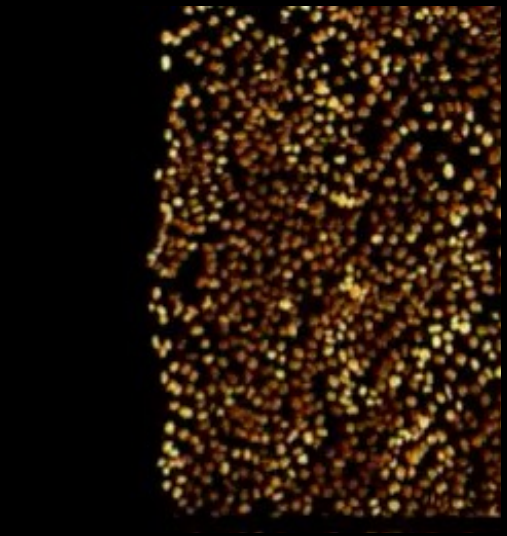






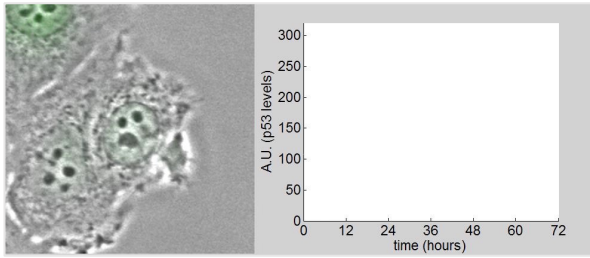
Tg(krt19:H2A-mCherry)





Emergent properties

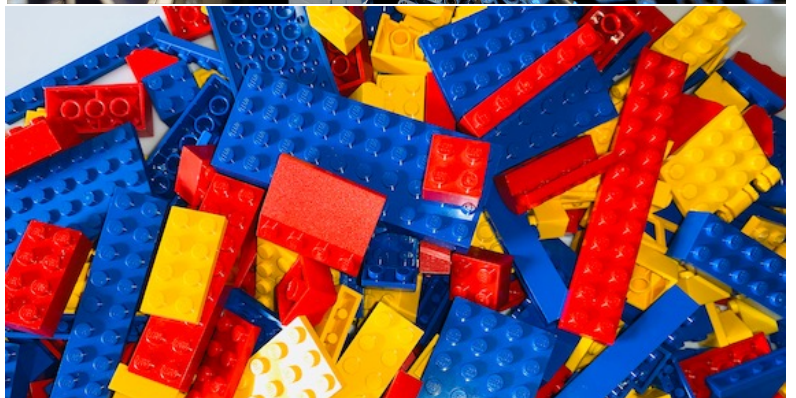
Biological dynamics



Design principles

?

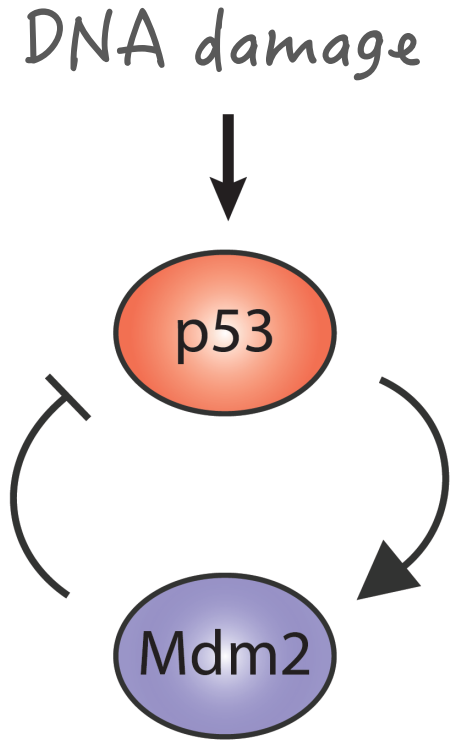
Individual components



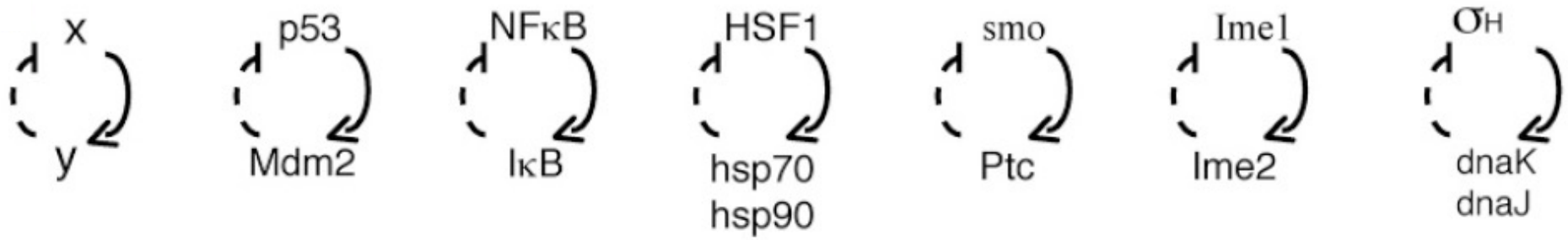
How do we find principles in biological oscillators?

Dynamics -> Principles

Molecular mechanism underlying the p53 oscillator

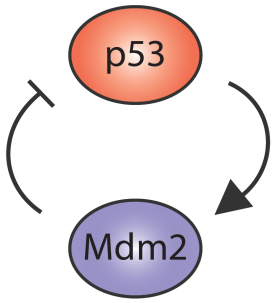


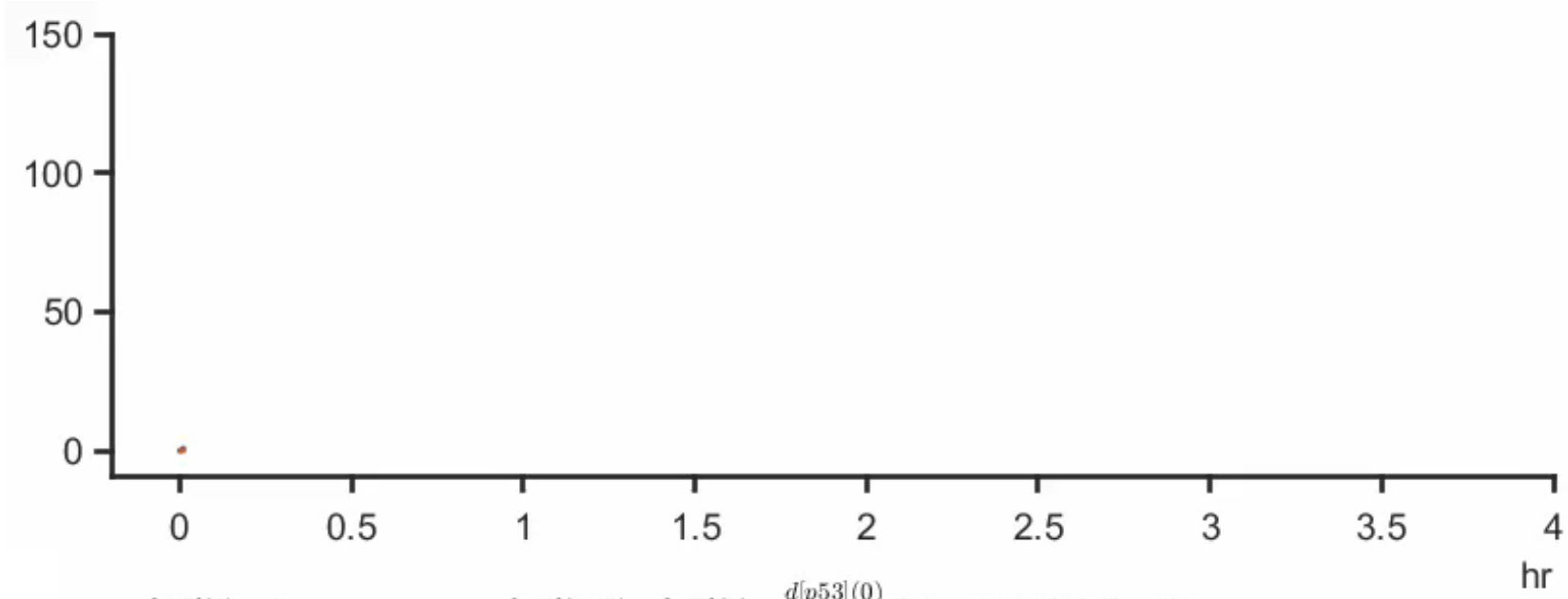
General molecular feature of biological oscillators



Nat Genet. 2004 Feb;36(2):147-50.

"Solve" the differential equations by computation





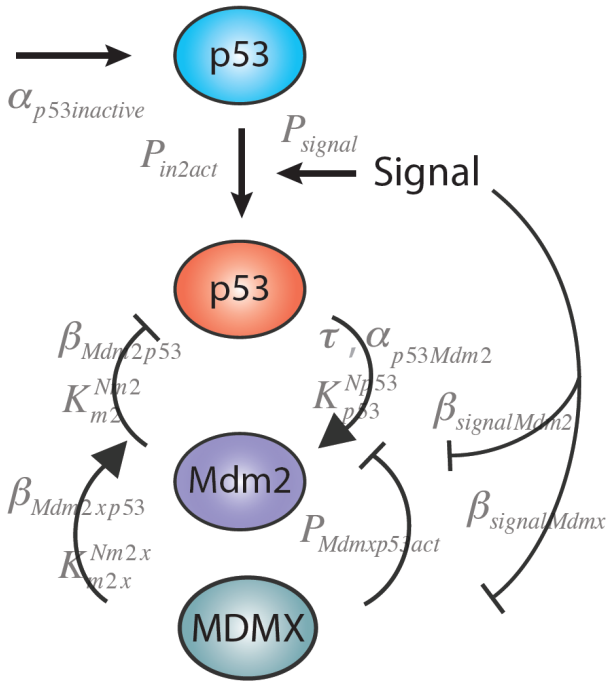
$$\frac{d[p53]}{dt} = \alpha - \beta[Mdm2]\frac{[p53]}{\gamma+[p53]}$$

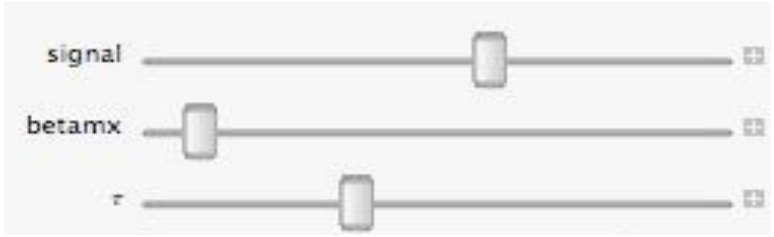
$$\frac{d[Mdm2]}{dt} = \psi[p53(t-\tau)] - \delta[Mdm2]$$

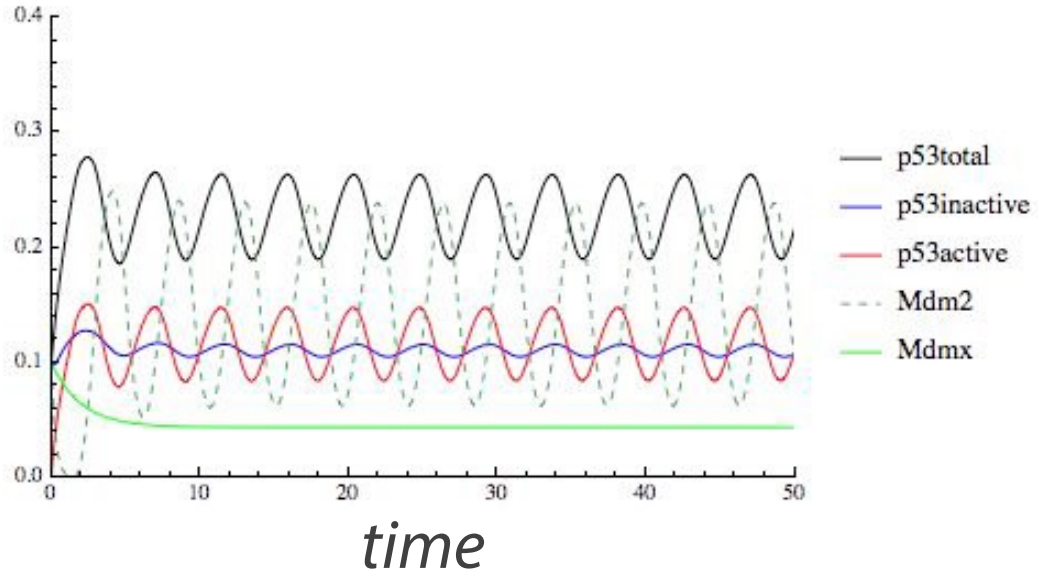
$$[p53](0) = 0 \qquad [p53](0.01) = [p53](0) + \frac{d[p53](0)}{dt} \times dt = 0 + 80 \times 0.01 = 0.8$$

$$[Mdm2](0) = 0 \qquad [Mdm2](0.01) = [Mdm2](0) + \frac{d[Mdm2](0)}{dt} \times dt = 0 + 0 \times 0.01 = 0$$

In silico exploration of regulators for p53 dynamics

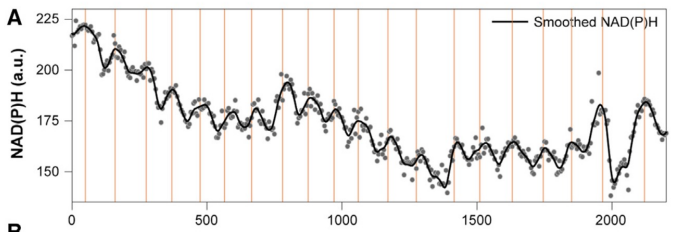


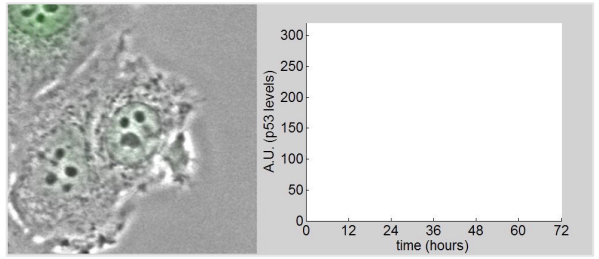




General principles governing biological oscillators

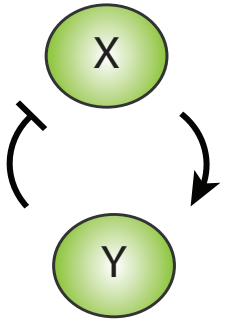
High-quality quantitative dataset





Simplifying theory

Delayed negative feedback
e.g., multi-step regulations…



Deeper simplifying theory

???

How do biological oscillators emerge during evolution?

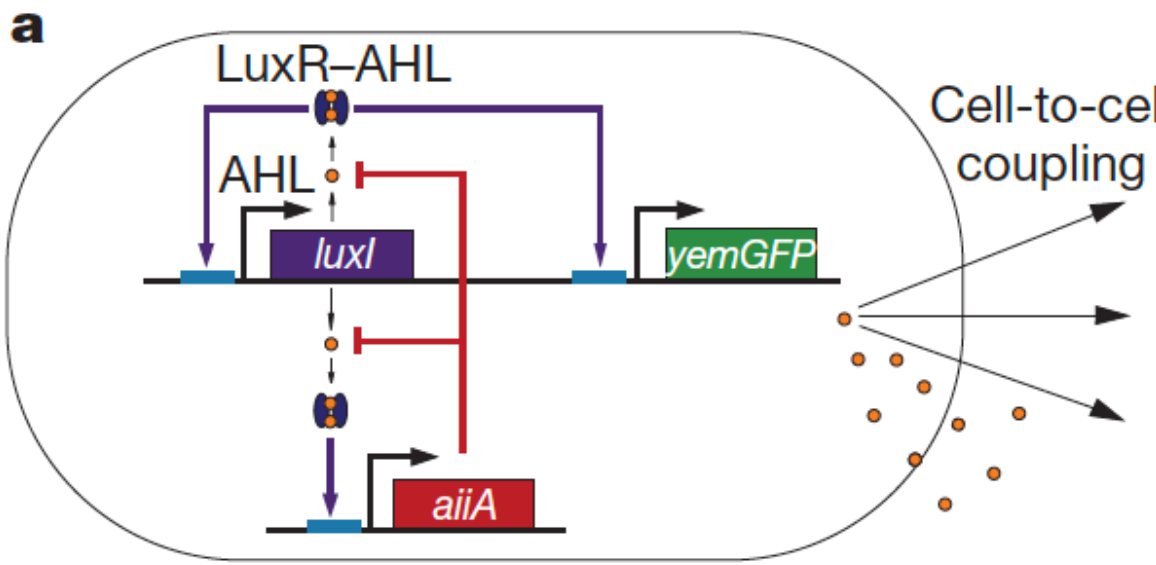
Can we predict when and where biological oscillators arise?

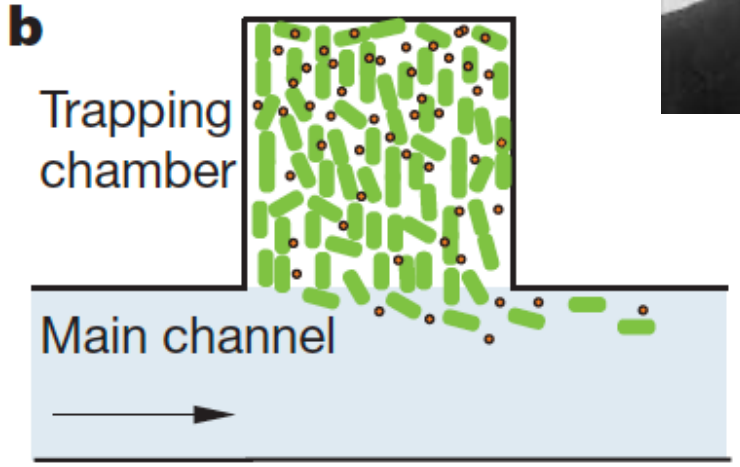
Q4: Do you have a dream?

Any?

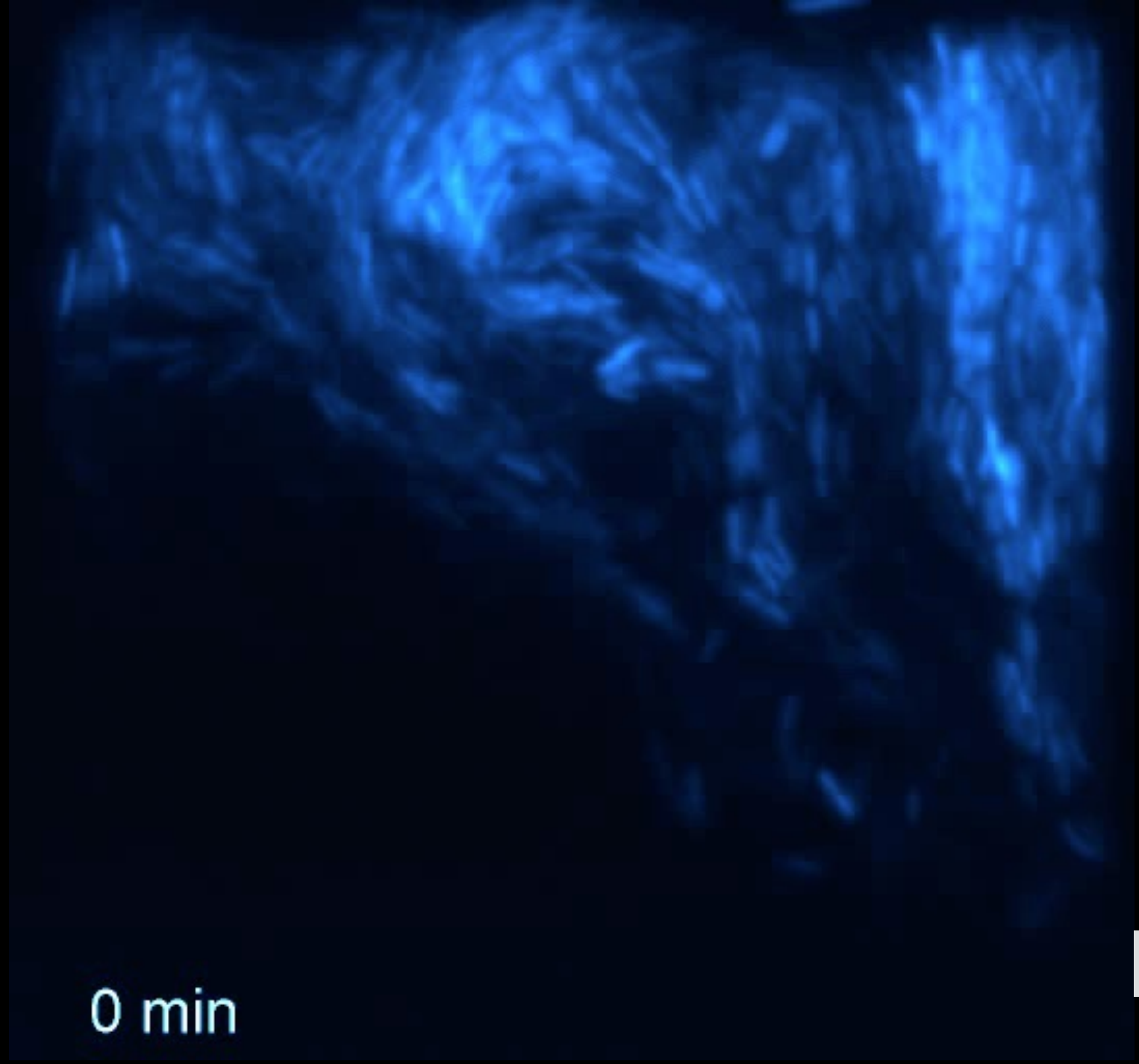
Tool-building in biology based on design principles

Synthetic oscillator --- a genetic circuit of negative feedback loop





Vol 463|21 January 2010|doi:10.1038/nature08753



Vol 463|21 January 2010|doi:10.1038/nature08753

2 min

Synthetic biological switches in human cells

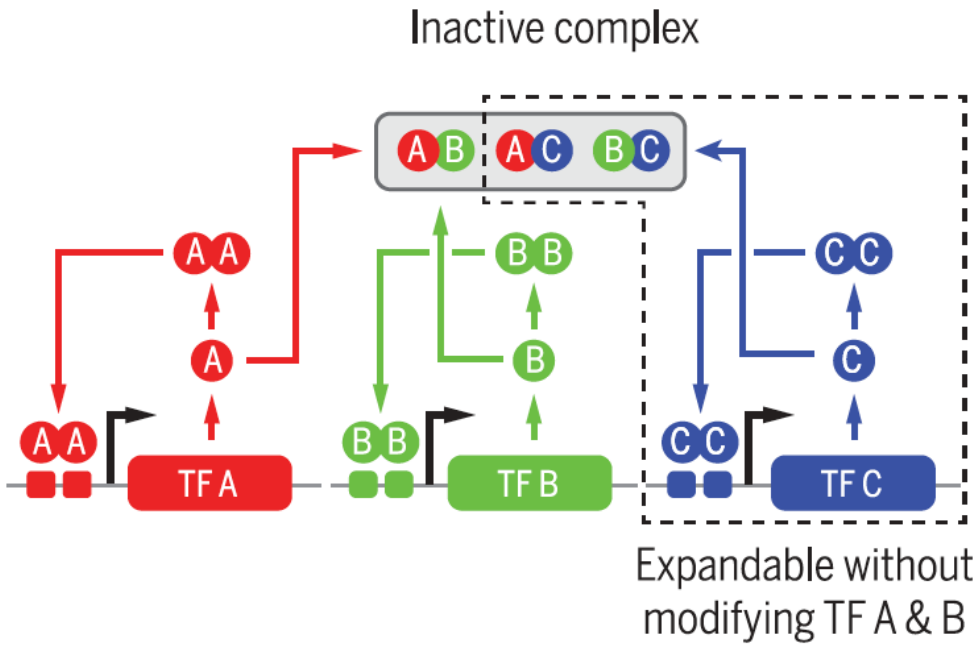
RESEARCH ARTICLE

SYNTHETIC BIOLOGY

Synthetic multistability in mammalian cells

Ronghui Zhu[1], Jesus M. del Rio-Salgado[1], Jordi Garcia-Ojalvo[2], Michael B. Elowitz[1,3]*

MultiFate: a synthetic multistable circuit architecture



Zhu *et al.*, *Science* **375**, 284 (2022)

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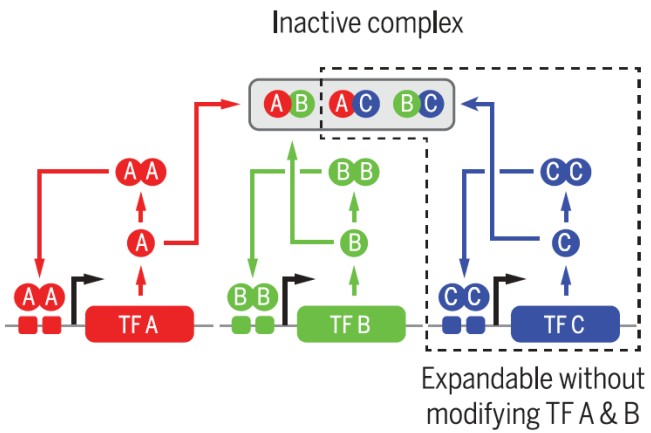
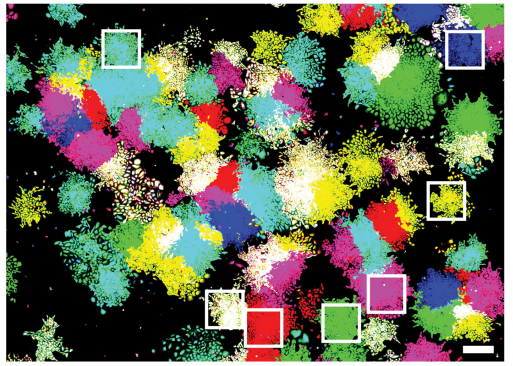
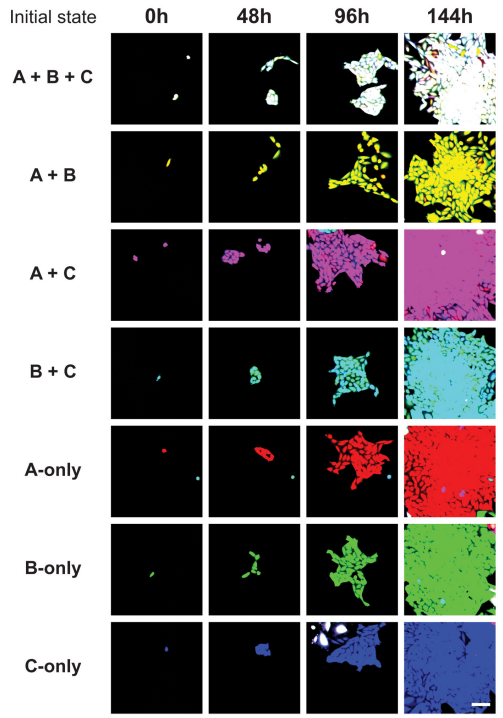
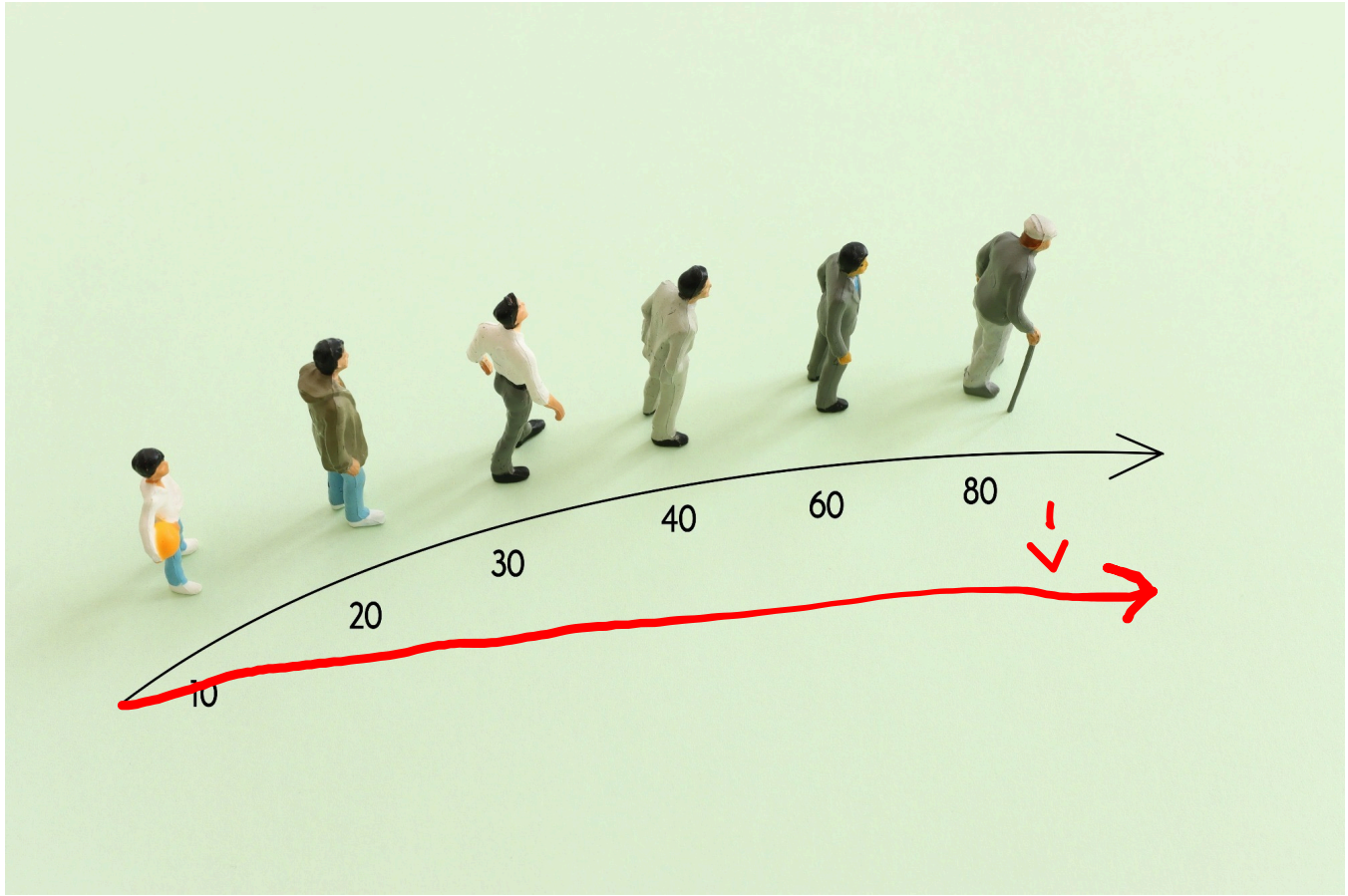






Zhu *et al.*, *Science* **375**, 284 (2022)

Harnessing design principles to create new kind of biology



RESEARCH ARTICLE

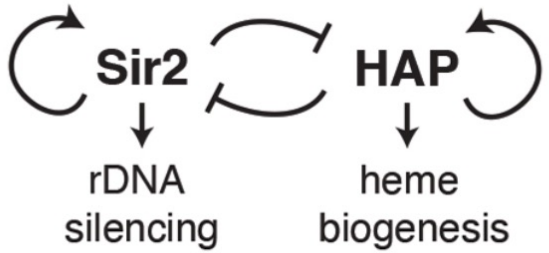
SYNTHETIC BIOLOGY

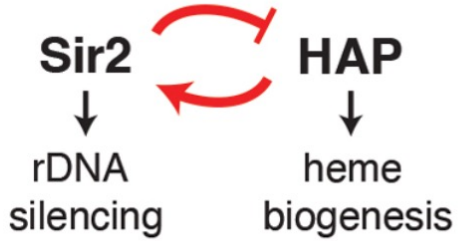
Engineering longevity—design of a synthetic gene oscillator to slow cellular aging

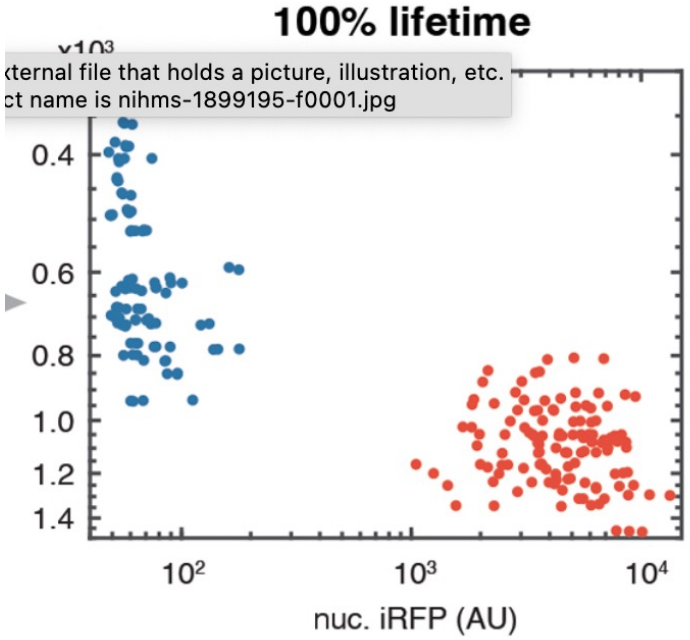
Zhen Zhou[1], Yuting Liu[1], Yushen Feng[1], Stephen Klepin[1], Lev S. Tsimring[2], Lorraine Pillus[1,3], Jeff Hasty[1,2,4], Nan Hao[1,2,4]*

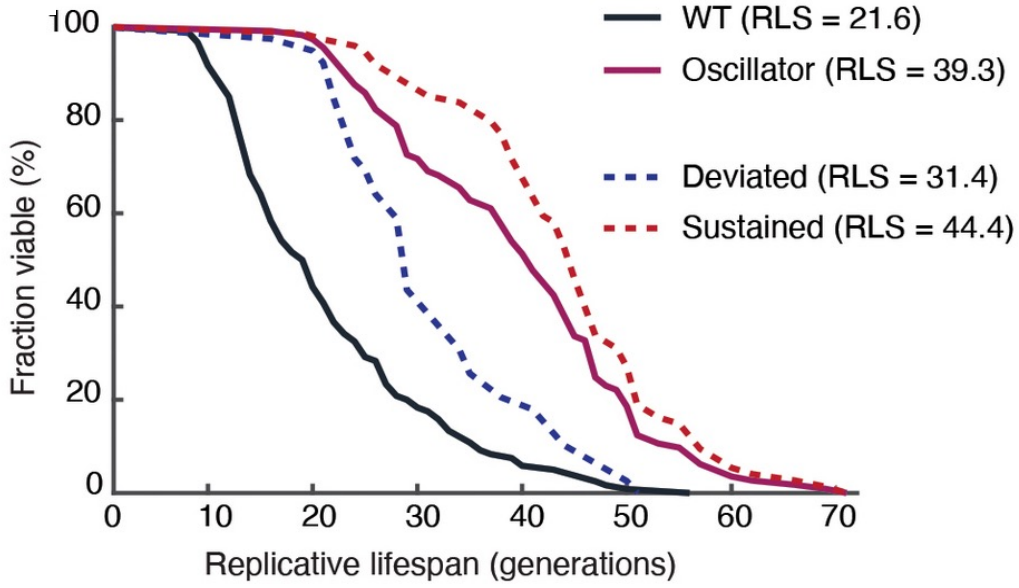
Science 27 Apr 2023, Vol 380, Issue 6643, pp. 376-381

Converting a bistable system to an oscillatory system









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量化/系統生物學的 why, when and what

Sheng-hong Chen, 陳昇宏 助研究員
Institute of Molecular Biology, 分子生物研究所
Academia Sinica, 中央研究院

高中生命科學研究人才培育計畫, April/13/2024