Design Principles In Biology: A Dynamical Systems Approach

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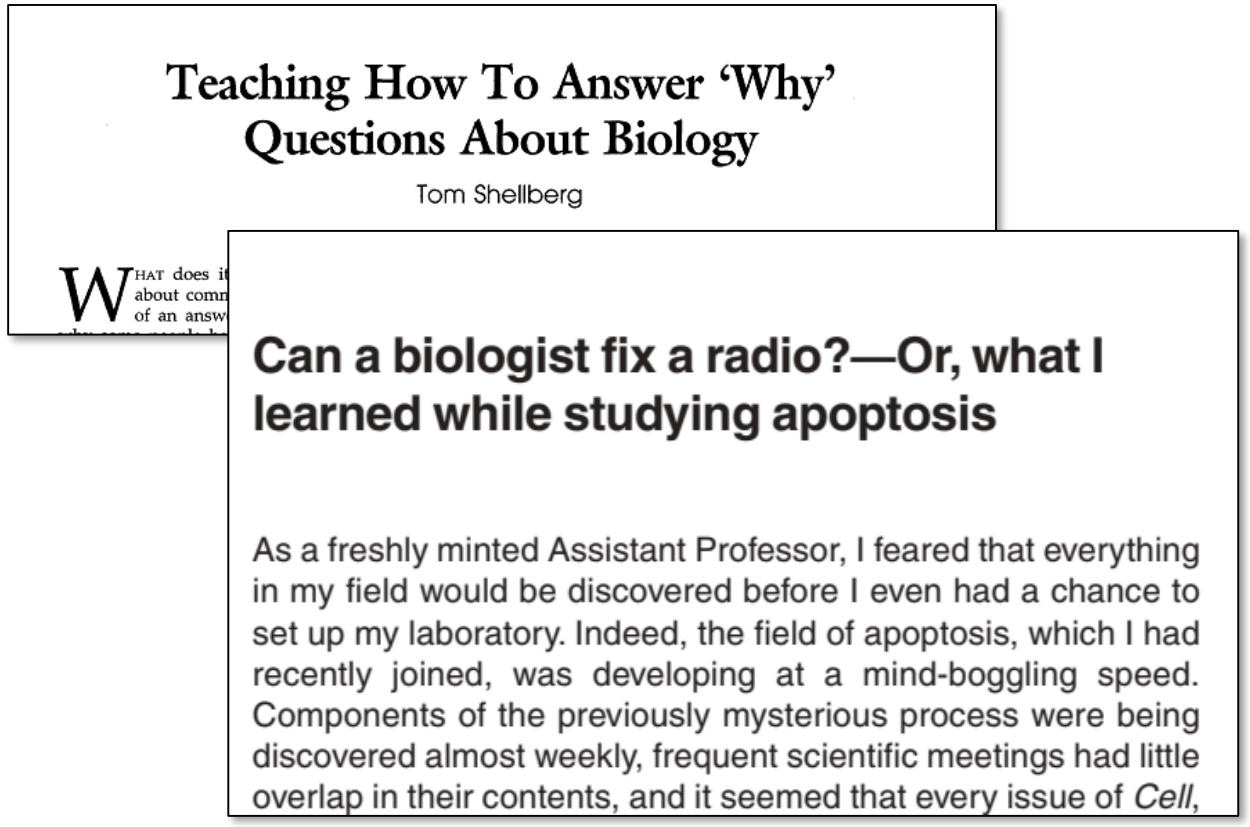
We Looked Up And Asked Why

There are “Worlds Hidden in Plain Sight” with unanswered questions

But How To Ask The Question?



Teaching How To Answer 'Why' Questions About Biology

Tom Shellberg

WHAT does it about comm of an answ

Can a biologist fix a radio?—Or, what I learned while studying apoptosis

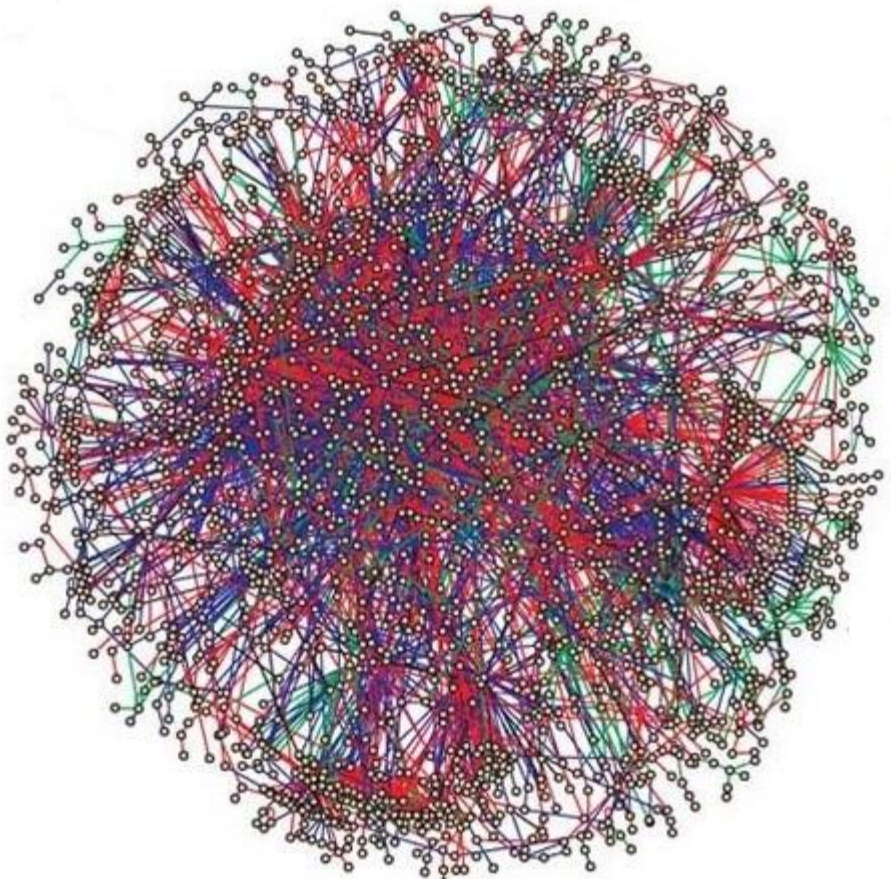
As a freshly minted Assistant Professor, I feared that everything in my field would be discovered before I even had a chance to set up my laboratory. Indeed, the field of apoptosis, which I had recently joined, was developing at a mind-boggling speed. Components of the previously mysterious process were being discovered almost weekly, frequent scientific meetings had little overlap in their contents, and it seemed that every issue of *Cell*,

The meaning of Why/How differs:

Case specific 'mechanistic' explanation

Generalized explanation

Oh! It’s Complex

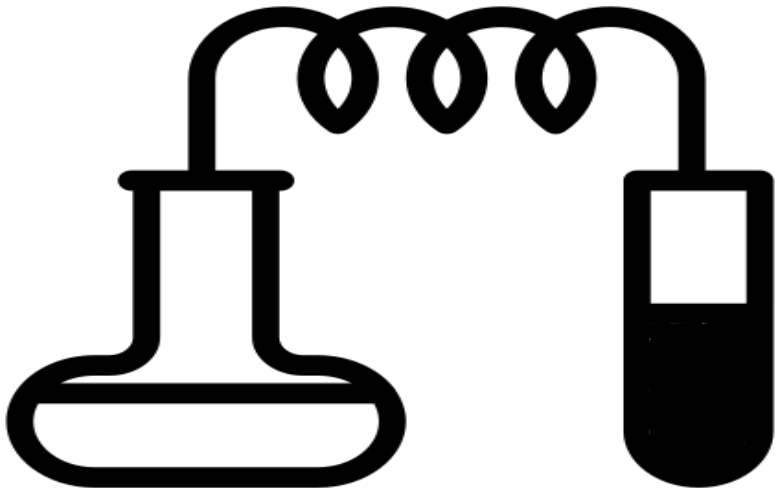


The System:

- Heterogenous (Multi-components)
- Non-linear interactions
- Dynamical
- Open
- Non-equilibrium

- Limited information
- Uncertainties

Understanding Design Principles



Mechanistic details of a phenomena

Generalized rules & design principles

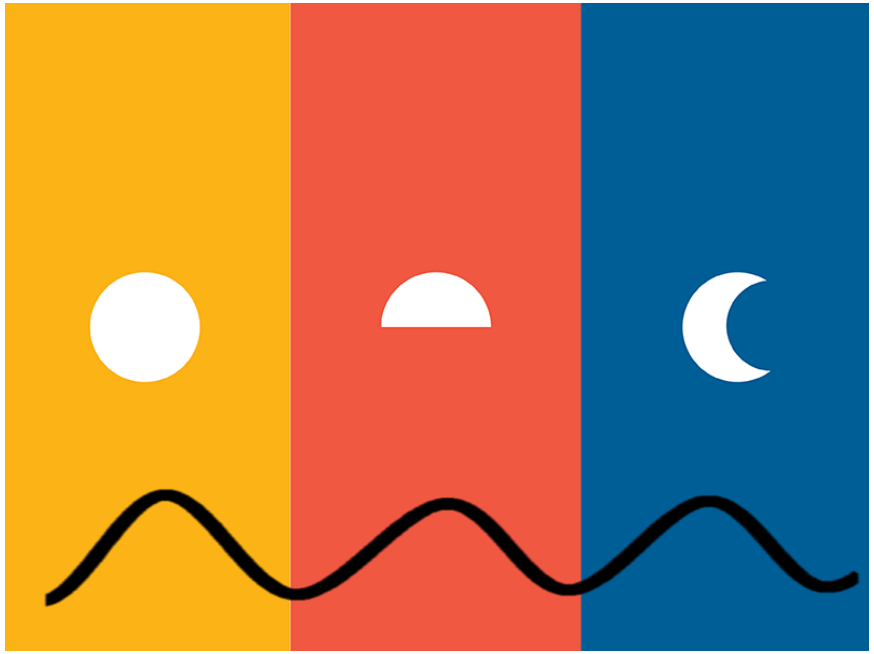
$f(x)$

A Toy Model

{ What is possible. / What is not possible. }

Similarity among apparently different complex phenomenon

Biological Clocks

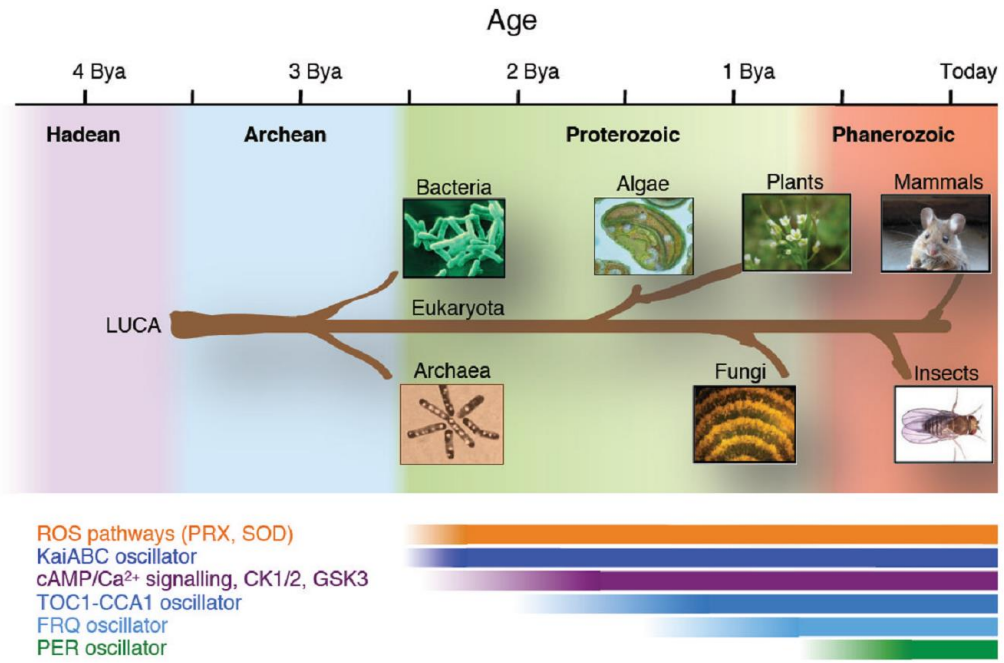


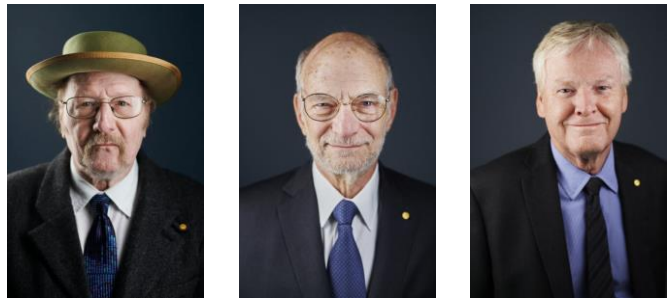
Circadian clock: Primary clock in our body

It is synchronized with environmental light

Similar clocks are present in other organisms, including plants and microbes.

How Will You Study The Clock?





Jeffrey C. Hall M. Rosbash M. W. Young

- Mutant Analysis
- Identifying homologous molecules
- Over-expression/under-expression systems
- Biochemical studies
- Structural analysis

Fig ref: Green et. al., Nature 2012/ Nobel Prize Web Page

What Makes A Clock?

Fig ref: Pinterest

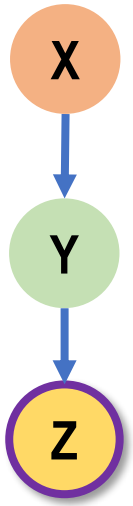
What Makes A Clock?

- **Has a robust periodic oscillator**
- Ability to synchronisation with another clock
- Suitable read-out

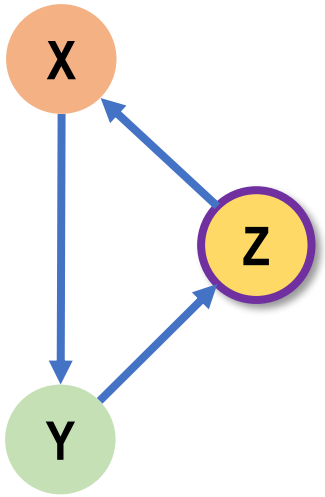
All biological clocks must have these three properties

Fig ref: Pinterest

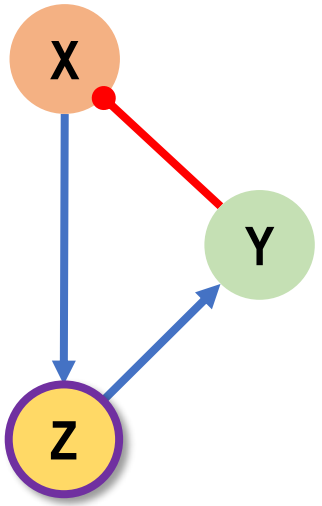
Which Molecular Circuit Generates Oscillation?



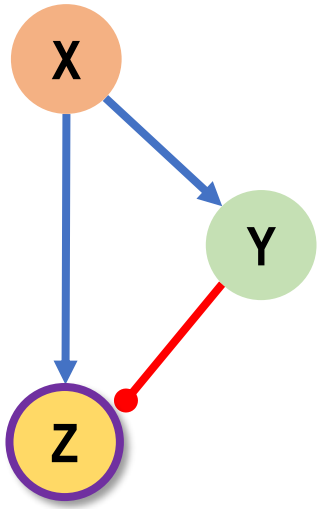
Linear Cascade



Positive Feedback

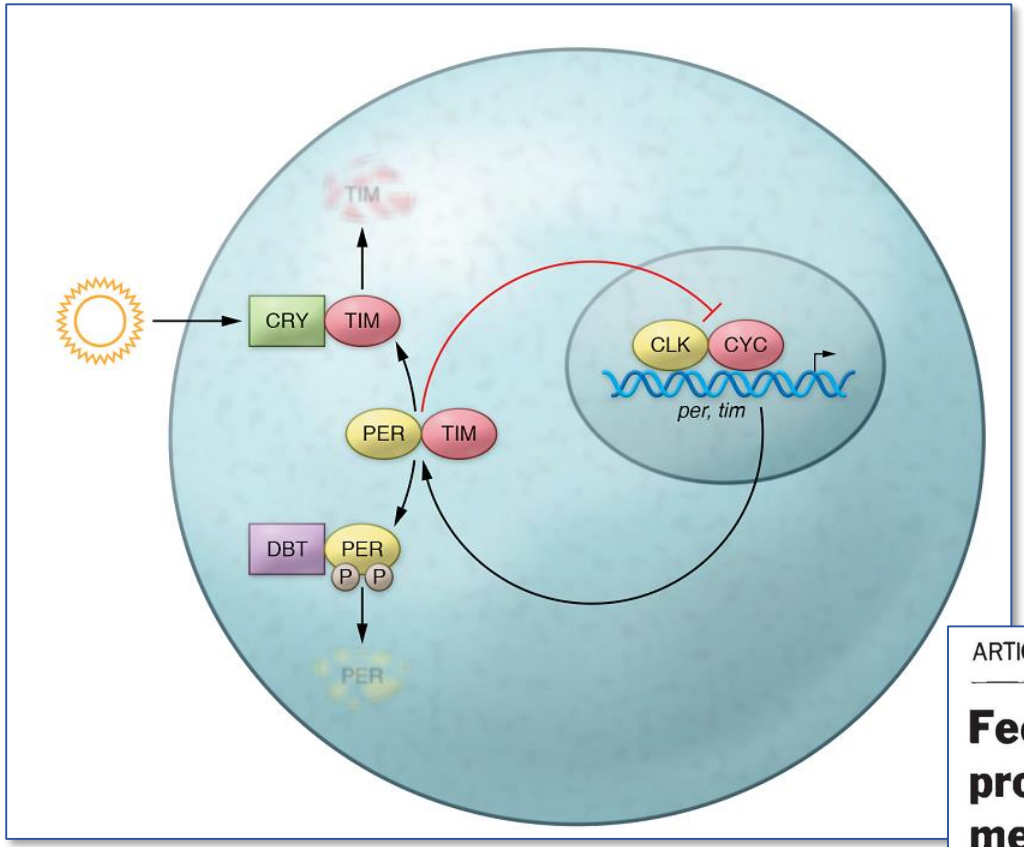


Negative Feedback



Incoherent Feedforward

Negative Feedback in Circadian Clock



ARTICLES

Feedback of the *Drosophila period* gene product on circadian cycling of its messenger RNA levels

Paul E. Hardin*†, Jeffrey C. Hall† & Michael Rosbash*†

* Howard Hughes Medical Institute and † Department of Biology, Brandeis University, Waltham, Massachusetts 02254, USA

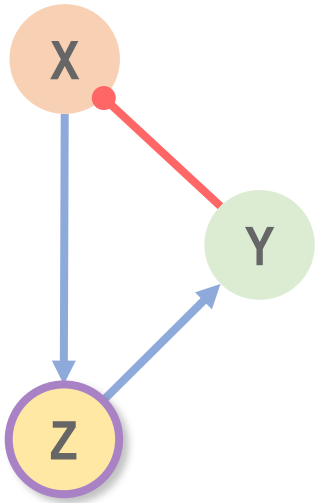
Fig ref: Sehgal, JCI, 2018 / Nature 1990

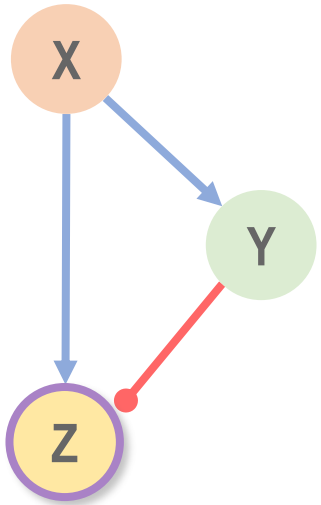
Oscillation with Negative Feedback

Goodwin Model (1965)

$$\frac{dx}{dt} = \frac{a}{k_m + k_i y} - \delta_x$$

$$\frac{dy}{dt} = k_y x - \delta_y$$





Linear Cascade

Positive Feedback

Negative Feedback

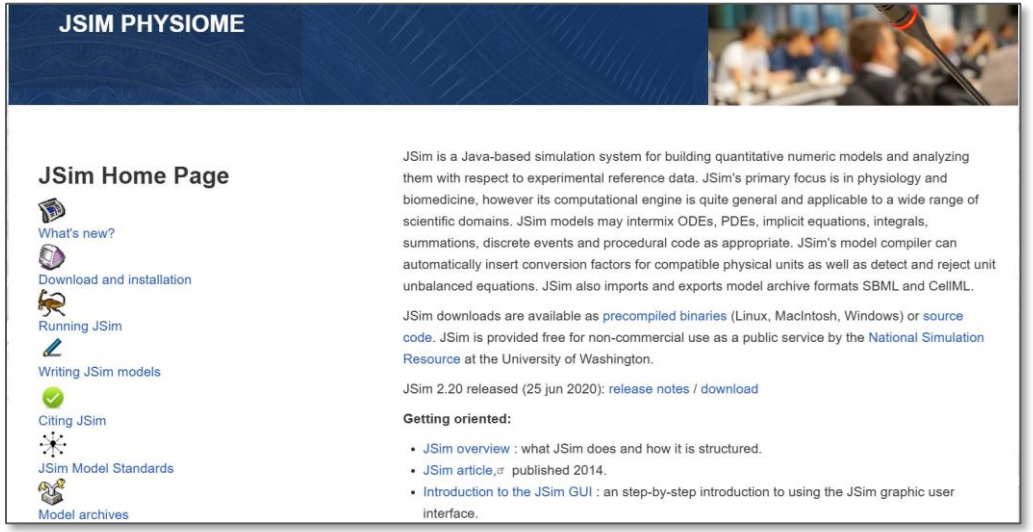
Incoherent Feedforward

Numerical Simulation of the Model

Algorithms: Euler, Runge–Kutta etc

Write your own program: C, Python, **Julia**, MATLAB

Simulation software: Copasi, DBSolveOptimum,
KINSOLVER, GEPASI, JigCell, **JSim**



https://www.imagwiki.nibib.nih.gov/physiome/jsim

Oscillation with Negative Feedback

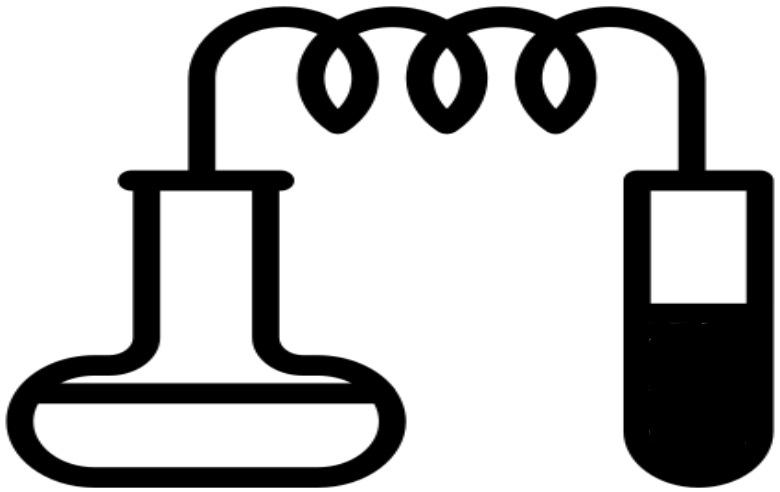
Modified Goodwin Model:

$$\frac{dx}{dt} = \frac{a}{k_m + k_i z^n} - \delta_x x$$

$$\frac{dy}{dt} = k_y x - \delta_y y$$

$$\frac{dz}{dt} = k_z y - \delta_z z$$

Understanding Design Principles



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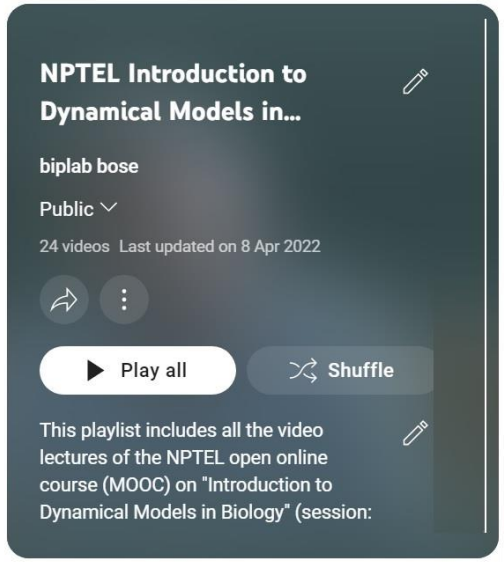
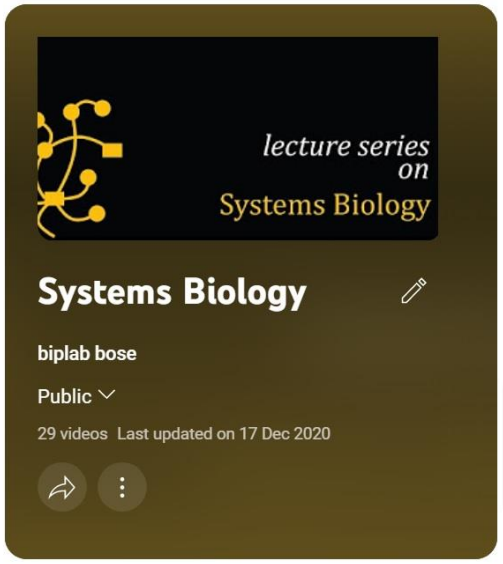
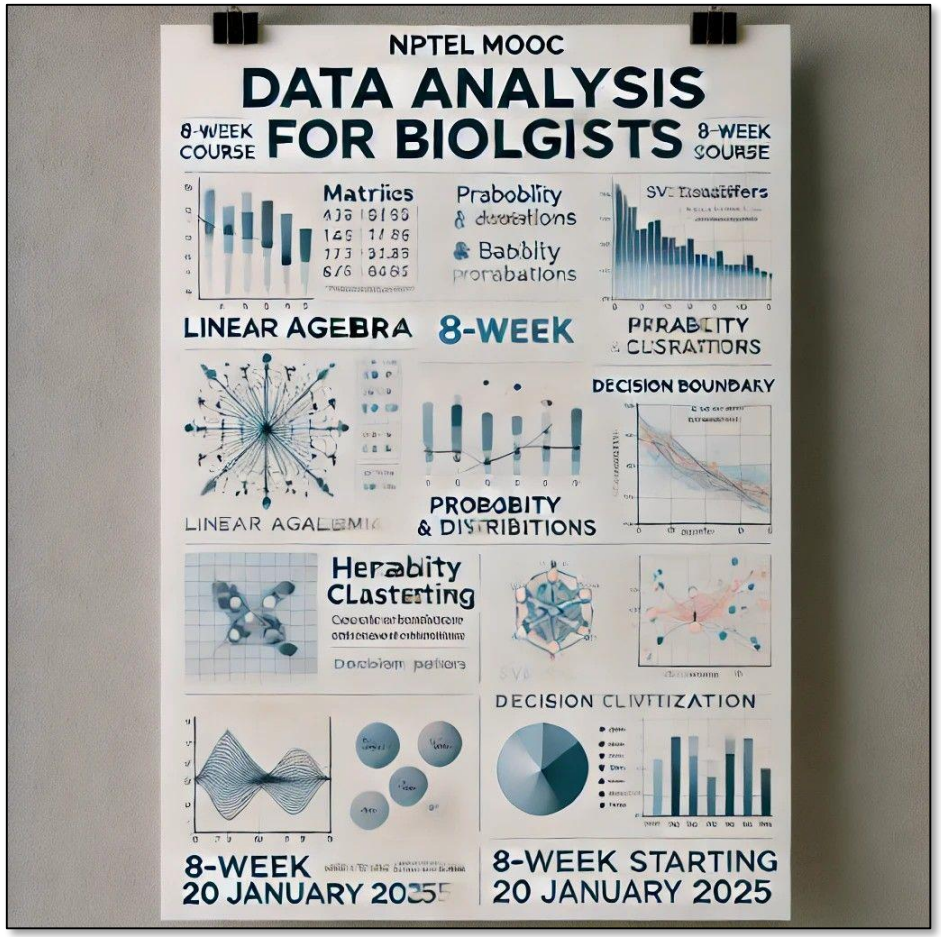




https://www.youtube.com/@sysbio

https://github.com/biplabbose/Systems_Biology_Textbook



NPTEL Course
Data Analysis For Biologists

8 weeks
20th January 2025

https://www.youtube.com/@sysbio

www.linkedin.com/in/biplab-bose-0807267