

CALCULATING CANCER CAUSES (CLEVERLY)

THE ROLE OF HPC IN SYSTEMS BIOLOGY

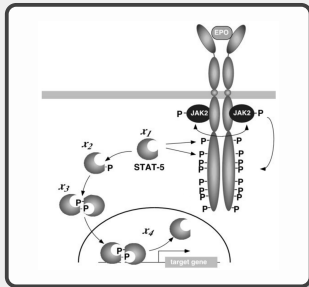
SEVERIN BANG

INSTITUTE OF PHYSICS, UNIVERSITY OF FREIBURG

NOVEMBER 28, 2022

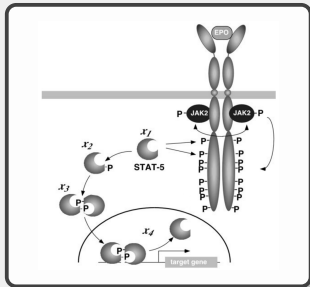
SYSTEMS BIOLOGY?

1. Cartoon:



SYSTEMS BIOLOGY?

1. Cartoon:



2. Equations:

$$\dot{x}_1 = -k_1 x_1 \text{EpoR}_A$$

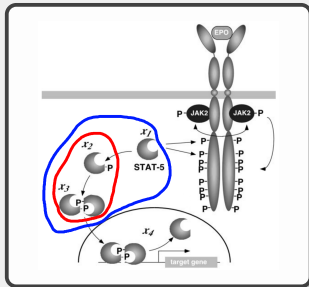
$$\dot{x}_2 = +k_1 x_1 \text{EpoR}_A - k_2 x_2^2$$

$$\dot{x}_3 = \frac{1}{2} k_2 x_2^2 - k_3 x_3$$

$$\dot{x}_4 = +k_3 x_3$$

SYSTEMS BIOLOGY?

1. Cartoon:



2. Equations:

$$\dot{x}_1 = -k_1 x_1 \text{EpoR}_A$$

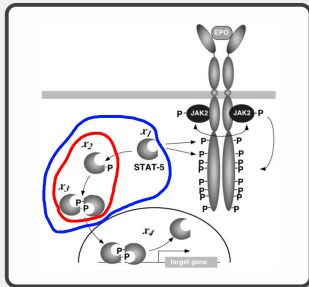
$$\dot{x}_2 = +k_1 x_1 \text{EpoR}_A - k_2 x_2^2$$

$$\dot{x}_3 = \frac{1}{2} k_2 x_2^2 - k_3 x_3$$

$$\dot{x}_4 = +k_3 x_3$$

SYSTEMS BIOLOGY?

1. Cartoon:



2. Equations:

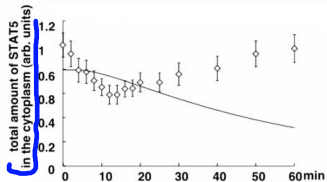
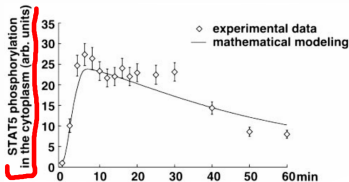
$$\dot{x}_1 = -k_1 x_1 \text{EpoR}_A$$

$$\dot{x}_2 = +k_1 x_1 \text{EpoR}_A - k_2 x_2^2$$

$$\dot{x}_3 = \frac{1}{2} k_2 x_2^2 - k_3 x_3$$

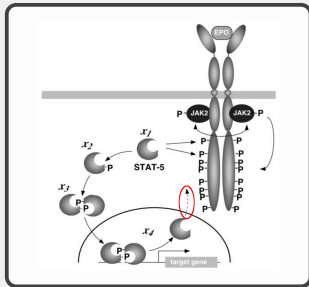
$$\dot{x}_4 = +k_3 x_3$$

3. Fits



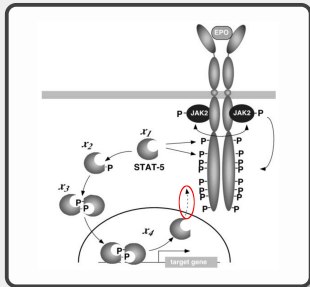
NOW LET ME TRY ONE THING...

1. Cartoon:



NOW LET ME TRY ONE THING...

1. Cartoon:



2. Equations:

$$\dot{x}_1 = +2k_4 x_3^T - k_1 x_1 \text{EpoR}_A$$

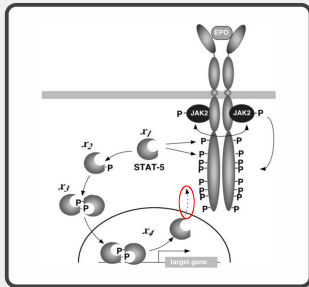
$$\dot{x}_2 = +k_1 x_1 \text{EpoR}_A - k_2 x_2^2$$

$$\dot{x}_3 = \frac{1}{2} k_2 x_2^2 - k_3 x_3$$

$$\dot{x}_4 = +k_3 x_3 - 2k_4 x_3^T$$

NOW LET ME TRY ONE THING...

1. Cartoon:



2. Equations:

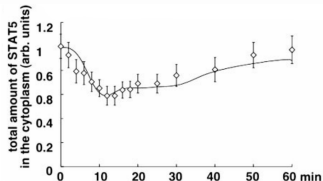
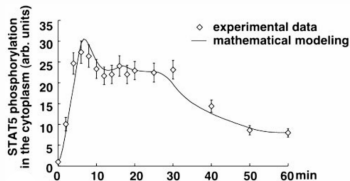
$$\dot{x}_1 = +2k_4x_3^T - k_1x_1EpoR_A$$

$$\dot{x}_2 = +k_1x_1EpoR_A - k_2x_2^2$$

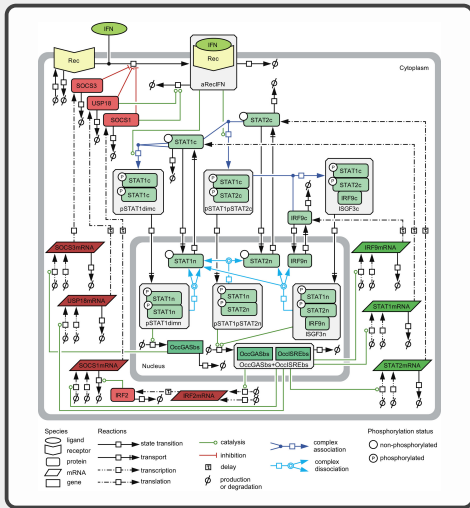
$$\dot{x}_3 = \frac{1}{2}k_2x_2^2 - k_3x_3$$

$$\dot{x}_4 = +k_3x_3 - 2k_4x_3^T$$

3. Fits



LARGER SYSTEMS

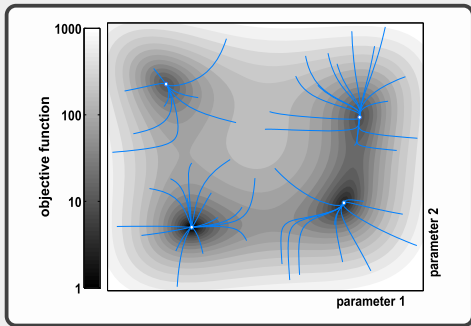


- Understand system to understand cancer causes
- 75 Equations
- 1918 Data points
- Need a lot of computational power to fit

WHY WOULD I WANT THAT?

- Mechanistic model: each parameter has biological meaning
- Investigate biologically not accessible parts
- Infer information about system from mathematical structure
- Identify key players in cancer development
- Screen for possible drug intervention points
- Use parametrized model to predict response and behavior (e.g. dosing strategy)

CALCULATION



Typical setup:

- ~30 nodes @ 64 cores
- 50 fits per node
- Runtime 15min – 30h

- Optimize likelihood
- Multi start fit:
 - ▶ Start with random parameters
 - ▶ Optimize until (local) optimum is reached
- Optimization is computationally hard
- Easily parallelizable
- ⇒ Perfect application for HPC cluster

CONCLUSION

- Dynamical modeling allows new insights in biological questions
- Today: new approaches exponentially increase available data
- More and more computational power is needed to tackle increased complexity

Thanks to:

- Prof. Jens Timmer & JetiLab
- C-TIP-HCC project of the LiSyM-cancer program of the BMBF
- Of course: bwForCluster Helix through bwHPC and DFG through grant INST 35/1597-1 FUGG
- The organizers
- You :)