



Towards a more open, collaborative, and integrated systems biology.

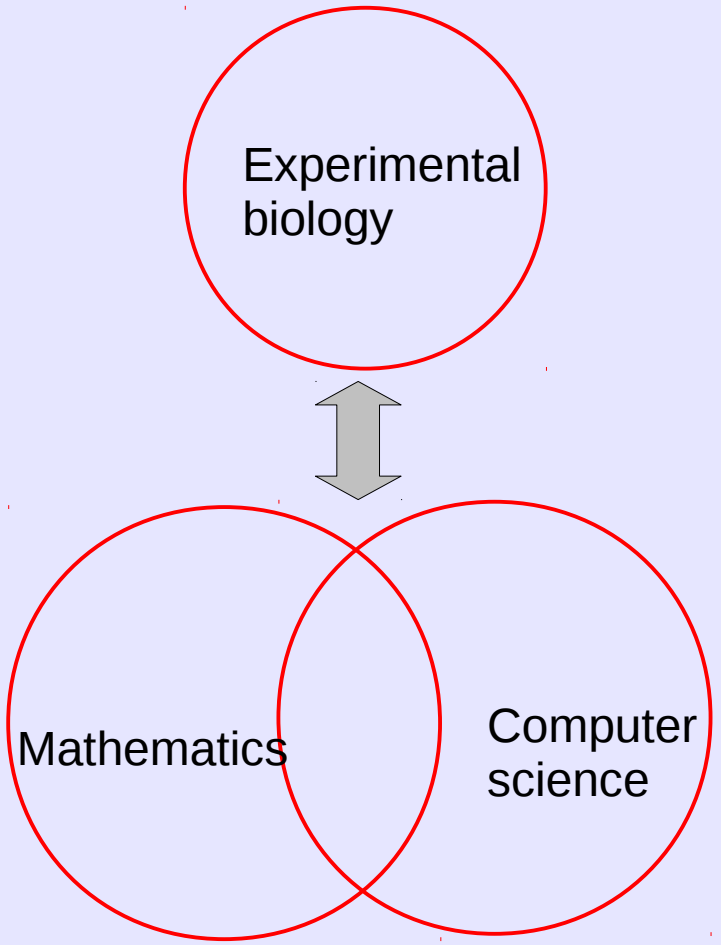
by

Tomáš Helikar, Ph.D.

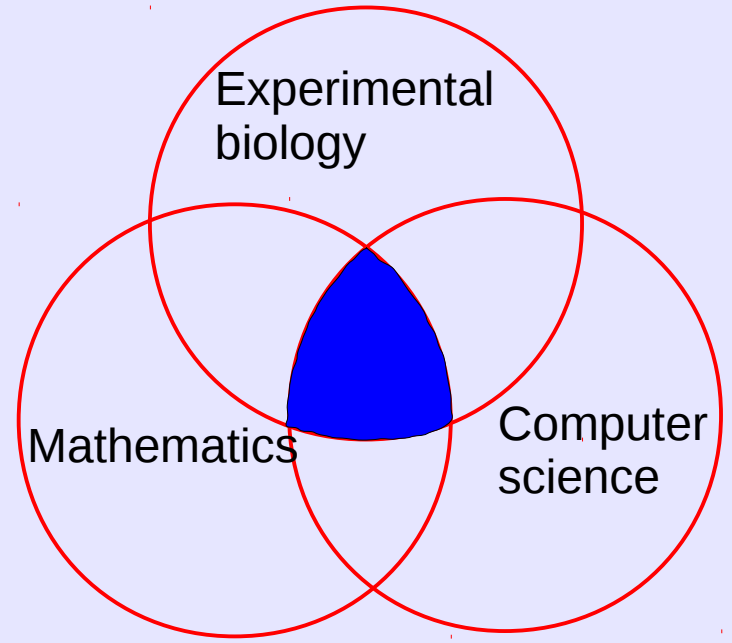
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March 28, 2012

Current state of Systems Biology



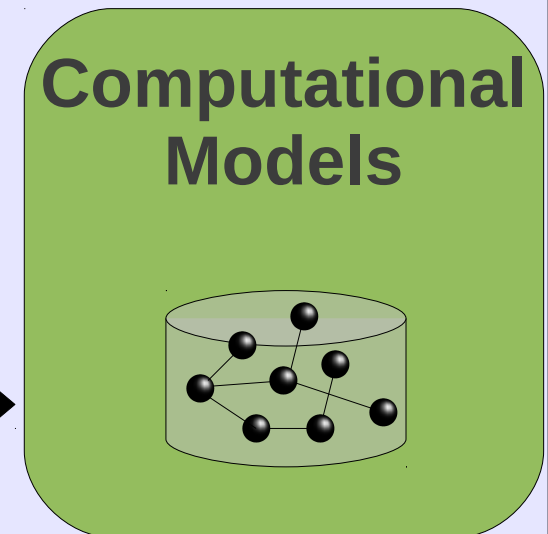
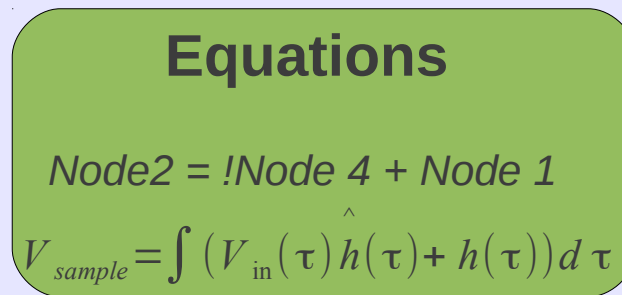
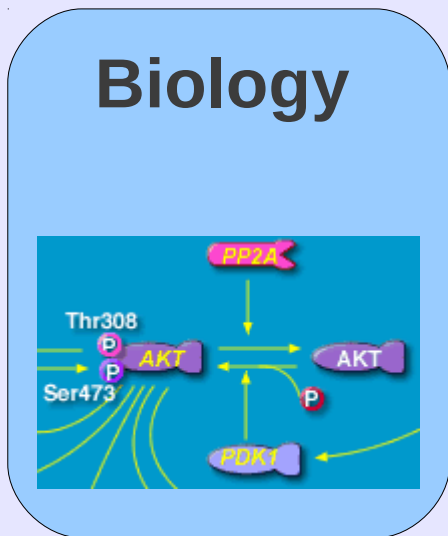
The "Ideal" Systems Biology





Current issues facing Systems Biology:

1. Modeling will not be embraced by biologists if it requires them to be computer scientists or mathematicians.



Negative Regulation Modules

Akt
When Rac is ON
(Rac activity condition)

RalBP1
When Rac is ON
(Rac activity condition)

P190RhoGAP
When Rac is ON
(Rac activity condition)

RhoGDI
Unless PAK is ON
(PAK activity condition)

Rac

RasGRF
When ECM AND Integrins are ON
(Cell attachment condition)

Tiam
When ECM AND Integrins are ON
(Cell attachment condition)

DOCK180
When ECM AND Integrins are ON
(Cell attachment condition)

Pix/Cool

- 1) When Gbg AND PAK are ON, then
 - a) Cdc42 AND Rac must be OFF, and
 - b) ECM AND Integrins must be ON (Cell attachment condition)
- 2) When Gbg is OFF, then
 - a) Cdc42 must be ON, and
 - b) ECM AND Integrins must be ON (Cell attachment condition) and
 - c) Rac must be OFF
- 3) When PAK is OFF, then
 - a) RhoGDI must be OFF, and
 - b) all other positive regulators must be OFF, and
 - c) ECM AND Integrins must be ON (Cell attachment), and
 - d) Cdc42 must be ON, and
 - e) Rac must be OFF

Positive Regulation Modules

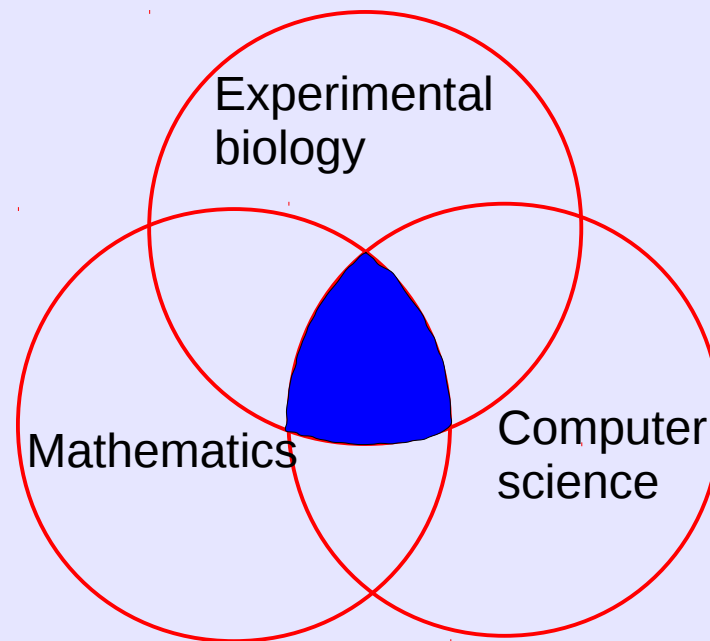


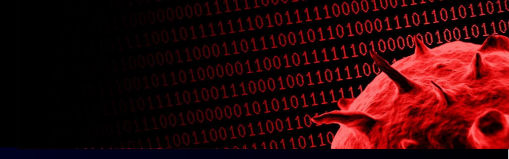
$$\begin{aligned}
 & (RasGRF \wedge \neg(RhoGDI \wedge \neg PAK) \wedge \neg(p190RhoGAP \wedge Rac) \wedge \neg(RalBP1 \wedge Rac) \\
 & \wedge ECM \wedge Integrins) \vee (Tiam \wedge \neg(RhoGDI \wedge \neg PAK) \wedge \neg(p190RhoGAP \wedge Rac) \\
 & \wedge \neg(RalBP1 \wedge Rac) \wedge (ECM \wedge Integrins)) \vee (Pix_{Cool} \wedge \neg(RhoGDI \wedge \neg PAK) \\
 & \wedge ((PAK \wedge G\beta\gamma \wedge ((\neg Cdc42 \wedge \neg Rac) \wedge (Integrins \wedge ECM)))) \vee (\neg G\beta\gamma \wedge (Cdc42 \\
 & \wedge (Integrins \wedge ECM) \wedge \neg Rac)) \vee (\neg PAK \wedge (\neg RhoGDI \wedge (\neg DOCK180 \wedge \neg(RhoGDI \wedge \neg PAK) \\
 & \wedge \neg(p190RhoGAP \wedge Rac) \wedge \neg(RalBP1 \wedge Rac) \wedge \neg RasGRF \wedge \neg(RhoGDI \wedge \neg PAK) \\
 & \wedge \neg(p190RhoGAP \wedge Rac) \wedge \neg(RalBP1 \wedge Rac) \wedge \neg Tiam \wedge \neg(RhoGDI \wedge \neg PAK) \\
 & \wedge \neg(p190RhoGAP \wedge Rac) \wedge \neg(RalBP1 \wedge Rac)) \wedge (Integrins \wedge ECM) \wedge Cdc42 \wedge \neg Rac)))) \\
 & \vee (DOCK180 \wedge \neg(RhoGDI \wedge \neg PAK) \wedge \neg(p190RhoGAP \wedge Rac) \wedge \neg(RalBP1 \wedge Rac) \\
 & \wedge (ECM \wedge Integrins))
 \end{aligned} \tag{1}$$



Current issues facing Systems Biology:

2. Current largest models are only a small fraction of the real cell. **No one group can build a model of the entire cell!**

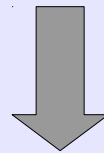




Current issues facing Systems Biology:

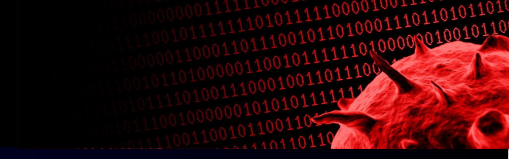
Possible Solution?

User Intuitive (“biologist-friendly”) collaborative software platform.

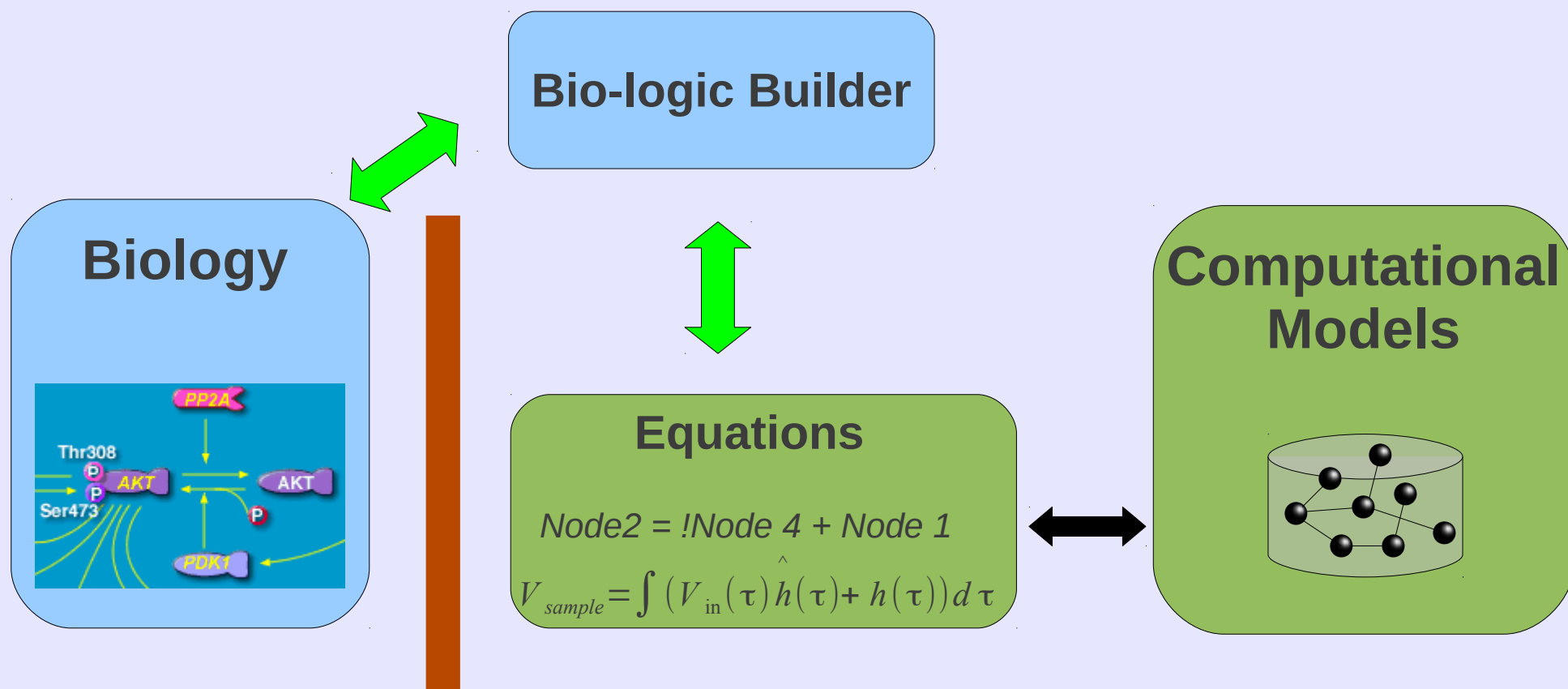


The Cell Collective

(<http://www.thecellcollective.org>)



User Intuitive (“biologist friendly”) collaborative software platform



User Intuitive (“biologist friendly”) collaborative software platform.

?Complete? Virtual Cell

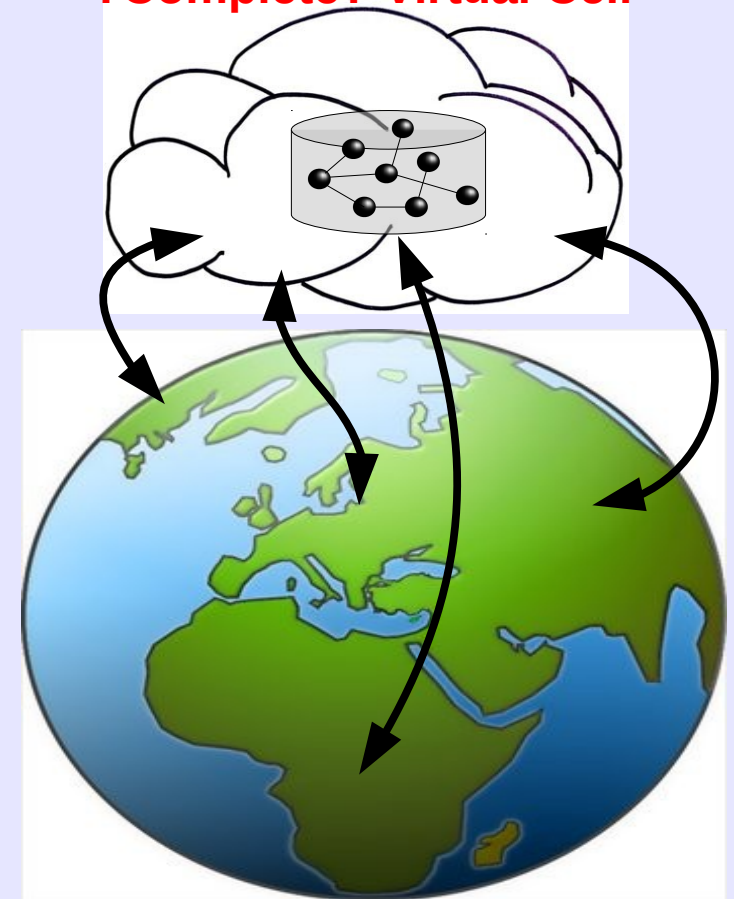
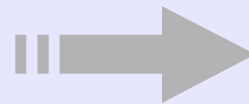
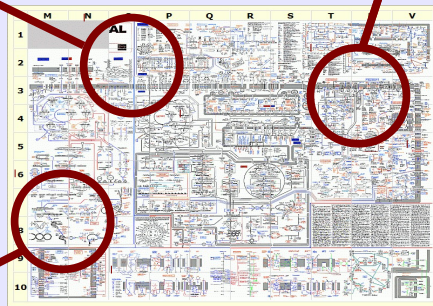
Cell Death
Regulation



Cell Motility



Cell Growth
Regulation





The Cell Collective

- Bio-logic Builder
- Model Management
- Knowledge base of protein dynamics
- (Real-time) Simulations & Analyses

The Cell Collective

• Simulations and Analyses

- Real-time simulations
- Sliders to allow users to modify dosages of extracellular signals (e.g., growth hormones) during a simulation.
- View the signal tracing of any node in the simulated model.

