

Negative feedback based simulations of bio-systems

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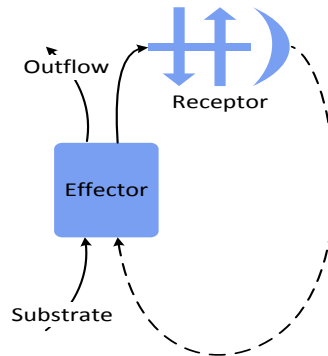
<http://nfs-qba.rhcloud.com/nfs/>

Motivation

- Bio-systems are very complex (even the smallest – **20k** protein-coding genes in a human cell)
- Simulation of bio-system is a must in order to develop e.g. new treatments
- Needs to take into account whole system (**holistic** approach)
- Current simulation approaches (approximate, precise) are not sufficient – either way too complex or losing necessary details
 - Most sophisticated example – Stanford bacteria cell, **40x simpler** than a human cell

Novel approach

- Bio-systems are open and therefore need to self-regulate
- Simplest self-regulator – **negative feedback (NF) loop**
- Idea from the „Systems biology” - model each *functional* component as a NF loop → construct a **functional proteome** of bio system



NF component

Effector

- delivers a product, output speed regulated by the Receptor

Receptor

- delivers signal turning off/on the Effector
- Signal is regulated by product concentration (*threshold*)

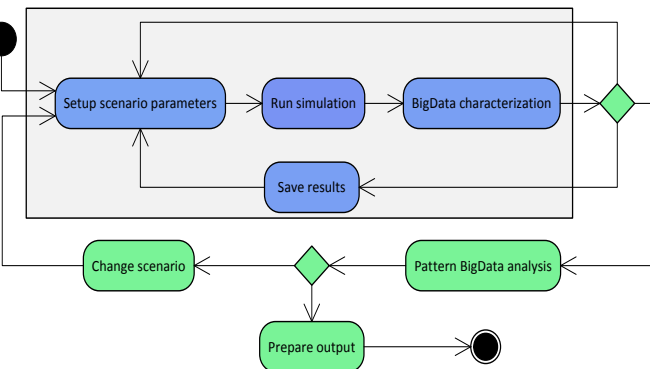
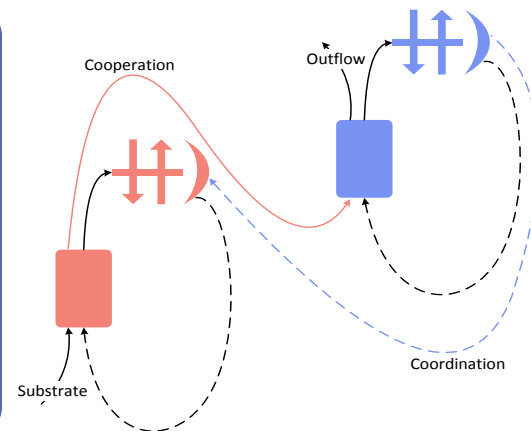
System structure

Cooperation – via Effector

- Other components can change Effector's parameters
- Receptor is not aware of the change – in fact, it's a **local** reaction on too high concentration of Effector's substrate
- Example – enzymatic cascade, where one enzyme delivers substrate to another one

Coordination – via Receptor

- Other components can order Receptor to change regulation threshold
- Such interaction is **global**, influencing whole NF component
- Example – hormonal control of cells



Observations

- Simulated cascades and cycles of NF components display complex regulation behaviour
- Cooperation/coordination relations work as expected

Future work

- Simulate well-known bio systems (e.g. glycolysis enzymatic cascade) to verify the system
- Search for *emergent properties* of more complex systems
- Build workflow utilizing NF simulation core to automate and speed-up search

1. Leszek Konieczny, Irena Roterman-Konieczna, Paweł Spólnik, Systems Biology: Functional Strategies of Living Organisms, Springer Dordrecht, New York, London 2013

2. Karr, Jonathan R. et al., A Whole-Cell Computational Model Predicts Phenotype from Genotype, Cell, Volume 150, Issue 2

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