Programming biological systems

by reverse-engineering reaction-diffusion

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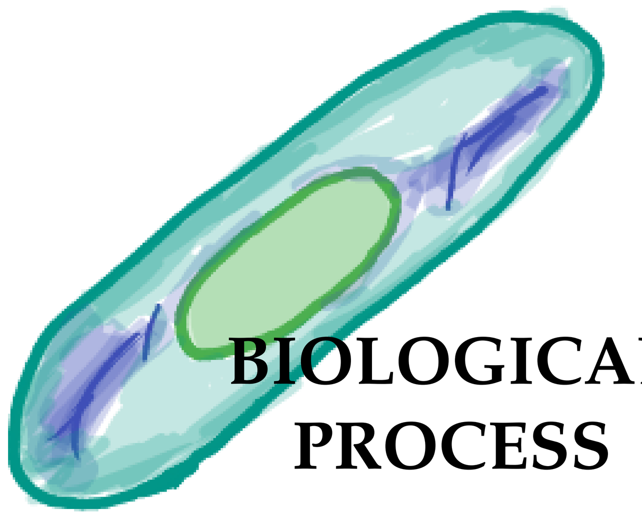
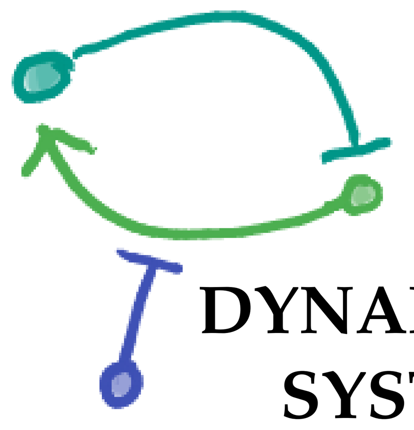


BIOLOGICAL PROCESS

systems biology

synthetic biology



DYNAMICAL SYSTEM

natural computation

```
for i in set :
    do this ;
    if this then...
```

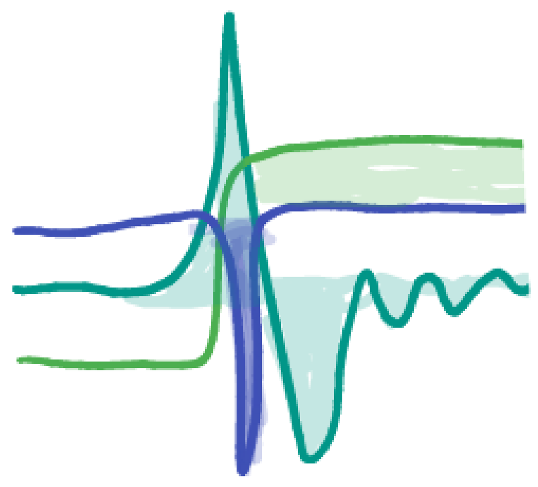
ALGORITHM

Motivation | Designing algorithms to be executed in living organisms

Is it possible to build a programming language that compiles into a chemical environment, allowing us to execute arbirary code in living cells? To produce appropriate adaptive responses given sensory input from enviroments, **living organisms perform asynchronous computations** using chemicals reaction networks [1].

```
for cell in lymph node :
    if type(cell) == "T" :
        cell.dna.append(sequence);
        cell.express(receptor)
    if "cancerSequence" in cell.dna :
        cell.init(apoptosis)
```

compile response function



infer reaction network

$$\partial_t \bar{\mathrm{p}}(t) = \overbrace{\bar{\mathrm{R}}(\bar{\mathrm{p}}|\theta)}^{\text{reaction network}} + \underbrace{\bar{\mathrm{S}}(t)}_{\text{sensory input}}$$

Algorithm → Dynamical System | Given a *response function* what is the *minimal* reaction network?

- 👍 Silicon devices executed code on arithmetic logic units, which are described by signal-response functions
- 👎 Networks of logical units are **controlled by clocks** limiting algorithms to **synchronous sequential logic**
- 👍 Chemical reaction networks can be inferred from cellular processes data [2]
- 👎 No general mapping exists that takes model complexity into consideration

What is the general routine for *reducing complexity* in reaction networks?

- 👍 For *known time-scale separations* one can reduce models, introducing memory effects [3]
- 👎 There exist *no relevance determination* methods beyond empirical sensitivity analysis [4]

How does evolution lead to *complexity increase* in network motifs such as switches and clocks?

- 👍 Relationship between robustness and evolvability has been investigated [5]
- 👎 Evolutionary relationships between different chemical networks have not been quantified

Dynamical System | Given a *steady state pattern* what is the *minimal* reaction-diffusion network?

- 👍 Dynamics of local equilibria show promising analysis beyond linear stability [6]
- 👎 Need to design attractors in phase space; no description in phase space exists

$$\partial_t \rho(t) = \overbrace{R(\rho)}^{\text{reaction}} + \underbrace{D\,\partial_x^2 \rho(t)}_{\text{diffusion}}$$

$R(\rho)$ is a vector, multinomial in the components of ρ

References

[1] Neil Dalchau, Gregory Szép, et al. Computing with biological switches and clocks. *Natural Computing*, 6 2018.
[2] Nikhil Galagali. Bayesian inference of chemical reaction networks. 2016.
[3] George D.J. Phillies. Projection Operators and the Mori-Zwanzig Formalism. *Springer, New York, NY*, 2000.
[4] Luca Cardelli, Attila Csikász-Nagy, et al. Noise Reduction in Complex Biological Switches. *Scientific Reports*, 2016.
[5] Bryan C Daniels, Yan-Jiun Chen, et al. Sloppiness, robustness and evolvability in systems biology. *Current Opinion in Biotechnology*, 2008.
[6] J. Halatek and E. Frey. Rethinking pattern formation in reactiondiffusion systems. *Nature Physics*, 2 2018.