Programming biological systems

by reverse-engineering reaction-diffusion

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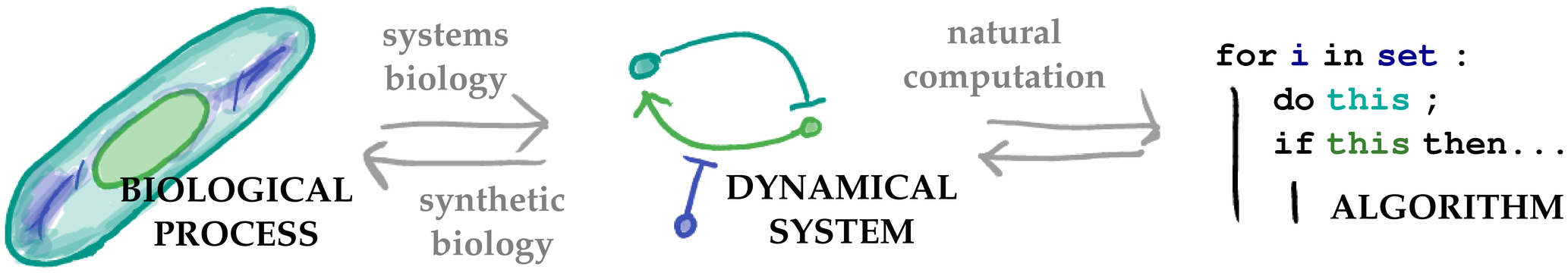
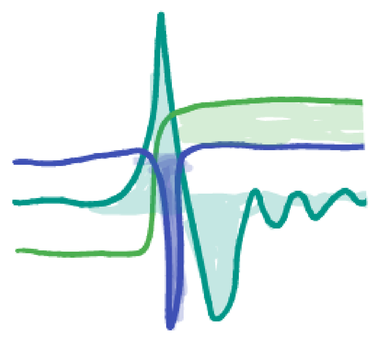


Motivation | **Designing algorithms to be executed in living organisms**

Is it possible to build a programming language that compiles into a chemical environment, allowing us to execute arbitrary code in living cells? To produce appropriate adaptive responses given sensory input from environments, **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 →

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

Leading Question | **Given a *response function* what is the *minimal* reaction network?**

- 👍 Asynchronous arithmetic logic units have been designed using chemical reaction networks [2]
- 👍 Chemical reaction networks can be inferred from processes data [3]
- 👎 No mapping between response function and network exists that minimises complexity

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

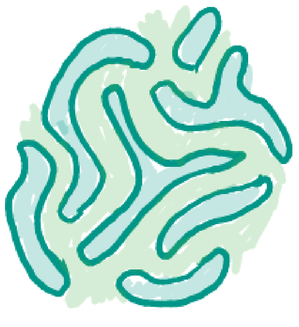
- 👍 For *known time-scale separations* one can reduce models, introducing memory effects [4]
- 👎 There exist no *unsupervised reduction* methods beyond empirical sensitivity analysis

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

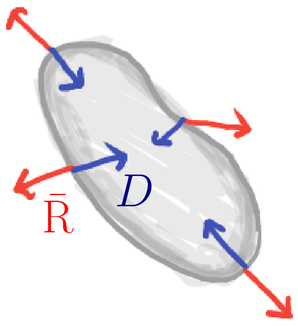
- 👍 Relationship between robustness and evolvability has been investigated [5]
- 👎 Evolutionary relationships between different chemical networks have not been quantified

Follow-up Question | **Given a *steady state pattern* what is the *minimal* reaction-diffusion network?**

- 👍 Dynamics of local equilibria show promising pattern formation analysis beyond linear stability [6]
- 👎 No geometric description of diffusive attractors in phase space exists; required for pattern design



geometrisation →



inference →

$$\partial_t \bar{\mathrm{p}}(\bar{\mathrm{x}}, t) = \overbrace{\bar{\mathrm{R}}(\bar{\mathrm{p}}|\theta)}^{\text{reaction network}} + D \underbrace{\partial^2_{\bar{\mathrm{x}}} \bar{\mathrm{p}}(\bar{\mathrm{x}}, t)}_{\text{diffusion}}$$

References

[1] Neil Dalchau, Gregory Szép, et al. Computing with biological switches and clocks. *Natural Computing*, 6 2018.

[2] Luca Cardelli, Marta Kwiatkowska, et al. Chemical reaction network designs for asynchronous logic circuits. *Natural computing*, 2018.

[3] Nikhil Galagali. Bayesian inference of chemical reaction networks. 2016.

[4] George D.J. Phillies. Projection Operators and the Mori-Zwanzig Formalism. *Springer, New York, NY*, 2000.

[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.

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