Fully Automated Attractor Analysis of Cyanobacteria Models

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Motivation: Cyanobacteria control

Control of cyanobacteria in a photo-bioreactor
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Model-based control ⇒ e-cyanobacterium.org
Problem: Attractor localisation with parameters

- Non-linear complex biological ODE models
- Parameter tuning controls attractors
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\[ p = 0.4 \quad \text{and} \quad p = 1.0 \]
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State of the art:

• Simulation, sampling, continuation
• Bifurcation theory and other analytical methods
• Depend on the type of the system
• Requires a skilled model analyst
• Computationally intensive, but hard to parallelise
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Method: Terminal strongly connected components

\[
\frac{dx_1}{dt} = f_1(x_1, \ldots, x_n) \\
\frac{dx_2}{dt} = f_2(x_1, \ldots, x_n) \\
\vdots \\
\frac{dx_n}{dt} = f_n(x_1, \ldots, x_n)
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3. Parallel parametrised divide and conquer algorithm for component detection
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2. Parameter uncertainty is captured by parametrised edges
3. Parallel parametrised divide and conquer algorithm for component detection
4. Each terminal component over-approximates an attractor
Clark et al. 2014
- Fluxes of inorganic carbon from cytosol to carboxysome
- Fixation using carbonic anhydrase and RuBisCO enzyme

Grimaud et al. 2014
- Time-dependent dynamics of nitrogen fixation
- Respecting the obligate nitrogen fixation and light limitation

Müller et al. (in devel.)
- Carbon fluxes in a laboratory scale photobioreactor
- Intercellular exchange, carbonate chemistry, and gas-to-liquid \( CO_2 \) transfer

Plyusnina et al. (in devel.)
- Electron transport on thylakoid membrane (photosynthesis)
Clark et al. 2014

- Fluxes and fixation of inorganic carbon
- Carbon dioxide concentrating mechanism (CCM)
- Model shows that CCM is not necessary for growth in media in equilibrium with concentration of 10% $CO_2$
- Activity of carbon-fixing enzyme $RuBisCO$
- Parameter *fast* affects rate of carbon fixation reaction

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1 Ryan L. Clark et al., Insights into the industrial growth of cyanobacteria from a model of the carbon-concentrating mechanism, AIChE Journal, 2014, https://doi.org/10.1002/aic.14310
Parameter $fast = 100$
Clark et al. – results

A single attractor across whole parameter range

$CO_2$ increases rapidly with fast, $HCO_3$ decreases for higher values
Other results

- Clark: Strong dependence on parameter \textit{fast}, 4 dimensions
- Grimaud: Independent on parameters $r_2$ and $r_4$, 4 dimensions
- Müller: Independent on parameter $kL_{A\text{-}CO_2\text{-}eff}$, 7 dimensions
- Plyusnina: 8 dimensions, strange non-trivial attractor
Software support: Pithya

http://pithya.ics.muni.cz/app/pithya
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Conclusions

- Dependence of attractors on parameters
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- Dependence of attractors on parameters
- Detection of terminal strongly connected components

Thank you for your attention!

Samuel Pastva
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• Fully automated and parallel
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