A Mathematical Framework for Building Oscillators in Reaction Networks

Joseph L. Hellerstein[a]

[a] *eScience Institute, University of Washington, Allen School of Computer Science, Seattle, WA, USA, 98195*

Abstract

Abstract

Keywords: Simulation, SBML, Software, Systems Biology

Introduction

1. Importance of oscillators in biology: circadian rhythms, filters, ... Indicate characteristics of importance: frequency, amplitude, phase. Controlling separately is tunable.
2. Models of biological oscillators. Number of species. Rate laws.
   (a) validation
   (b) requirements of oscillation (sufficiently non-linear)
   (c) insights into tunable
3. Requirements of theoretical oscillator: biological credibility
   (a) Non-negative concentrations
   (b) Credible kinetics
4. Summary of contribution
   (a) Oscillatory reaction network with linear rate laws. ODEs are a system of linear differential equations. Counter example to claim that the reaction network must be "sufficiently non-linear".
   (b) Closed form solution for the time domain behavior of the 2 species linear oscillatory network. Since linear network, initial conditions matter. There are no limit cycles.

Email address: `jlheller@uw.edu` (Joseph L. Hellerstein)

(c) The closed form solution provides a mathematical framework that provides insights into tuning non-linear oscillators. Changing amplitude while keeping frequency constant. Phase shifts.

Methods

1. Jacobian for 2 species, two reactions, mass action
2. Requirements for sustained oscillation: $T = 0$, $D > 0$
3. $T > 0$: self catalyzing
4. $D > 0$: inhibition through degradation. Requires care on operating region.
5. Solution to homogeneous system. Issue – need an offset. Calculating solution vectors using imaginary and real parts of eigenvectors.
6. Particular solution.
7. Full solution. Requires trig equality.

Results

1. Validation of the solution via simulations
2. What parts of the oscillator can be removed if unconcerned about certain elements of control like amplitude and phase?
3. Interpretations
   (a) Must have u_1, u_2 be non-zero in order to get an offset so that there are non-zero values for the two species.
   (b) Large frequency (α) approximation
   (c) Large δ approximation
4. Robustness

Conclusions

References