

Enzyme rhythms in model linear_chain4.speedy

Model name: linear_chain4

o Optimisation problem

- Protein turnover time $1 \text{ s} = 0.0167 \text{ min}$
- Perturbed parameter(s) : x1
- Perturbation frequency f : 0.0333/s (period 30 s)
- Scored quantity: v4
- Fitness-averaged fitness
- No posttranslational rhythms allowed
- Standard frequency considered f : 0.0333/s (period 30 s)

o Model properties:

- inactive_enzymes: 0
- balanced_reference_state: 1
- consider_external_rhythm: 1
- adaptive_rhythm: 1
- spontaneous_rhythm: 0
- spontaneous_rhythm_at_omega: 0
- has_spontaneous_rhythm_and_inactive_enzymes: 0

o No beneficial autonomous oscillation found

o Fitness changes after external perturbation at frequency $f=0.0333/s$

- Change by perturbation alone (xx): $-1.25e-09$
- Change by adaption synergies (xu): 0.00348
- Change by periodic enzyme (uu): -0.0012
- Change by enzyme mean shift (u): $7.04e-10$
- Total fitness change : 0.00228
- Fitness gain by adaption : 0.00228
- Maximum adaptive fitness found (in tested range) at frequency $f=0.0891/s$ (period 11.2 s)
- Predicted max. fitness change (adaptive, num. opt, full ampl. constraints) at frequency $f=0.0891$: 0.00282

o autonomous oscillations?

- No beneficial autonomous oscillations (2nd order, amplitude below 1/2 of mean) found at frequency $f = 0.0333/s$ (principal synergy = -0.0501): Predicted fitness change -0.000389

o Numerical calculation (responsive, $f=0.0333$)

- Fitness change (fitness-averaged): $-2.68e-09$
- Fitness change (state-averaged): $-1.43e-09$

o Numerical calculation (adaptive, $f=0.0333$)

- Fitness change (fitness-averaged): 0.00235
- Fitness change (state-averaged): 0.00297

o Numerical calculation (autonomous rhythm, amplitude below 1/2 of mean, $f=0.0333$)

- Fitness change (fitness-averaged) : $5.47e-06$
- Fitness change (state-averaged): $5.47e-06$

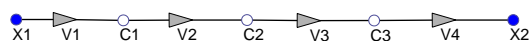


Figure 1: Network and reference flux

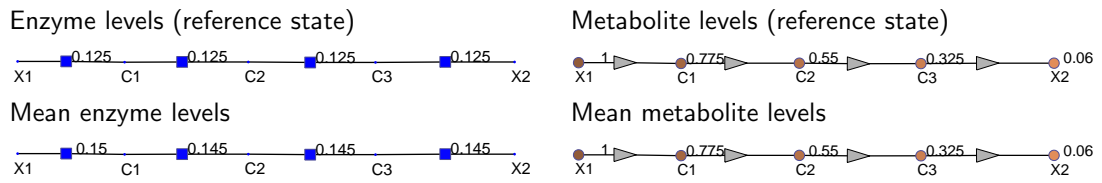


Figure 2: Reference state (top) and mean state during oscillation (bottom).

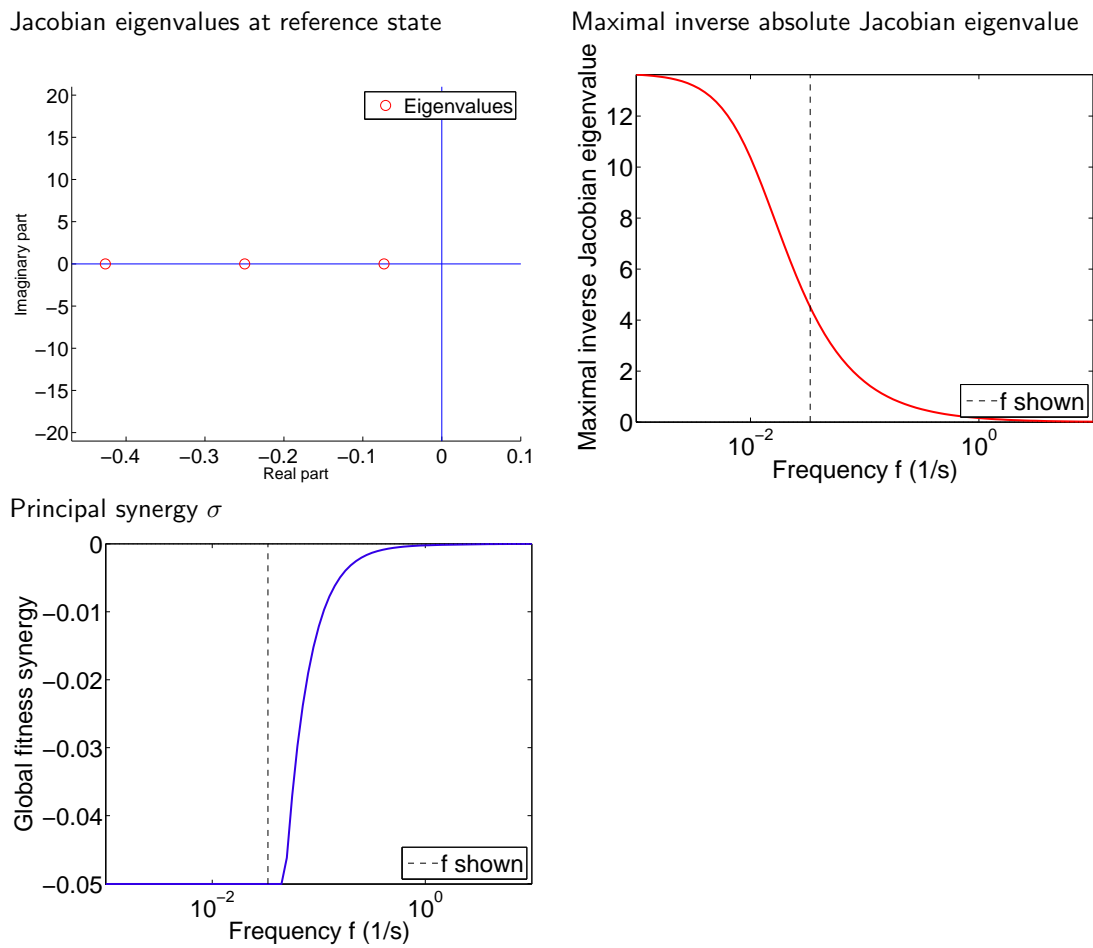
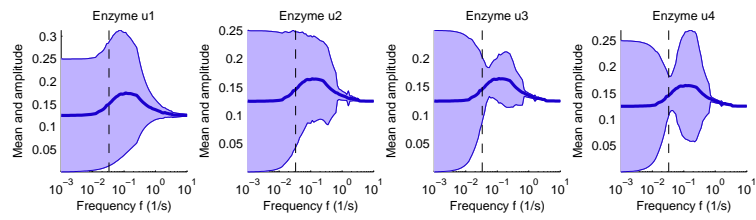
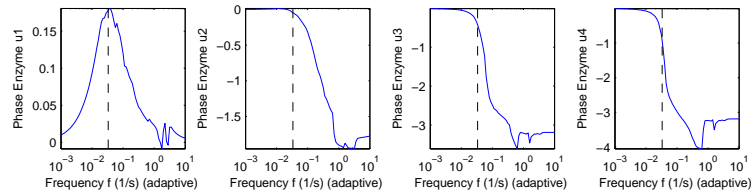


Figure 3: Control analysis. Left: Global fitness synergy (maximal fitness curvature eigenvalue), as a function of the frequency. Right: Relative amplitudes of individual enzymes for the least wasteful enzyme mode (components of the leading fitness curvature eigenvector).

Protein level and enzyme activity (mean and amplitude)



Phase angles $[0, 2\pi]$



Fitness change

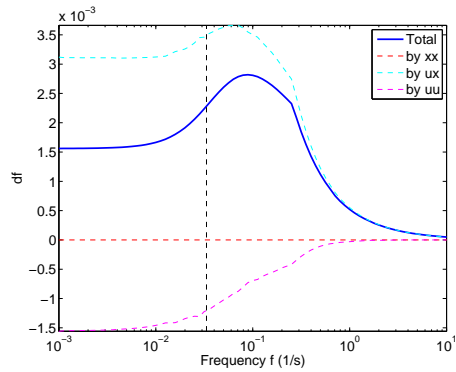


Figure 4: Adaptive oscillations. Left: amplitudes of protein levels (blue) and modification (grey). Right: phase shifts.

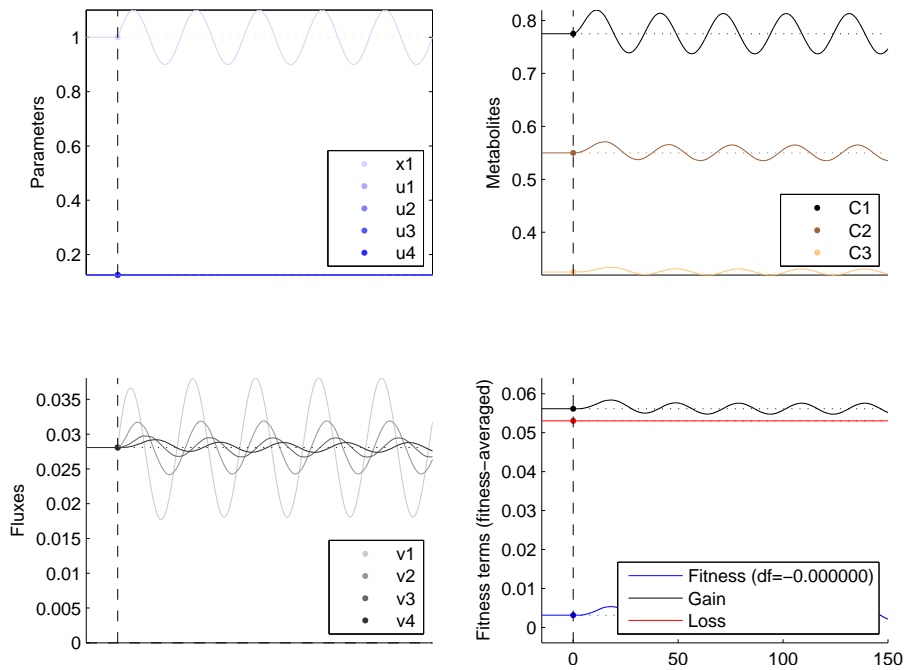


Figure 5: Numerical calculations: responsive oscillations (curves). Dynamic effects of oscillations. The panels show different types of variables: (i) Optimal periodic enzyme levels; (ii) internal metabolite levels; (iii) reaction fluxes; (iv) fitness, benefit, and cost. Perturbation frequency see first page.

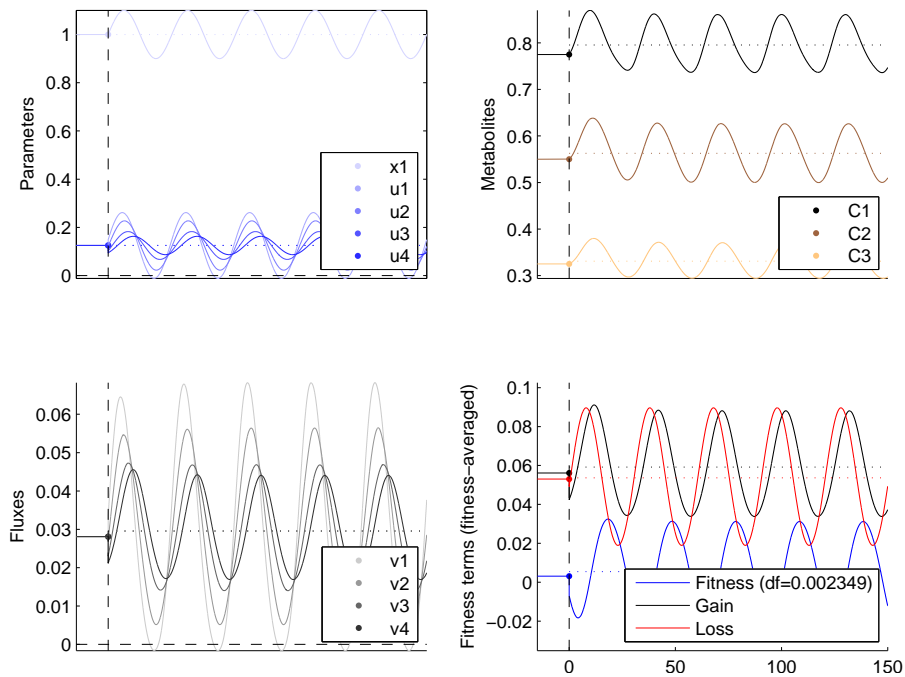
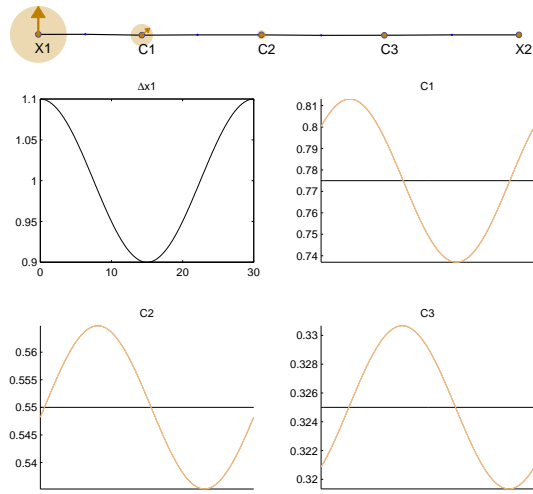


Figure 6: Numerical calculations: adaptive oscillations (curves). Dynamic effects of oscillations. The panels show different types of variables: (i) Optimal periodic enzyme levels; (ii) internal metabolite levels; (iii) reaction fluxes; (iv) fitness, benefit, and cost. Perturbation frequency see first page.

Responsive oscillations (concentrations)



Responsive oscillations (fluxes)

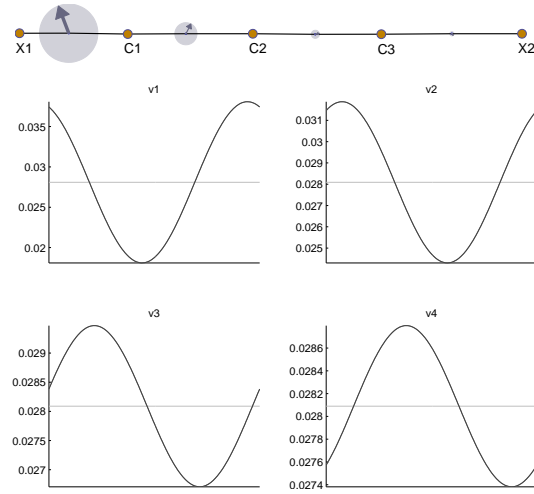
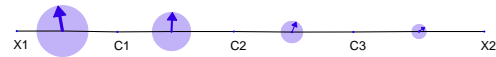
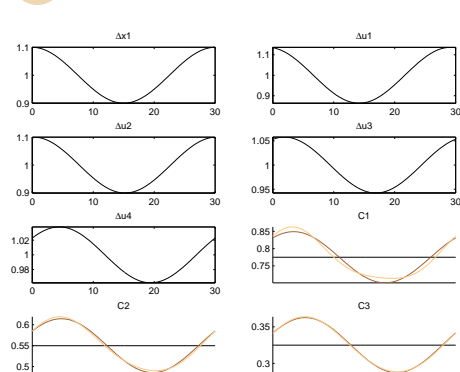
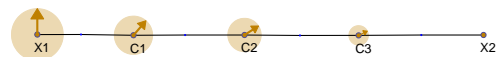


Figure 7: Responsive oscillations (local expansion; arrows: absolute changes) Perturbation frequency see first page.

Adaptive oscillations (enzymes)



Adaptive oscillations (metabolites)



Adaptive oscillations (fluxes)

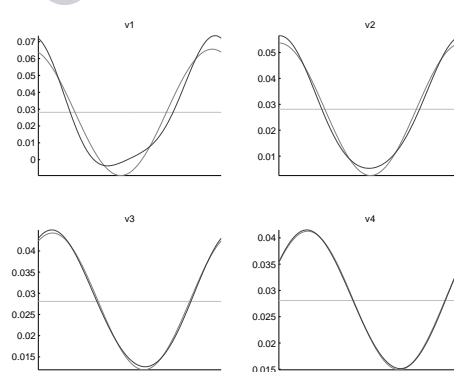
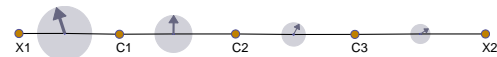


Figure 8: Adaption to forced oscillations (local expansion; arrows: absolute changes). Perturbation frequency see first page.

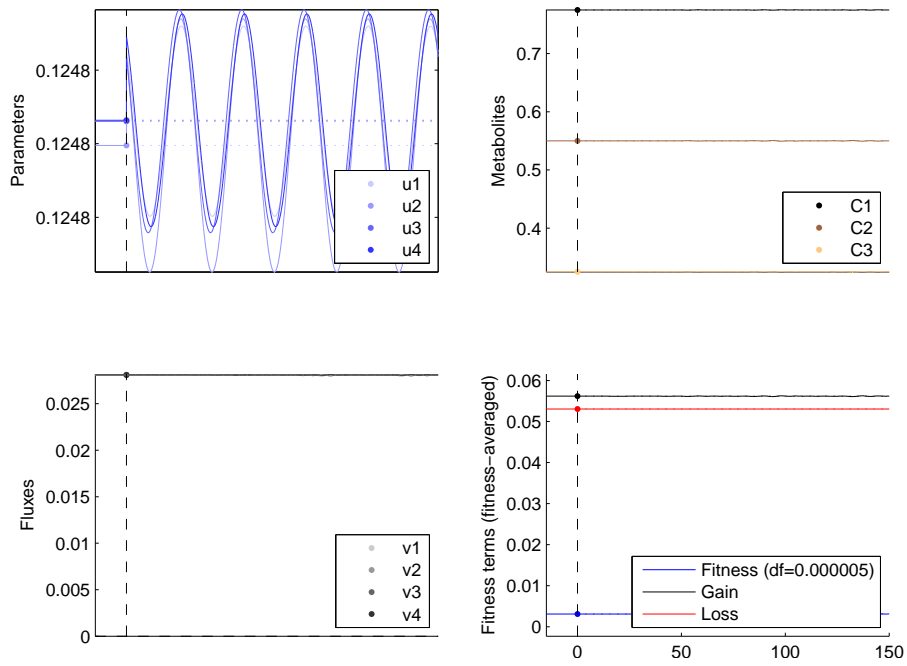


Figure 9: Tentative spontaneous oscillations. Perturbation frequency see first page.

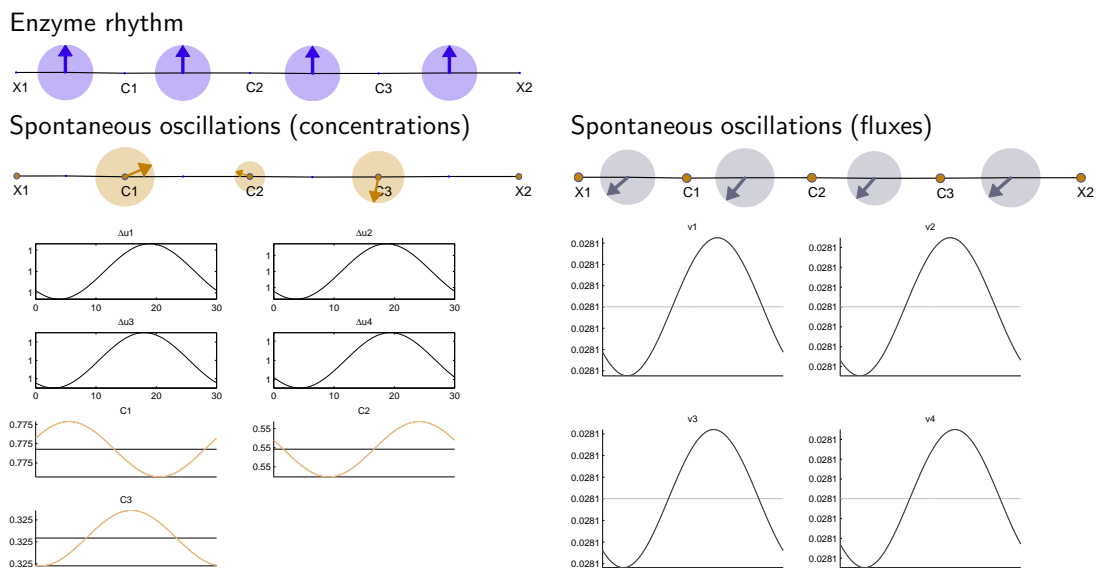
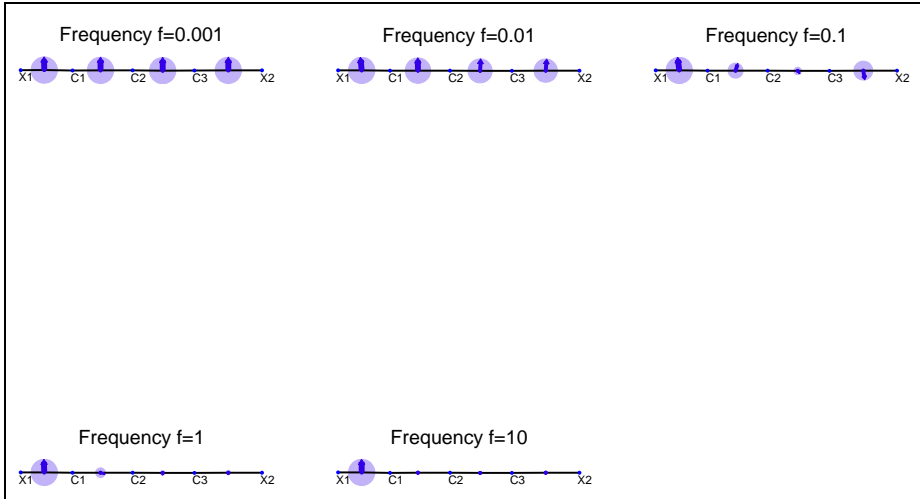


Figure 10: Tentative spontaneous oscillations (local expansion; arrows: absolute changes). Perturbation frequency see first page.

Adaptive



Least costly spontaneous

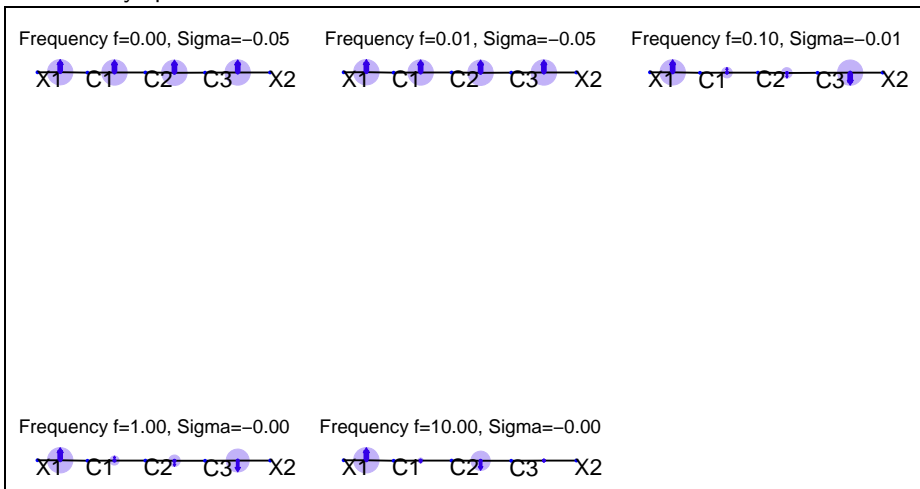
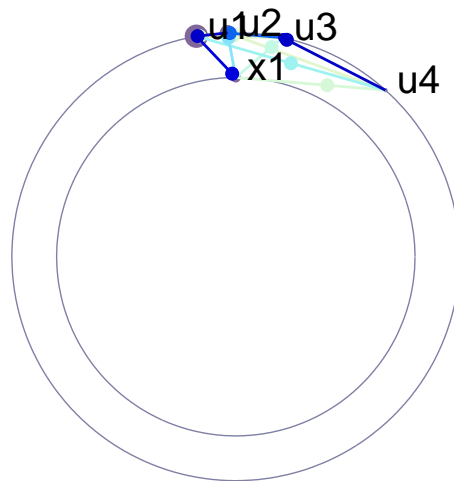
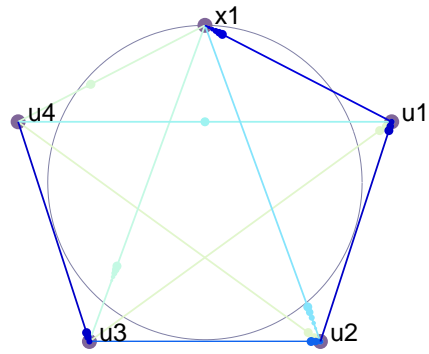


Figure 11: Potential oscillations at various frequencies (local expansion).

Synergies

Synergy phase plot



Synergies on network

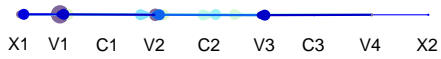


Figure 12: Periodic economic potentials and direct enzyme values.