

Enzyme rhythms in model linear_chain4_irrev.speedy

Model name: linear_chain4_irrev

o Optimisation problem

- Protein turnover time $1 \text{ s} = 0.0167 \text{ min}$
- Perturbed parameter(s) : x1
- Perturbation frequency f : $0.25/\text{s}$ (period 4 s)
- Scored quantity: v4
- Fitness-averaged fitness
- No posttranslational rhythms allowed
- Standard frequency considered f : $0.25/\text{s}$ (period 4 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 self-induced oscillation found

o Fitness changes after external perturbation at frequency $f=0.25/\text{s}$

- Change by perturbation alone (xx): -0.00639
- Change by adaption synergies (xu): 2.13
- Change by periodic enzyme (uu): -0.992
- Change by enzyme mean shift (u): $-4.46e-10$
- Total fitness change : 1.14
- Fitness gain by adaption : 1.14
- Maximum adaptive fitness found (in tested range) at frequency $f = 0.282/\text{s}$ (period 3.55 s)
- Predicted max. fitness change (adaptive, num. opt, full ampl. constraints) at frequency $f = 0.282$: 1.14

o Self-induced oscillations?

- No beneficial self-induced oscillations (2nd order, amplitude below 1/2 of mean) found at frequency $f = 0.25/\text{s}$ (principal synergy = -0.0241): Predicted fitness change -0.5

o Numerical calculation (responsive, $f=0.25$)

- Fitness change (fitness-averaged): -0.0136
- Fitness change (state-averaged): -0.00723

o Numerical calculation (adaptive, $f=0.25$)

- Fitness change (fitness-averaged): 1.12
- Fitness change (state-averaged): 2.05

o Numerical calculation (self-induced rhythm, amplitude below 1/2 of mean, $f=0.25$)

- Fitness change (fitness-averaged) : $-2.72e-06$
- Fitness change (state-averaged): $-2.72e-06$

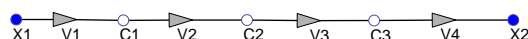


Figure 1: Network and reference flux

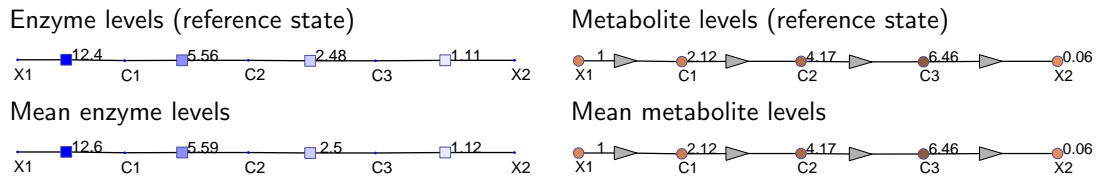


Figure 2: Reference state (top) and mean state during oscillation (bottom).

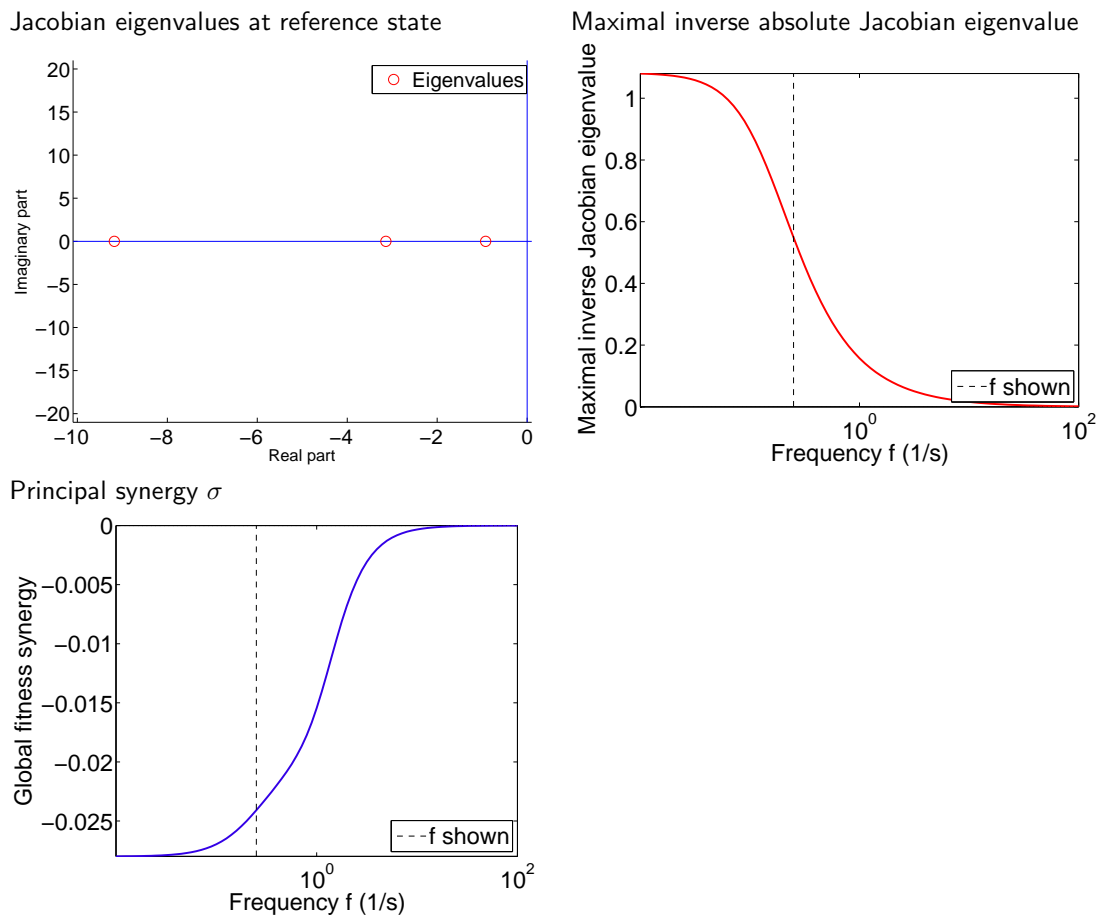
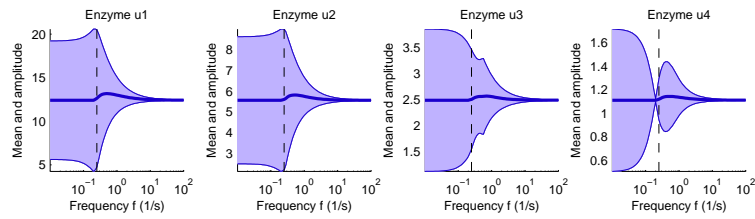
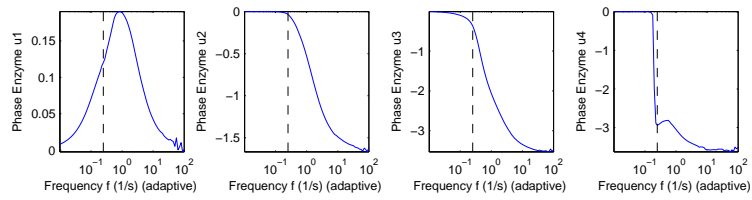


Figure 3: Control analysis. Left: Global fitness synergy (maximal fitness curvature eigenvalue), as a function of the frequency. Right: Relative amplitudes of individual enzymes for the least wasteful enzyme mode (components of the leading fitness curvature eigenvector).

Protein level and enzyme activity (mean and amplitude)



Phase angles $[0, 2\pi]$



Fitness change

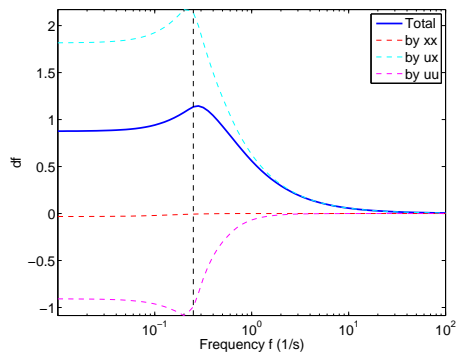


Figure 4: Adaptive oscillations. Left: amplitudes of protein levels (blue) and modification (grey). Right: phase shifts.

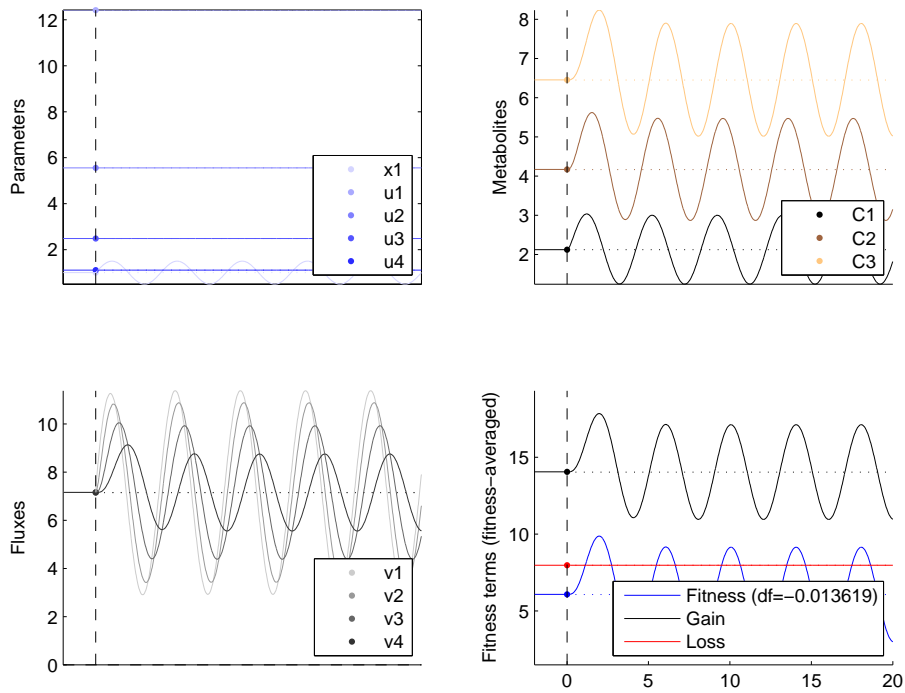


Figure 5: Numerical calculations: responsive oscillations (curves). Dynamic effects of oscillations. The panels show different types of variables: (i) Optimal periodic enzyme levels; (ii) internal metabolite levels; (iii) reaction fluxes; (iv) fitness, benefit, and cost. Perturbation frequency see first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

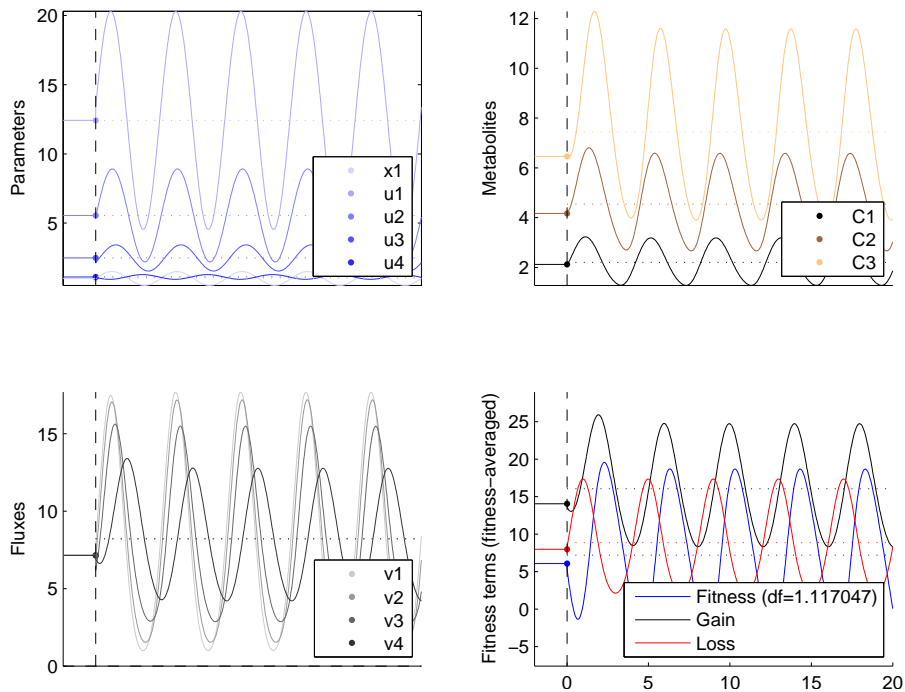


Figure 6: Numerical calculations: adaptive oscillations (curves). Dynamic effects of oscillations. The panels show different types of variables: (i) Optimal periodic enzyme levels; (ii) internal metabolite levels; (iii) reaction fluxes; (iv) fitness, benefit, and cost. Perturbation frequency see first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

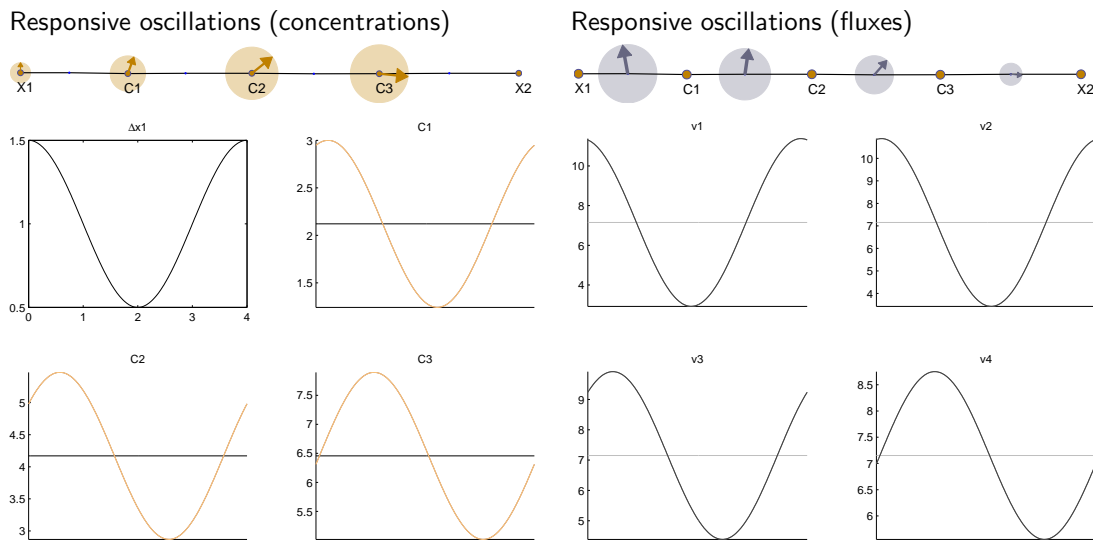


Figure 7: Responsive oscillations (local expansion; arrows: absolute changes) Perturbation frequency see first page.

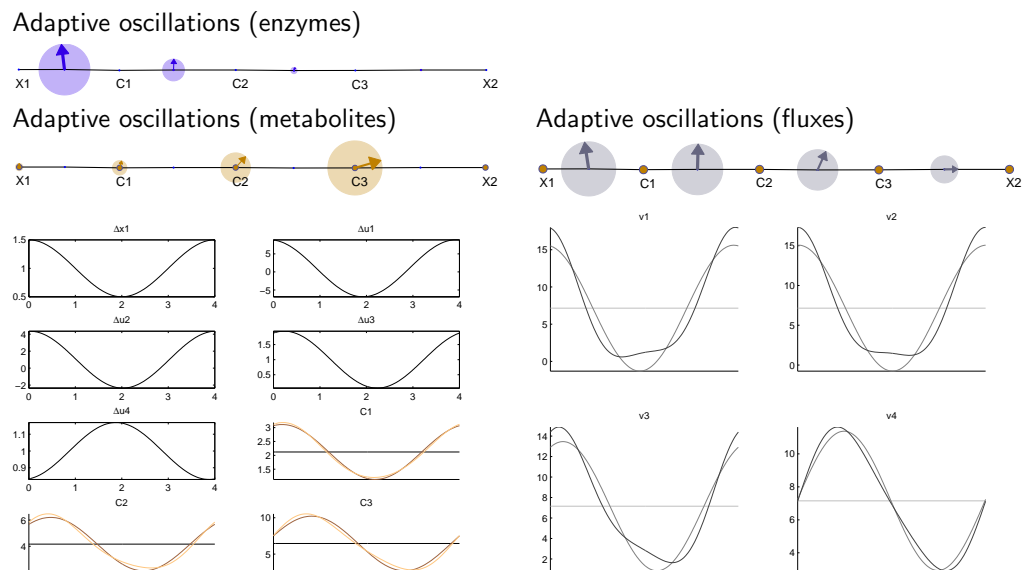


Figure 8: Adaption to forced oscillations (local expansion; arrows: absolute changes). Perturbation frequency see first page.

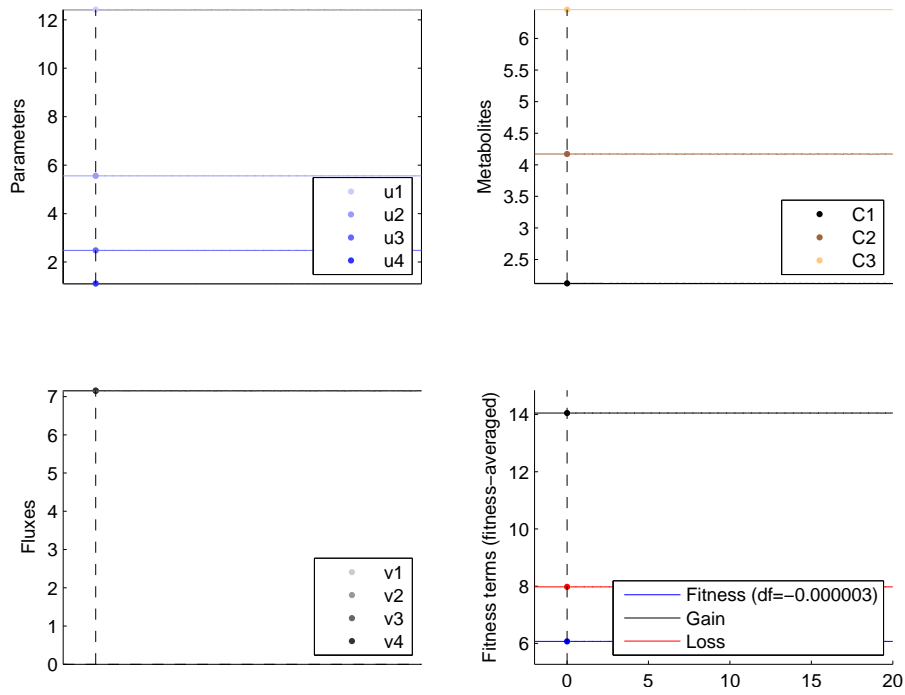
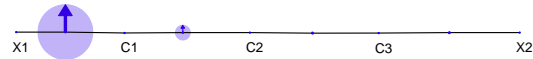
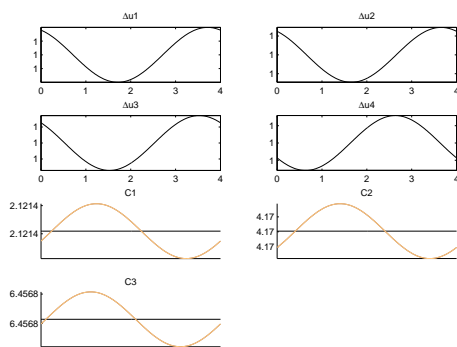
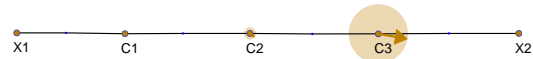


Figure 9: Tentative spontaneous oscillations. Perturbation frequency see first page.

Enzyme rhythm



Spontaneous oscillations (concentrations)



Spontaneous oscillations (fluxes)

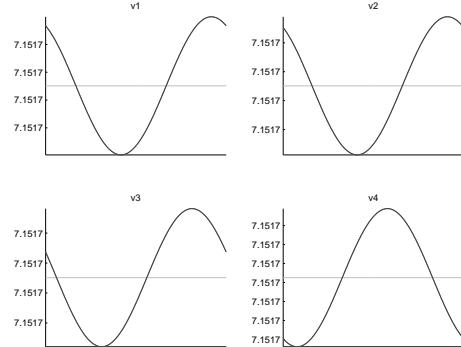
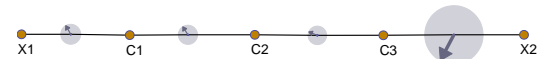
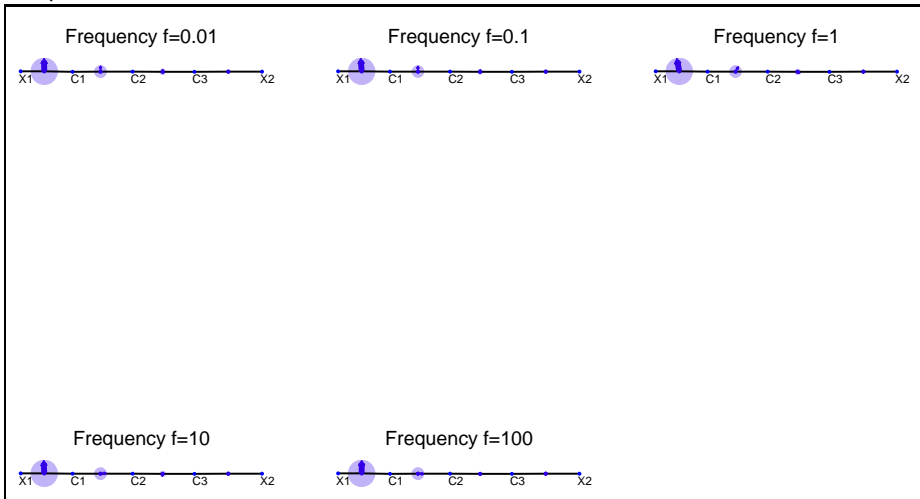


Figure 10: Tentative spontaneous oscillations (local expansion; arrows: absolute changes). Perturbation frequency see first page.

Adaptive



Least costly spontaneous

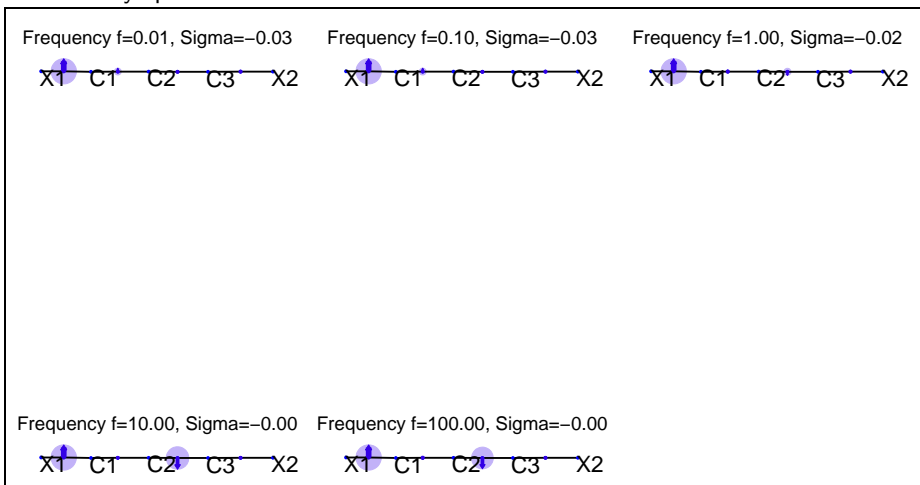


Figure 11: Potential oscillations at various frequencies (local expansion).