Enzyme rhythms in model linear_chain4

Model name: linear_chain4

o Optimisation problem
- Protein turnover time 1.8e+03 s = 30 min
- Perturbed parameter(s) : x1
- Perturbation frequency f : 0.0333/s (period 30 s)
- Scored quantity: v4
- Fitness-averaged fitness
- 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 self-induced 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): 0.00203
- Change by periodic enzyme (uu): -0.00141
- Change by enzyme mean shift (u): -1.57e-09
- Total fitness change : 0.00062
- Fitness gain by adaption : 0.00062
- Maximum adaptive fitness found (in tested range) at frequency f =0.794/s (period 1.26 s)
- Predicted max. fitness change (adaptive, num. opt, full ampl. constraints) at frequency f =0.794: 0.00154

o Self-induced oscillations?
- No beneficial self-induced 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): 0.00158
- Fitness change (state-averaged): 0.00182

o Numerical calculation (self-induced rhythm, amplitude below 1/2 of mean, f=0.0333)
- Fitness change (fitness-averaged) : 9.2e-07
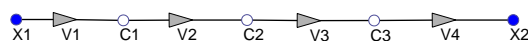- Fitness change (state-averaged): 9.2e-07

Figure 1: Network and reference flux

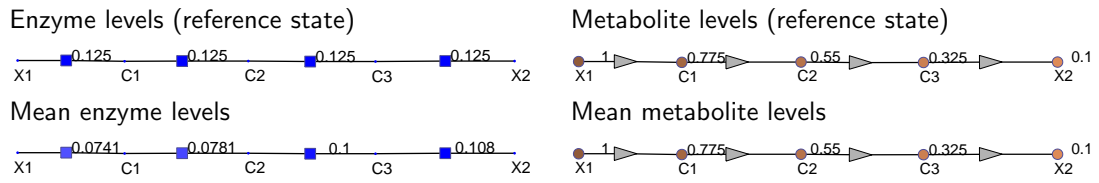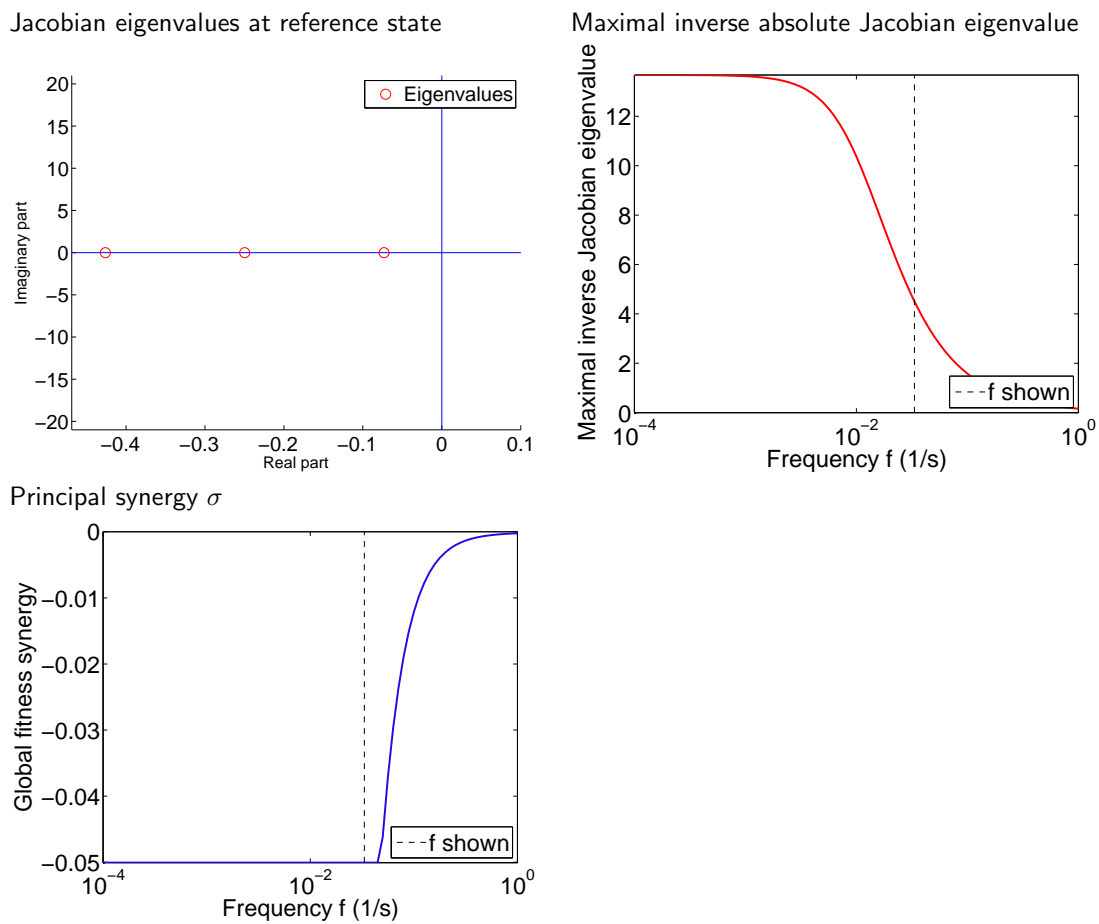Figure 2: Reference state (top) and mean state during oscillation (bottom).

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)
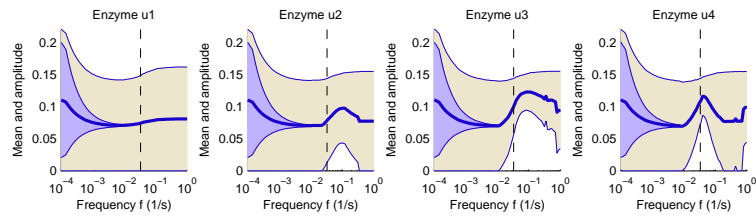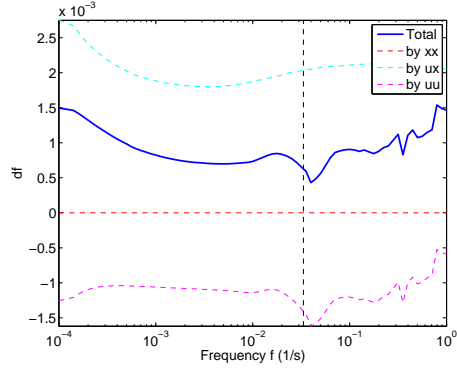

Phase angles $[0, 2\pi]$
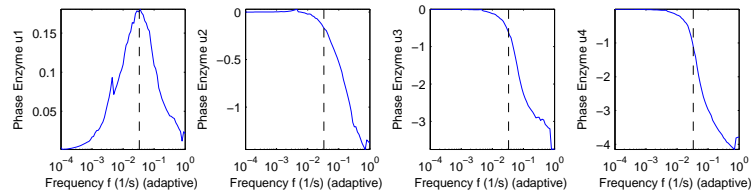
Fitness change

Figure 4: Adaptive oscillations. Left: amplitudes of protein levels (blue) and modification (grey). Right: phase shifts.
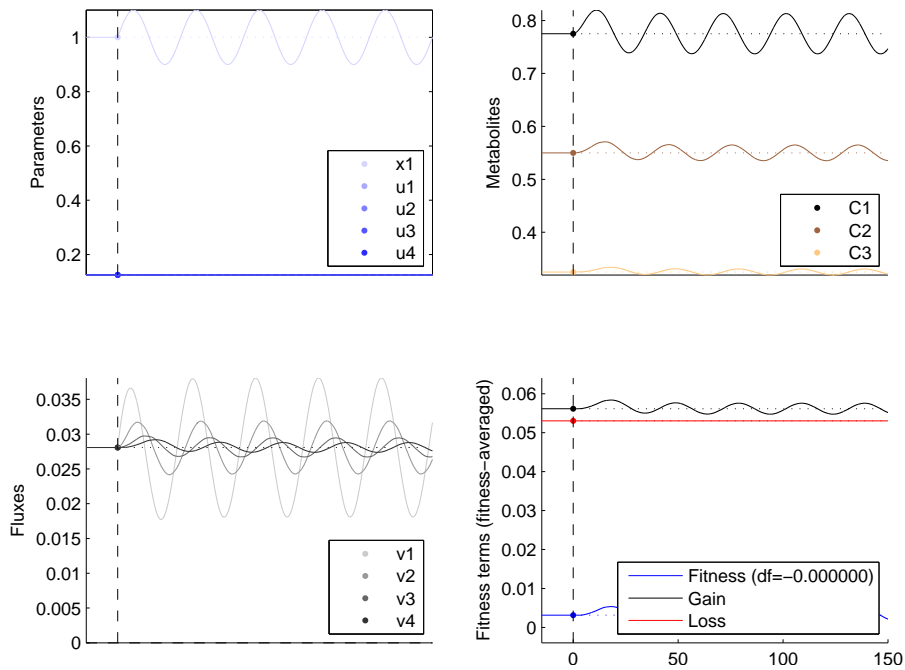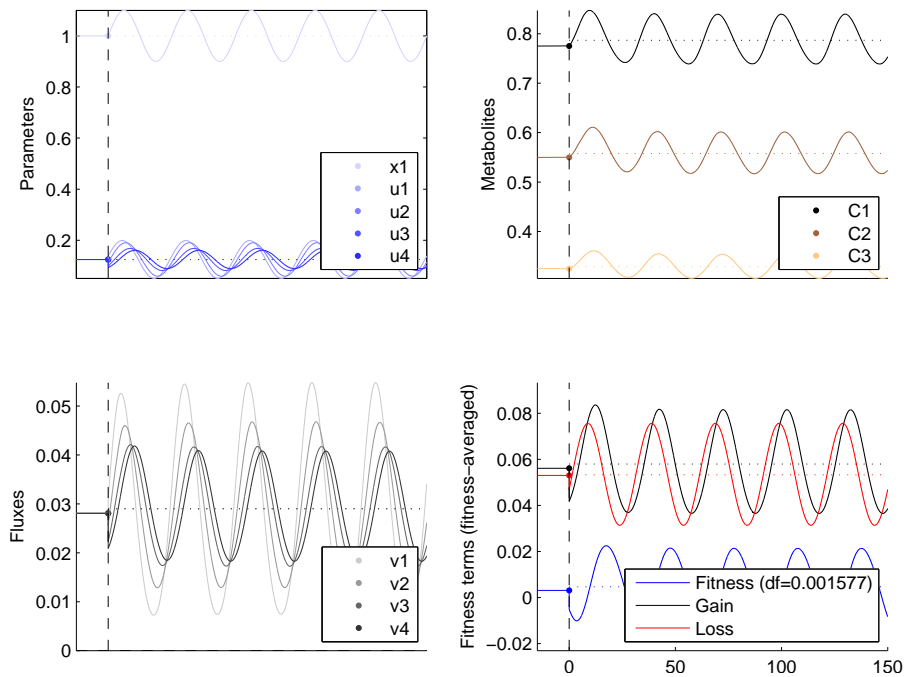
Figure 5: Numerical calculations: responsive oscillations (curves). Dynamic effects of oscillations. The panels show different types of variables: (i) Optimal periodic enzyme levels; (ii) internal metabolite levels; (iii) reaction fluxes; (iv) fitness, benefit, and cost. Perturbation frequency see first page.
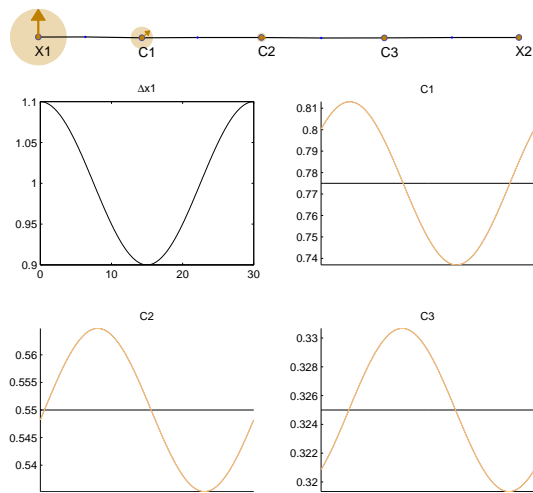

Figure 6: Numerical calculations: adaptive oscillations (curves). Dynamic effects of oscillations. The panels show different types of variables: (i) Optimal periodic enzyme levels; (ii) internal metabolite levels; (iii) reaction fluxes; (iv) fitness, benefit, and cost. Perturbation frequency see first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

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Responsive oscillations (concentrations)
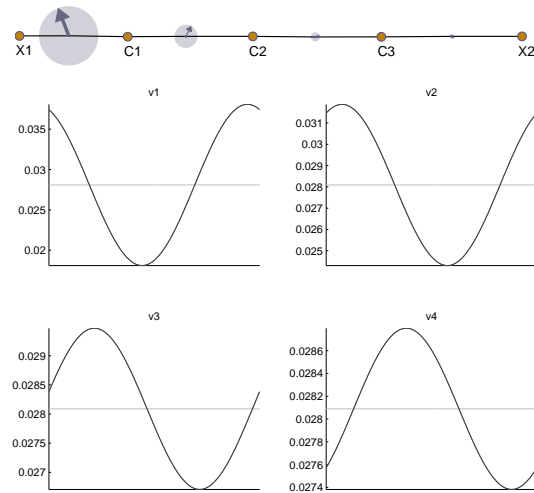

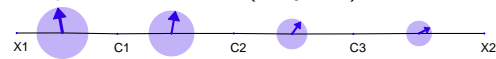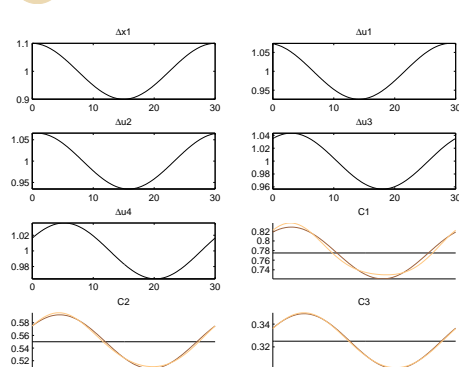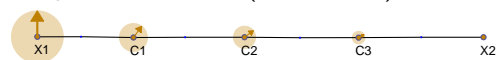## Responsive oscillations (fluxes)

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

Adaptive oscillations (enzymes)

Adaptive oscillations (metabolites)
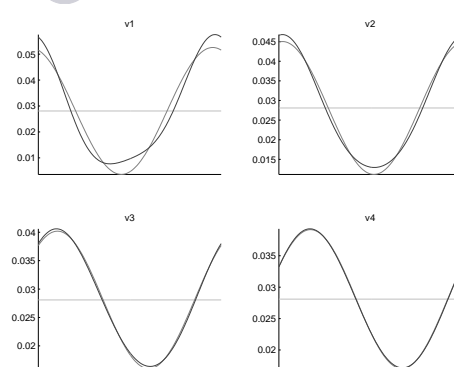

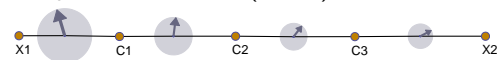## Adaptive oscillations (fluxes)

Figure 8: Adaption to forced oscillations (local expansion; arrows: absolute changes). Perturbation frequency see first page.
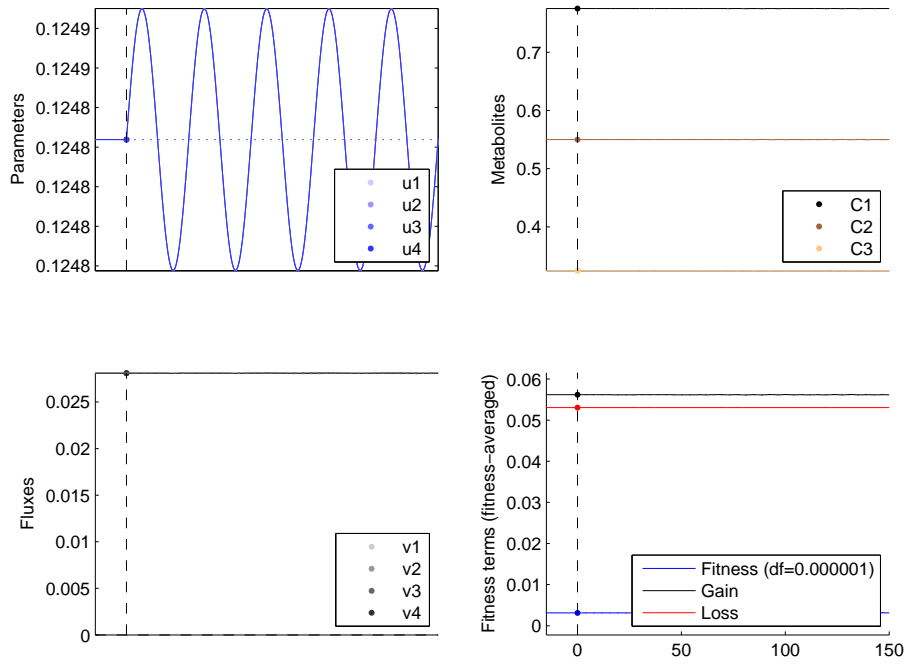
Figure 9: Tentative spontaneous oscillations. Perturbation frequency see first page.
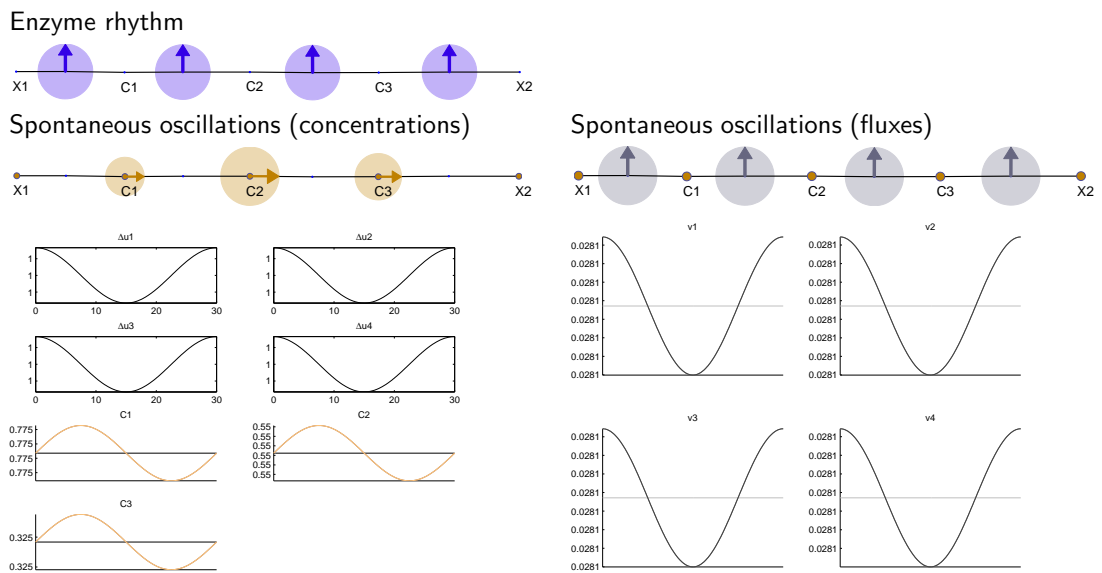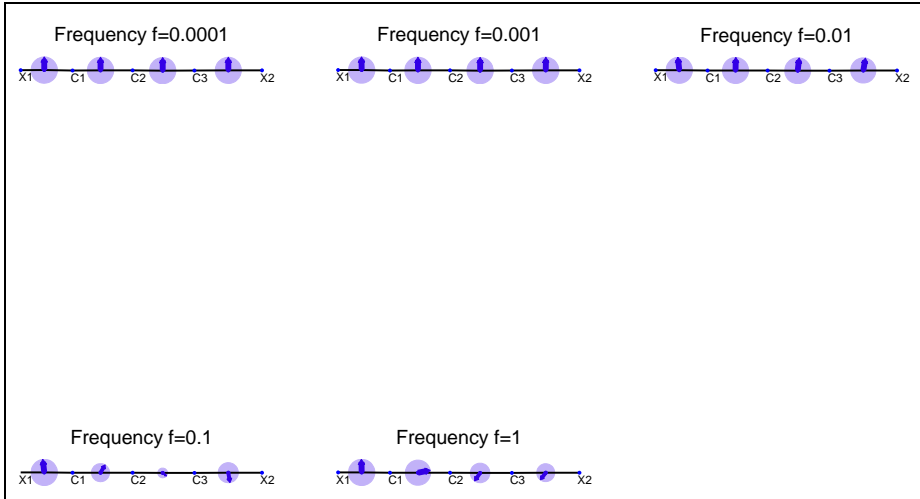

Figure 10: Tentative spontaneous oscillations (local expansion; arrows: absolute changes). Perturbation frequency see first page.
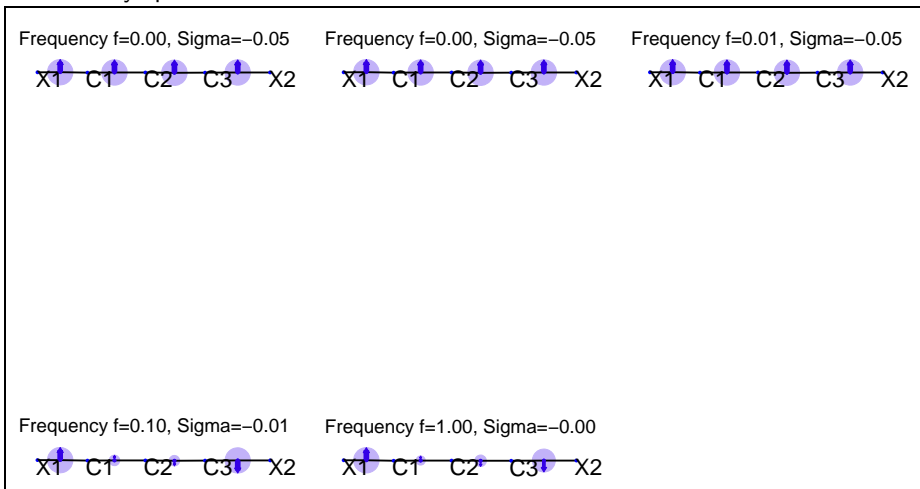
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Adaptive

Least costly spontaneous

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