

Enzyme rhythms in model ox_red_2.speedy

Model name: ox_red_2

o Optimisation problem

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

- Change by perturbation alone (xx): -0.0106
- Change by adaption synergies (xu): 0.00595
- Change by periodic enzyme (uu): -0.00297
- Change by enzyme mean shift (u): 0
- Total fitness change : -0.0076
- Fitness gain by adaption : 0.00297
- Maximum adaptive fitness found (in tested range) at frequency $f = 0.1/\text{s}$ (period 10 s)
- Predicted max. fitness change (adaptive, num. opt, full ampl. constraints) at frequency $f = 0.1$: -0.00401

o Self-induced oscillations?

- No beneficial self-induced oscillations (2nd order, amplitude below 1/2 of mean) found at frequency $f = 1/\text{s}$ (principal synergy = -0.531): Predicted fitness change -0.0422

o Numerical calculation (responsive, $f=1$)

- Fitness change (fitness-averaged): -0.0106
- Fitness change (state-averaged): -8.96e-05

o Numerical calculation (adaptive, $f=1$)

- Fitness change (fitness-averaged): -0.00761
- Fitness change (state-averaged): 0.0129

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

- Fitness change (fitness-averaged) : 7.06e-05
- Fitness change (state-averaged): 7.06e-05

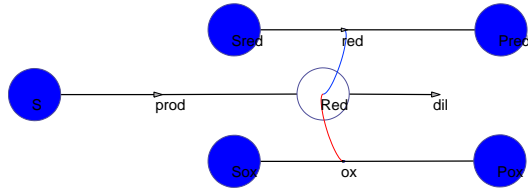


Figure 1: Network and reference flux

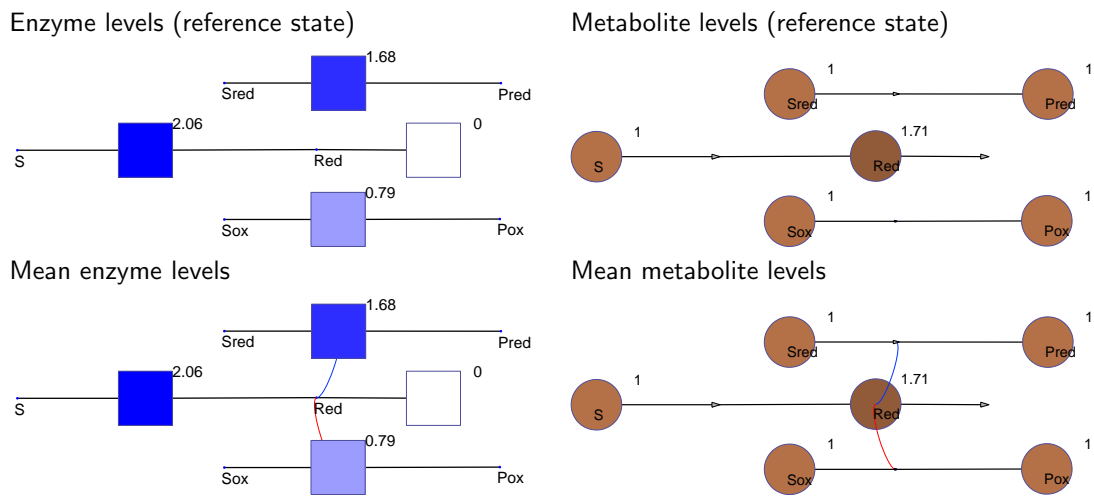
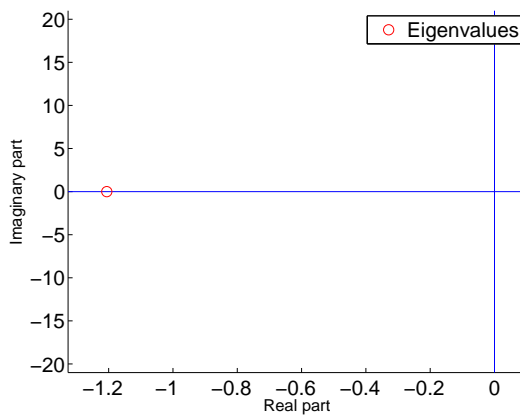
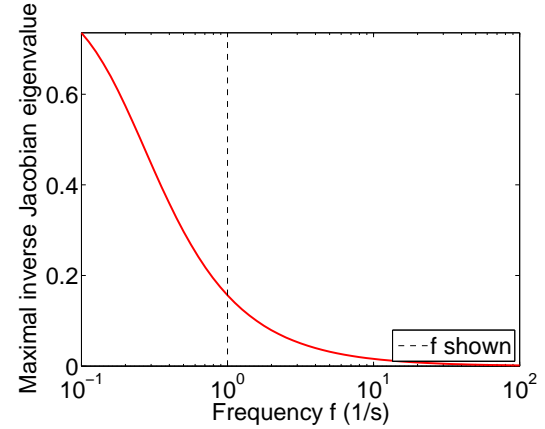


Figure 2: Reference state (top) and mean state during oscillation (bottom).

Jacobian eigenvalues at reference state



Maximal inverse absolute Jacobian eigenvalue



Principal synergy σ

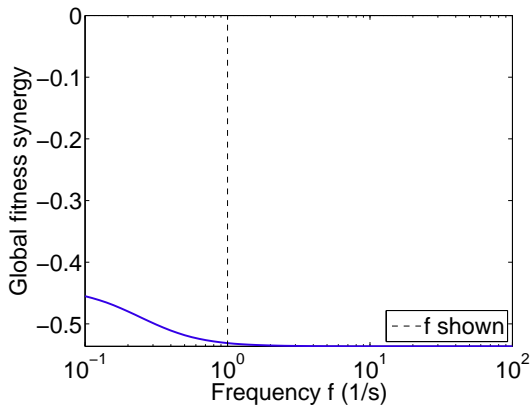
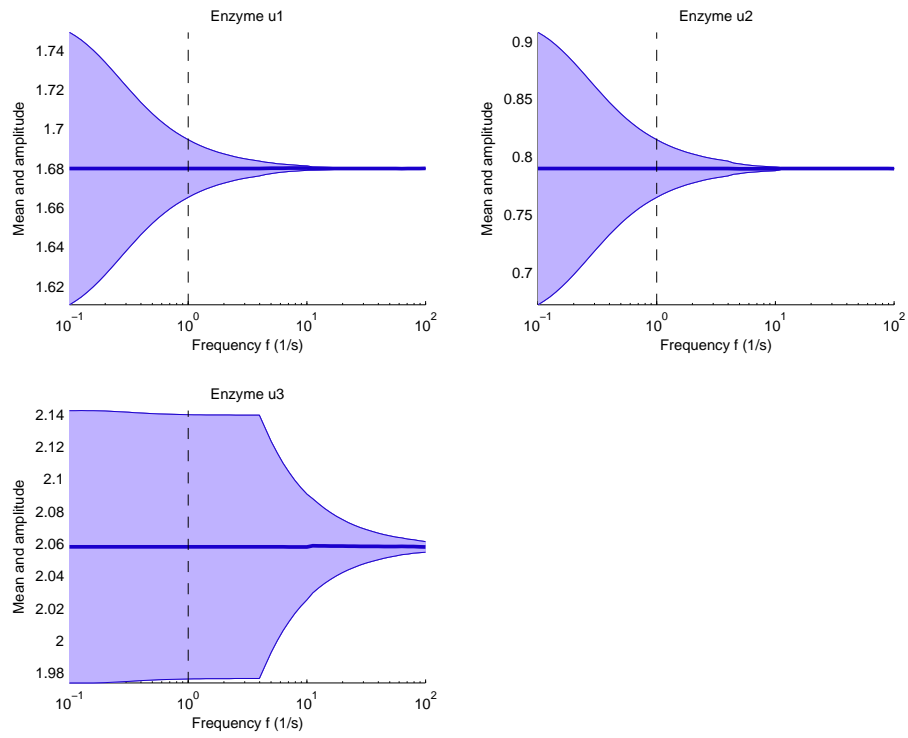
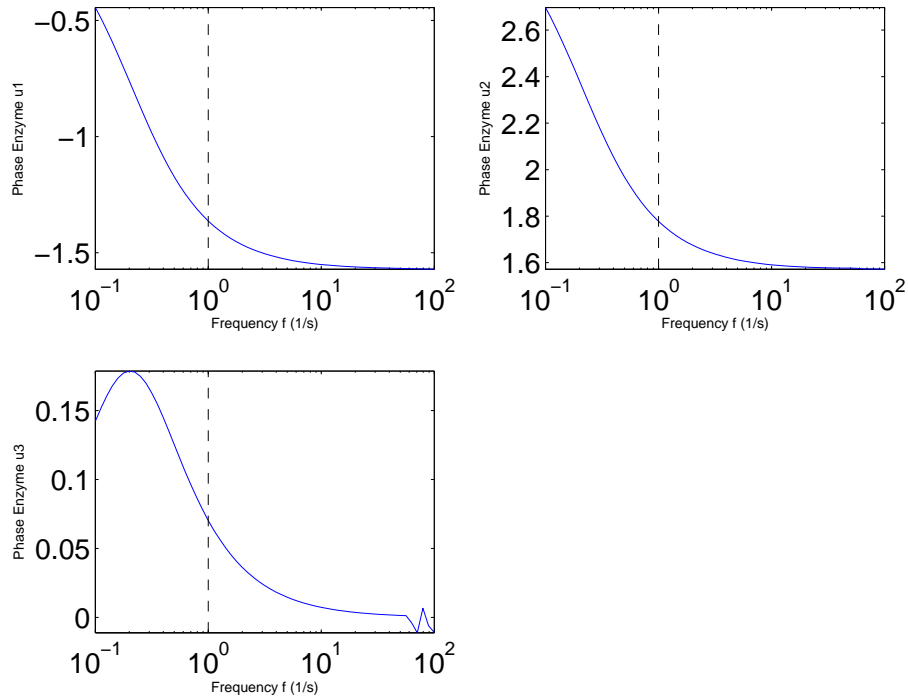


Figure 3: Control analysis. Left: Global fitness synergy (maximal fitness curvature eigenvalue), as a function of the frequency. Right: Relative amplitudes of individual enzymes for the least wasteful enzyme mode (components of the leading fitness curvature eigenvector).

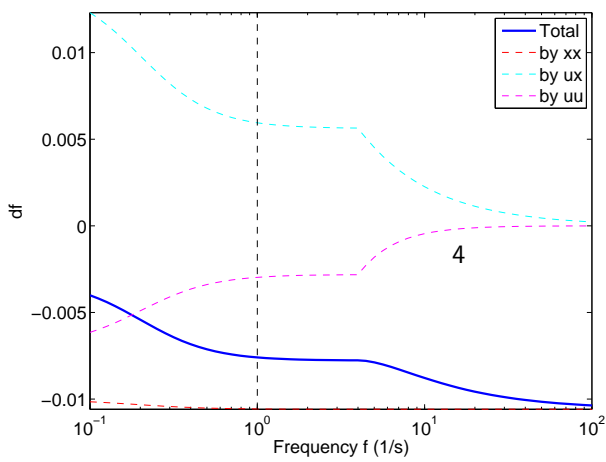
Protein level and enzyme activity (mean and amplitude)



Phase angles $[0, 2\pi]$



Fitness change



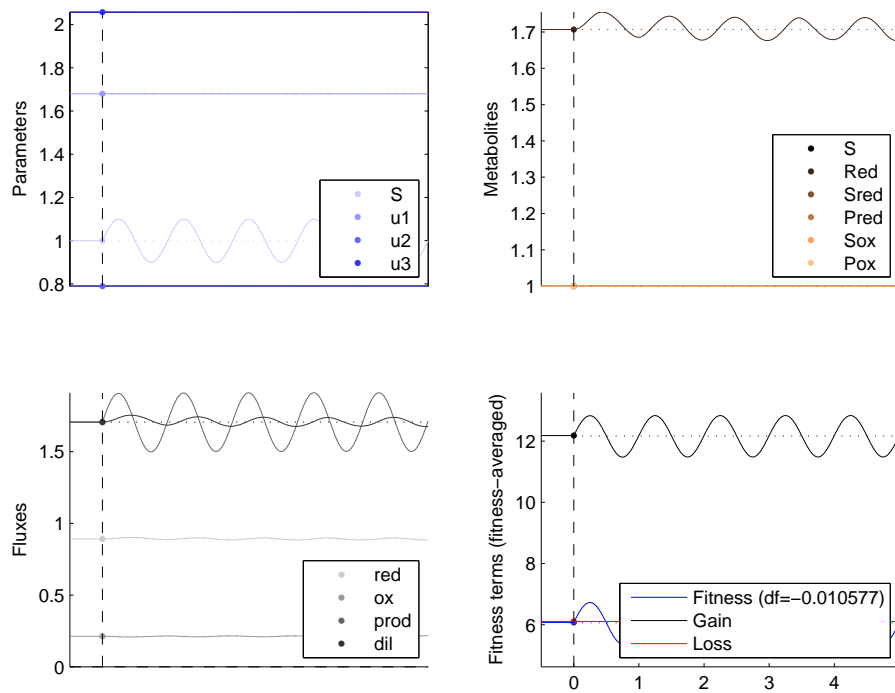


Figure 5: Numerical calculations: responsive oscillations (curves). Dynamic effects of oscillations. The panels show different types of variables: (i) Optimal periodic enzyme levels; (ii) internal metabolite levels; (iii) reaction fluxes; (iv) fitness, benefit, and cost. Perturbation frequency see first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

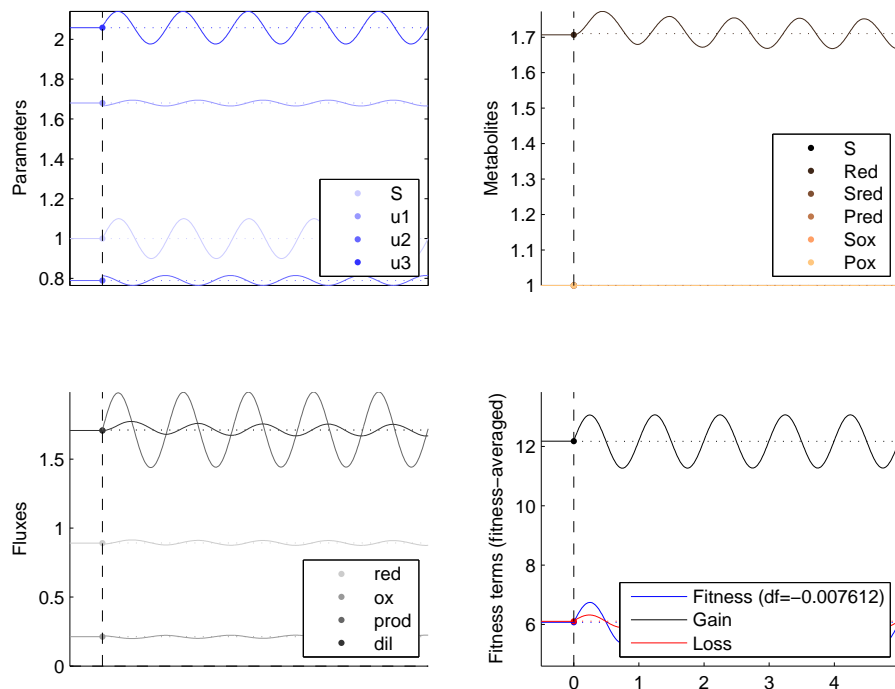
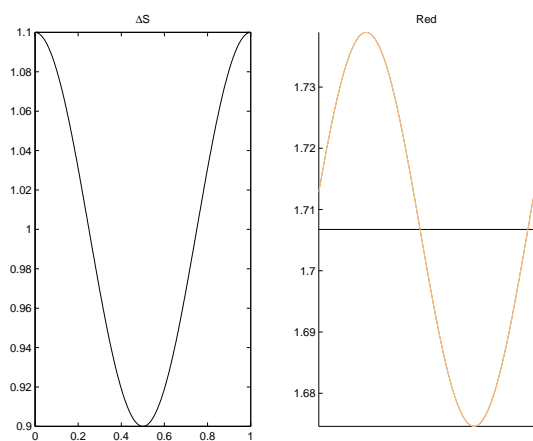
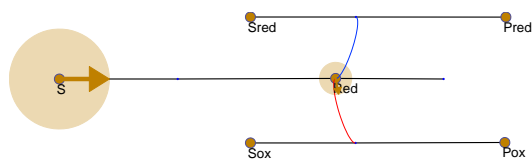


Figure 6: Numerical calculations: adaptive oscillations (curves). Dynamic effects of oscillations. The panels show different types of variables: (i) Optimal periodic enzyme levels; (ii) internal metabolite levels; (iii) reaction fluxes; (iv) fitness, benefit, and cost. Perturbation frequency see first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

Responsive oscillations (concentrations)



Responsive oscillations (fluxes)

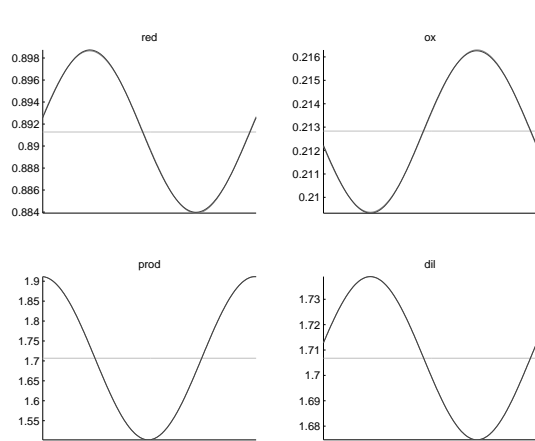
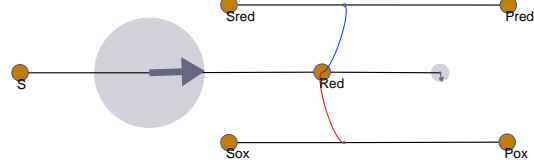
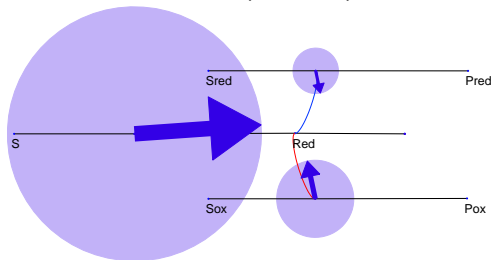
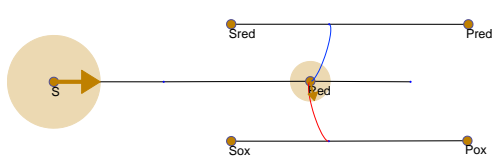


Figure 7: Responsive oscillations (local expansion; arrows: absolute changes) Perturbation frequency see first page.

Adaptive oscillations (enzymes)



Adaptive oscillations (metabolites)



Adaptive oscillations (fluxes)

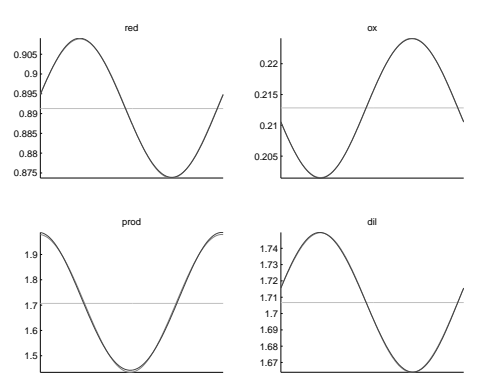
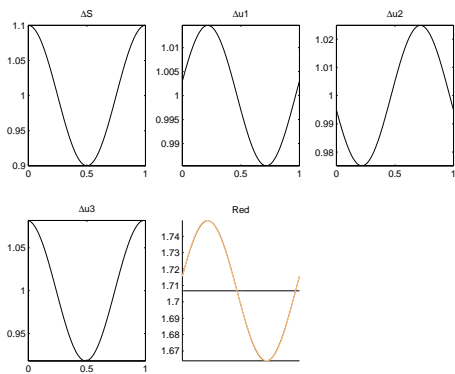
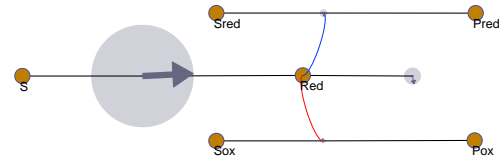


Figure 8: Adaption to forced oscillations (local expansion; arrows: absolute changes). Perturbation frequency see first page.

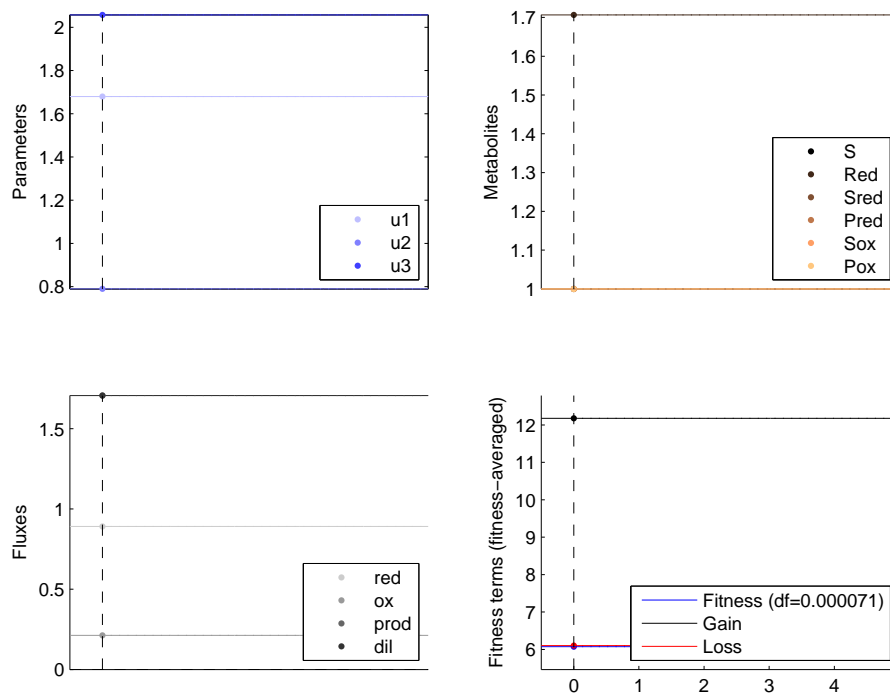
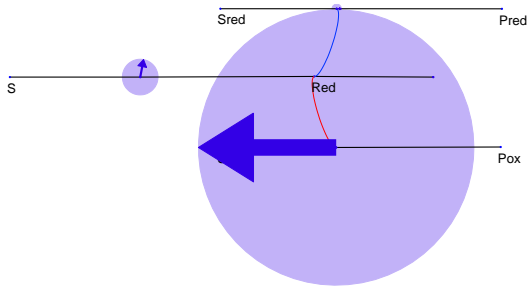
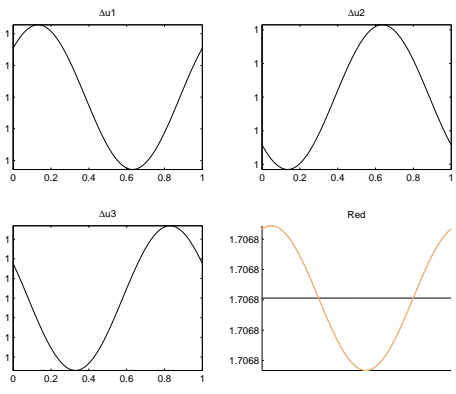
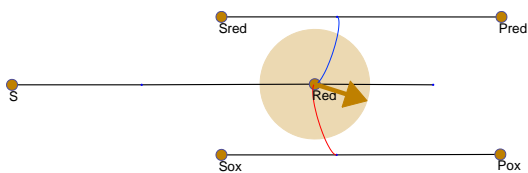


Figure 9: Tentative spontaneous oscillations. Perturbation frequency see first page.

Enzyme rhythm



Spontaneous oscillations (concentrations)



Spontaneous oscillations (fluxes)

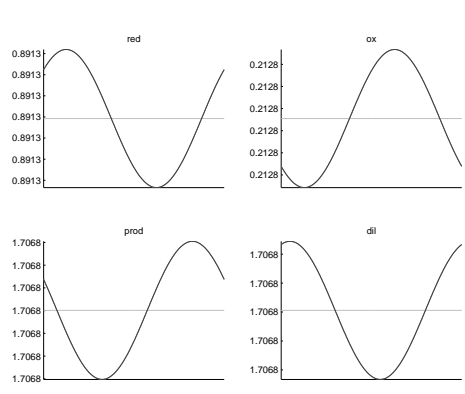
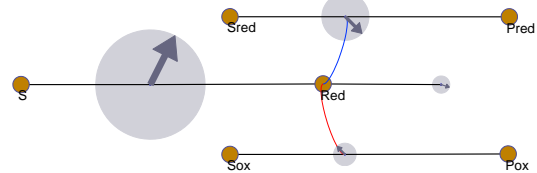
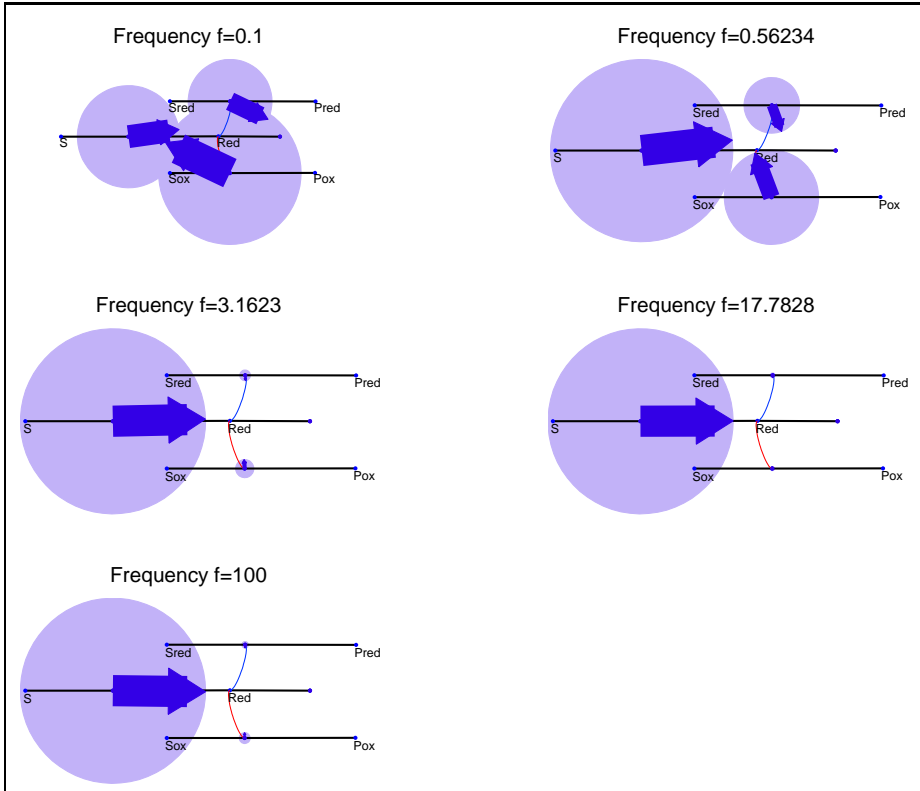


Figure 10: Tentative spontaneous oscillations (local expansion; arrows: absolute changes). Perturbation frequency see first page.

Adaptive



Least costly spontaneous

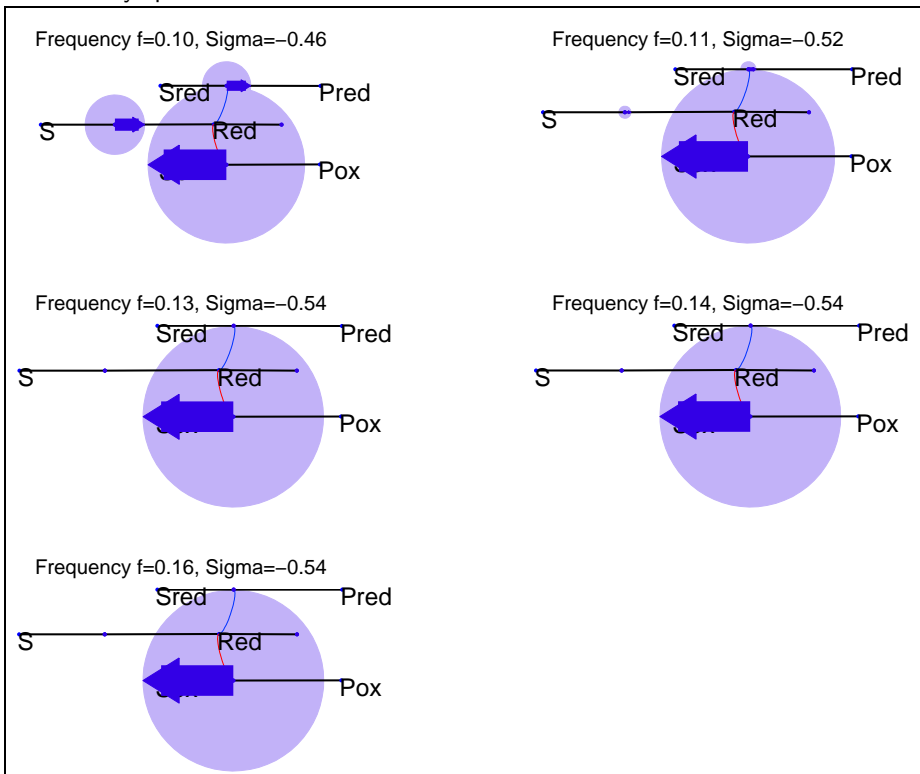


Figure 11: Potential oscillations at various frequencies (local expansion).