

Enzyme rhythms in model ox_red_1.speedy - spontaneous oscillations

Model name: ox_red_1

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: Ana
- State-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: 0
- spontaneous_rhythm: 1
- spontaneous_rhythm_at_omega: 0
- has_spontaneous_rhythm_and_inactive_enzymes: 0

o Beneficial self-induced oscillation found

- Maximum principal synergy found (in tested range) at frequency $f = 8.91/\text{s}$ (period 0.112 s)
- Maximum fitness found (in tested range) at frequency $f = 5.62/\text{s}$ (period 0.178 s)

o Fitness changes after external perturbation at frequency $f=1/\text{s}$

- Change by perturbation alone (xx): $4.73\text{e-}07$

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 = $7.58\text{e-}11$): Predicted fitness change $5.26\text{e-}12$

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

- Fitness change (fitness-averaged): -0.000158
- Fitness change (state-averaged): -0.000158

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

- Fitness change (fitness-averaged) : $-1.54\text{e-}05$
- Fitness change (state-averaged): $1.98\text{e-}05$

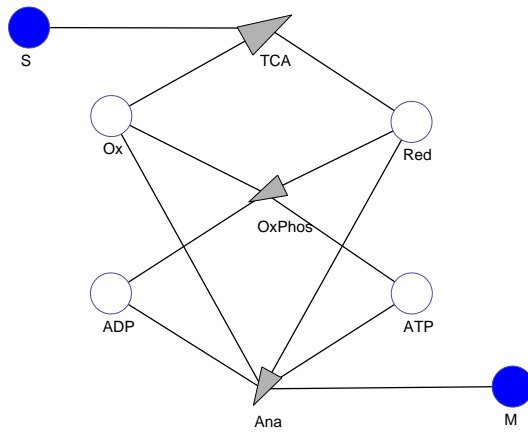
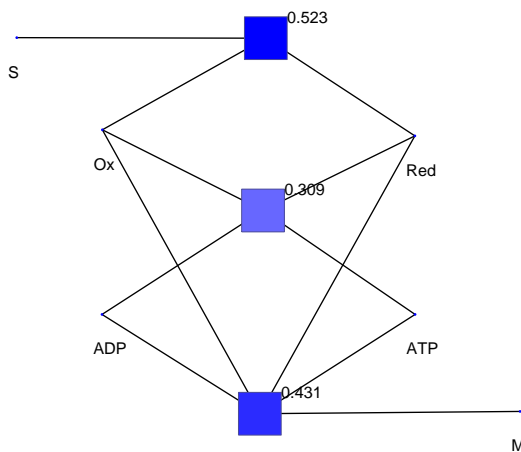
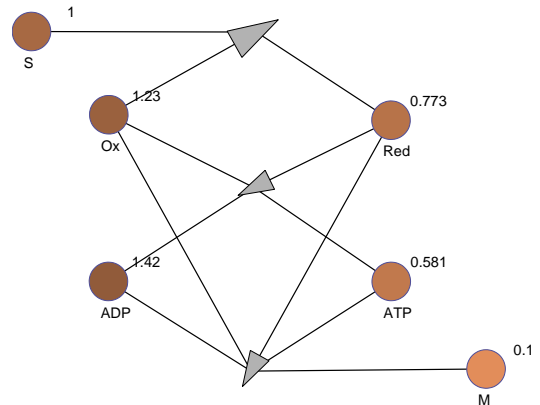


Figure 1: Network and reference flux

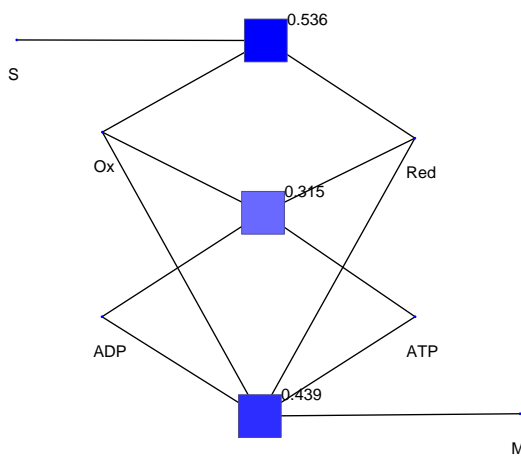
Enzyme levels (reference state)



Metabolite levels (reference state)



Mean enzyme levels



Mean metabolite levels

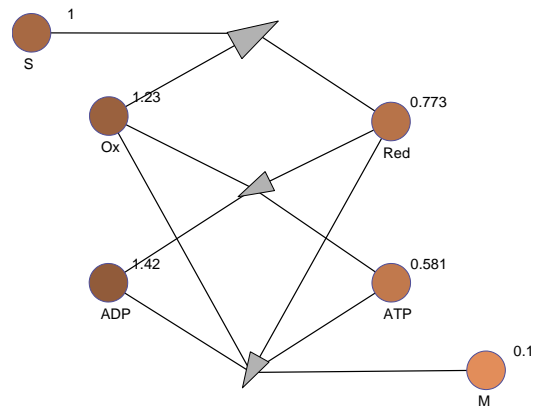


Figure 2: Reference state (top) and mean state during oscillation (bottom).

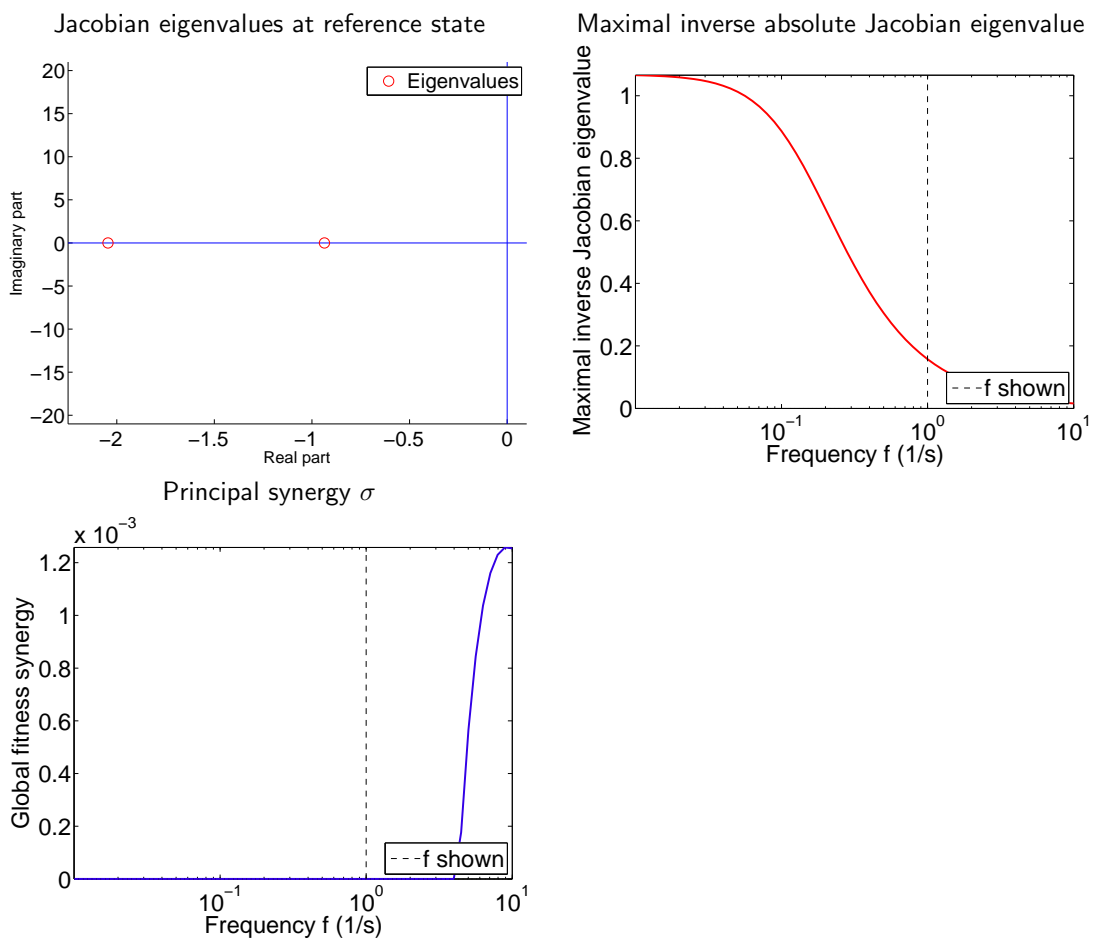
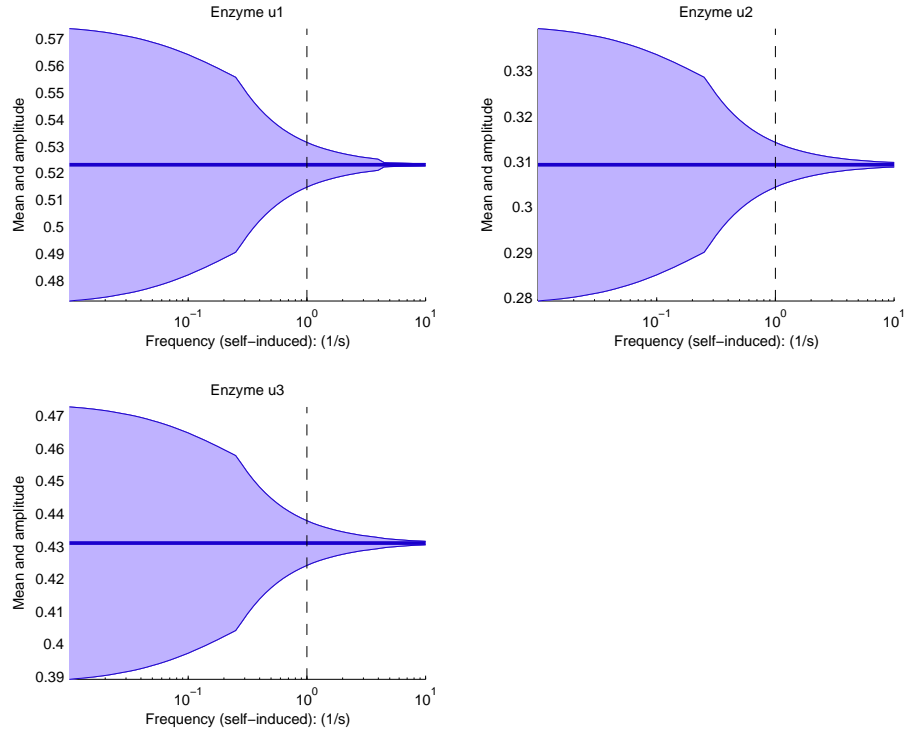
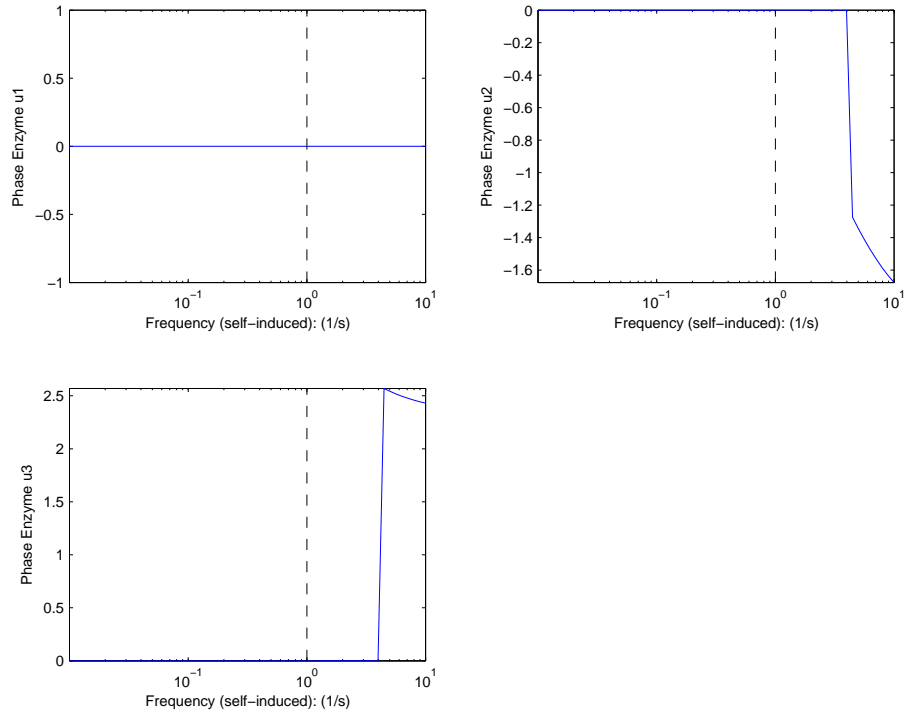


Figure 3: Control analysis: fitness curvatures. Left: Frequency-dependent fitness curvature eigenvalues. Right: relative sizes and phases of the individual enzyme levels (components of the leading fitness curvature eigenvector).

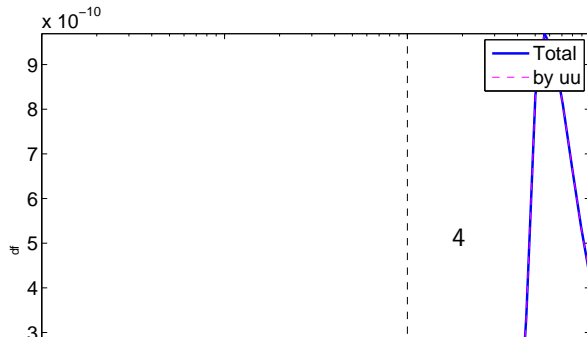
Protein level and enzyme activity (mean and amplitude)



Phase angles $[0, 2\pi]$



Fitness change



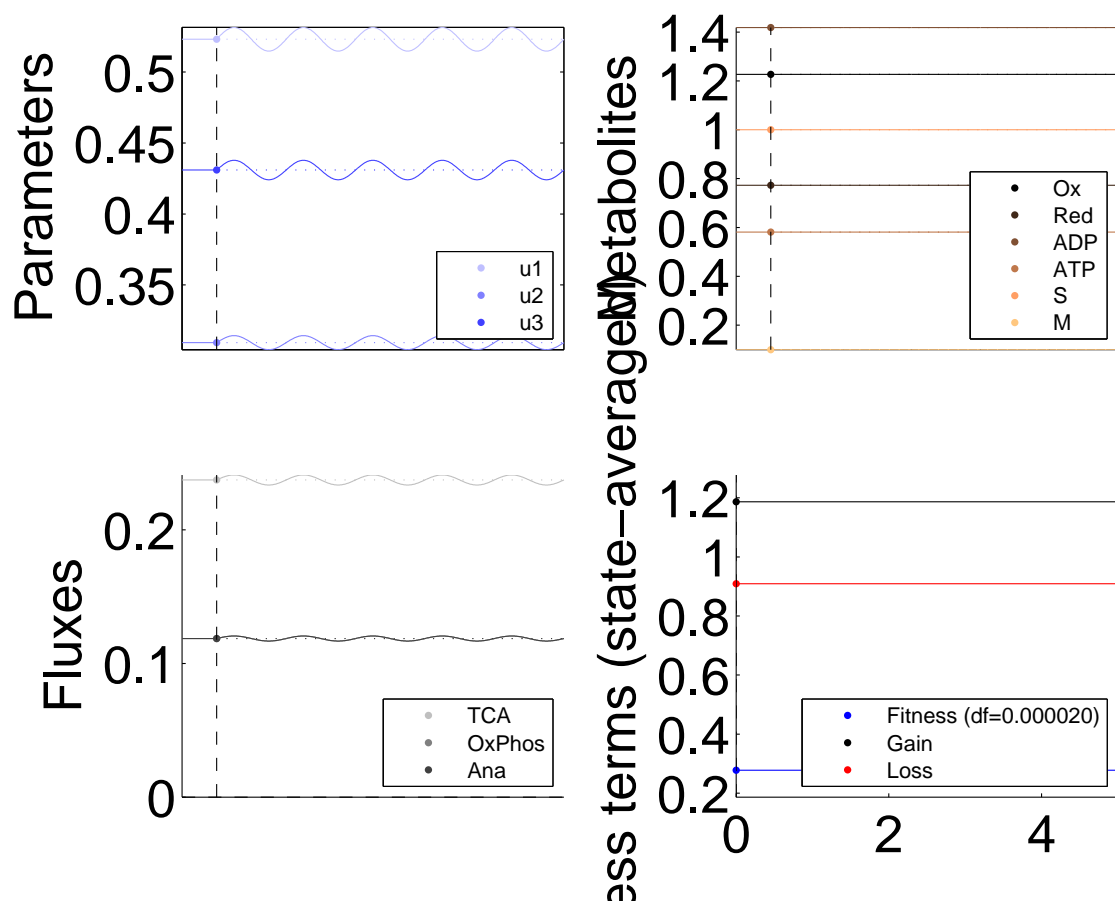
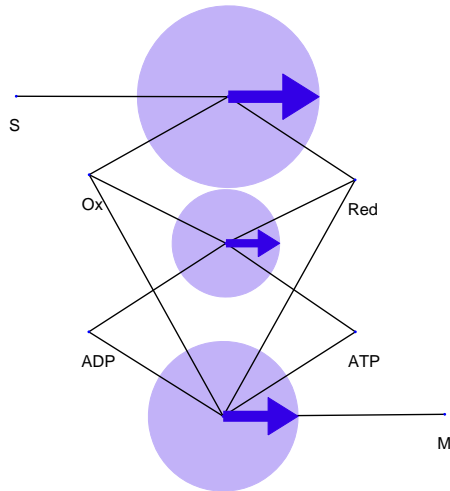
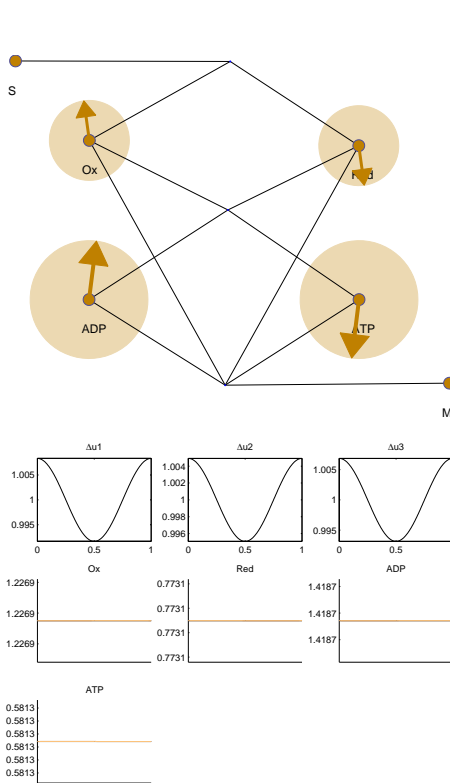


Figure 5: Numerical calculations: spontaneous oscillations. Perturbation frequency see first page.

Enzyme rhythm



Spontaneous oscillations (concentrations)



Spontaneous oscillations (fluxes)

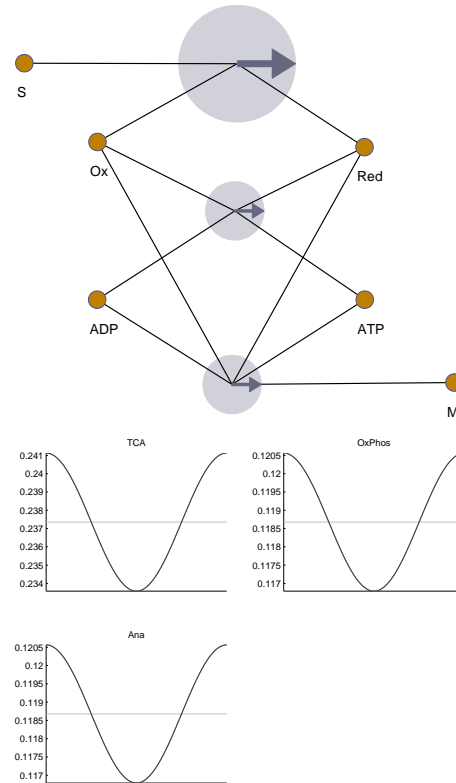


Figure 6: Spontaneous oscillations (local expansion; arrows: absolute changes). Perturbation frequency see first page.

Spontaneous oscillations

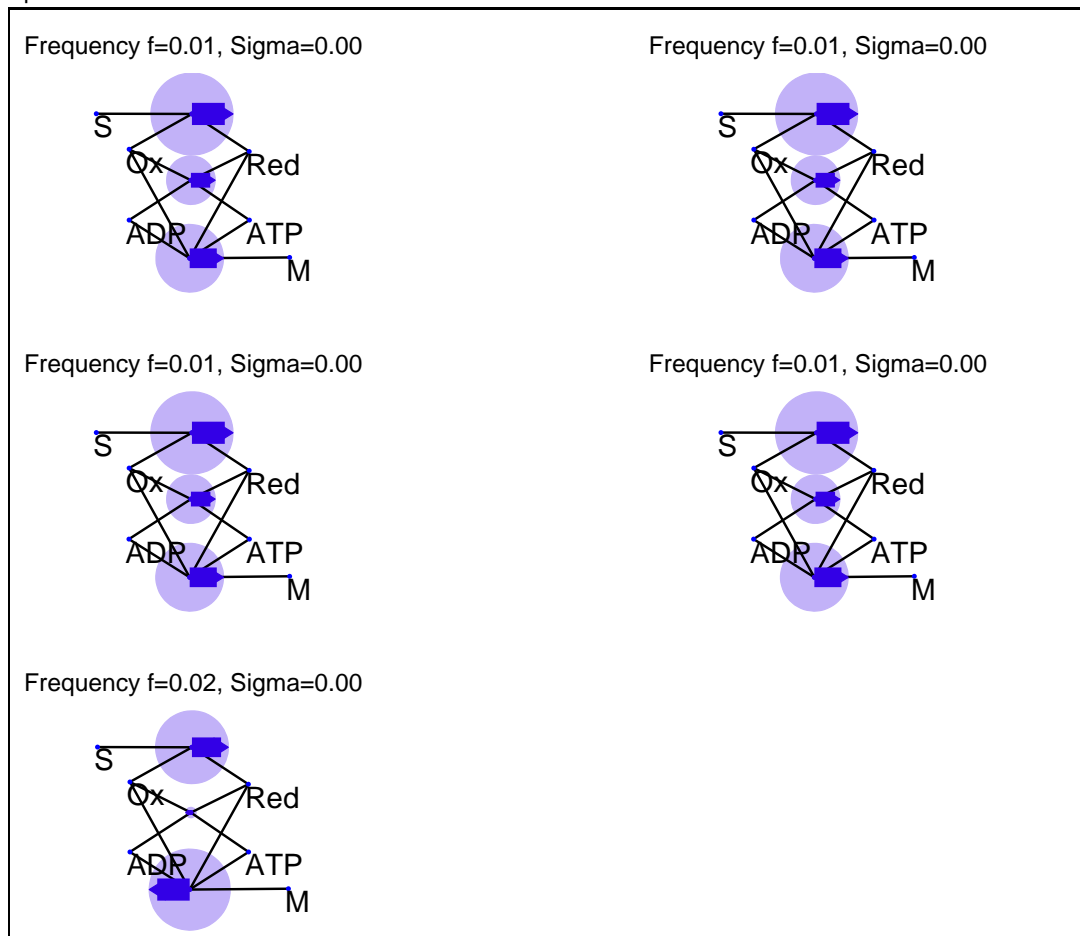


Figure 7: Spontaneous oscillations (or tendencies towards them) for various circular frequencies ω . If the maximal fitness curvatures λ is positive, the rhythm is beneficial (local expansion; arrows: absolute changes).