

## Enzyme rhythms in model ox\_red\_1 - spontaneous oscillations

Model name: ox\_red\_1

### o Optimisation problem

- Protein turnover time  $1.8e+03$  s = 30 min
- Perturbed parameter(s) : S
- Perturbation frequency  $f$  : 0.0333/s (period 30 s)
- Scored quantity: Ana
- State-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: 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  $f = 0.000282$ /s (period  $3.55e+03$  s)
- Maximum fitness found (in tested range) at frequency  $f = 0.0001$ /s (period  $1e+04$  s)

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

- Change by perturbation alone (xx):  $5.35e-05$

### 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 =  $7.58e-11$ ): Predicted fitness change  $5.26e-12$

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

- Fitness change (fitness-averaged): -0.000441
- Fitness change (state-averaged): -0.000441

### o Numerical calculation (self-induced rhythm, amplitude below 1/2 of mean, $f=0.0333$ )

- Fitness change (fitness-averaged) :  $2.14e-07$
- Fitness change (state-averaged):  $2.23e-07$

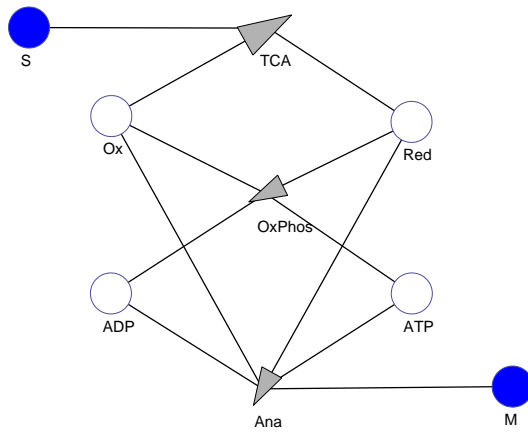
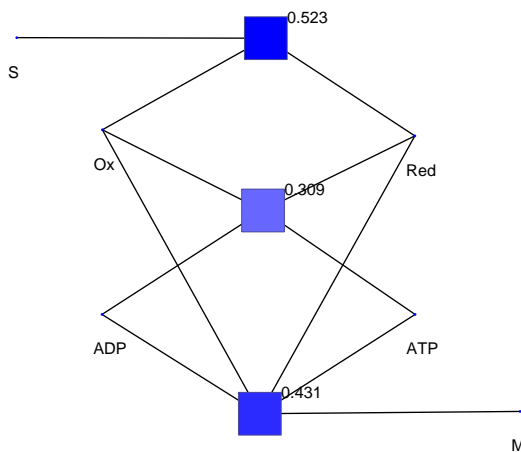
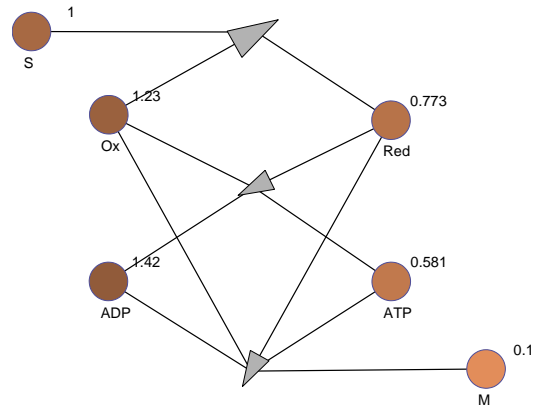


Figure 1: Network and reference flux

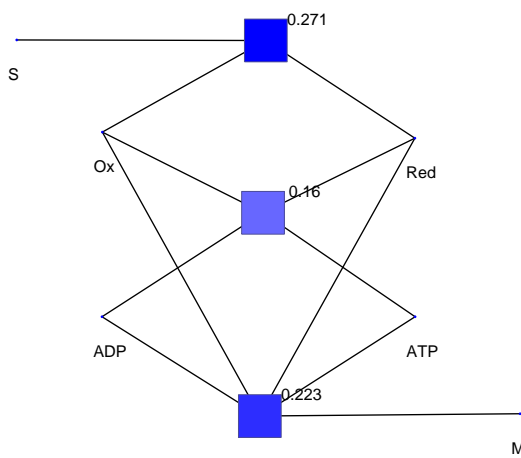
Enzyme levels (reference state)



Metabolite levels (reference state)



Mean enzyme levels



Mean metabolite levels

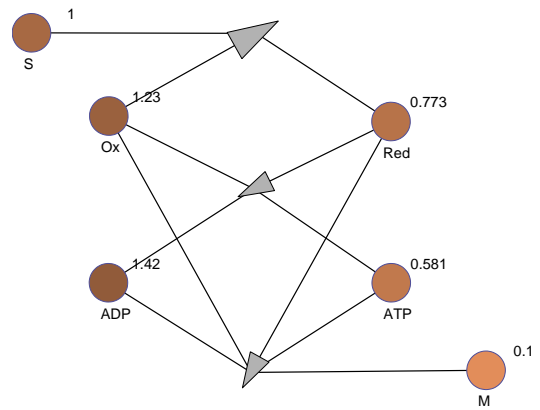


Figure 2: Reference state (top) and mean state during oscillation (bottom).

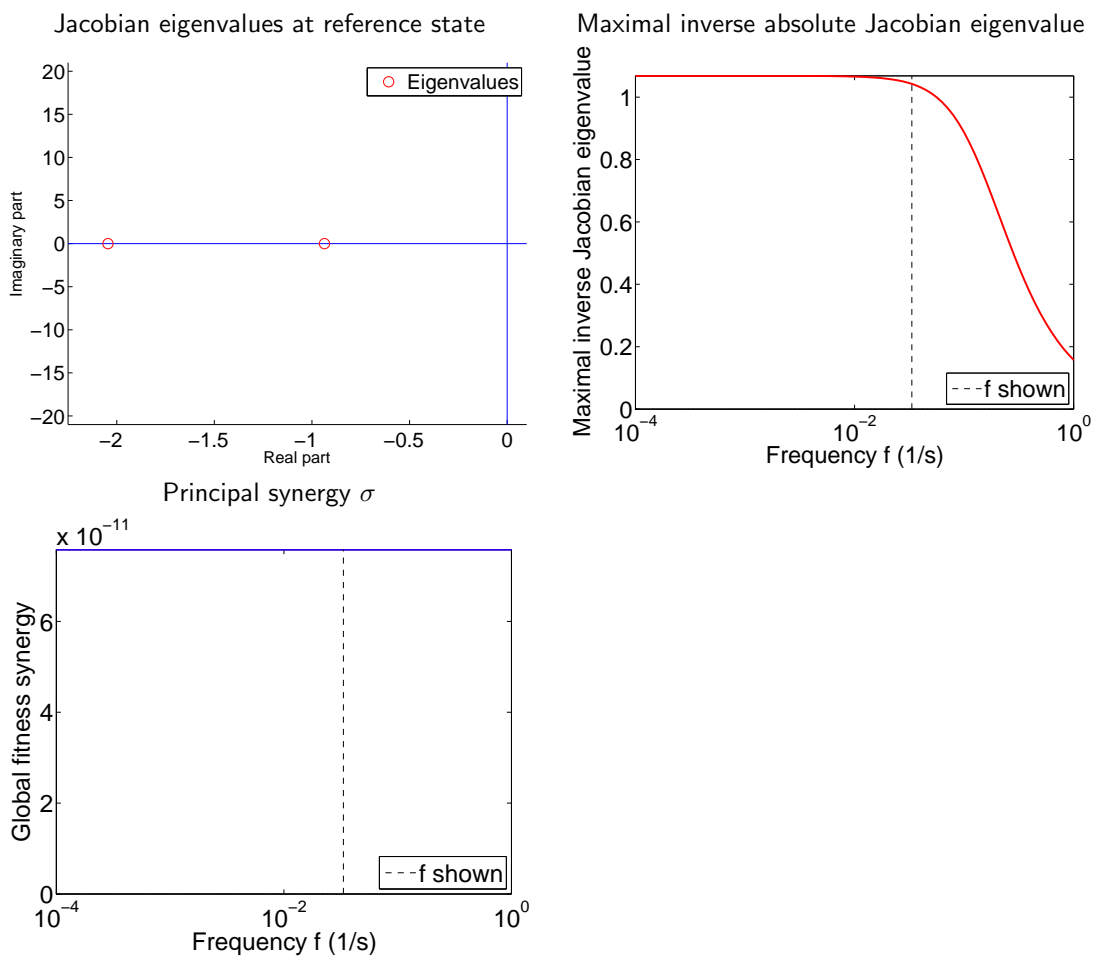
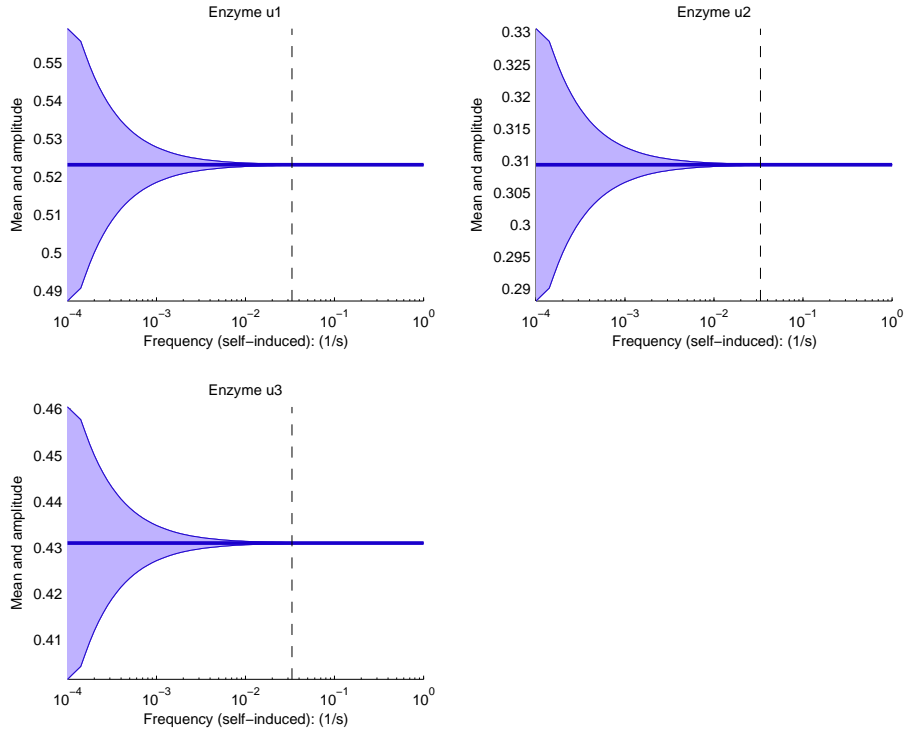
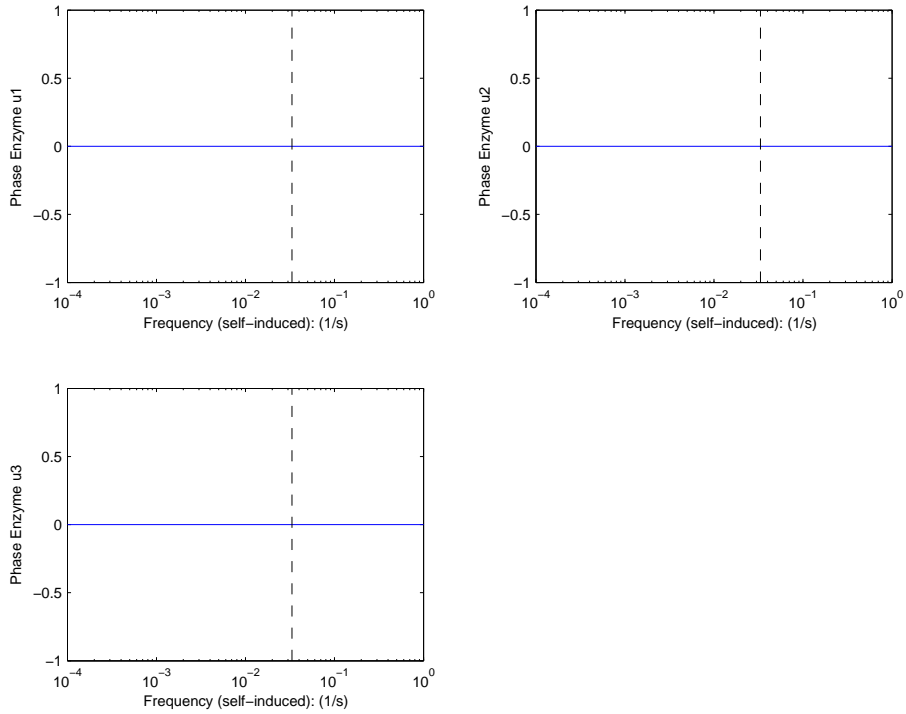


Figure 3: Control analysis: fitness curvatures. Left: Frequency-dependent fitness curvature eigenvalues. Right: relative sizes and phases of the individual enzyme levels (components of the leading fitness curvature eigenvector).

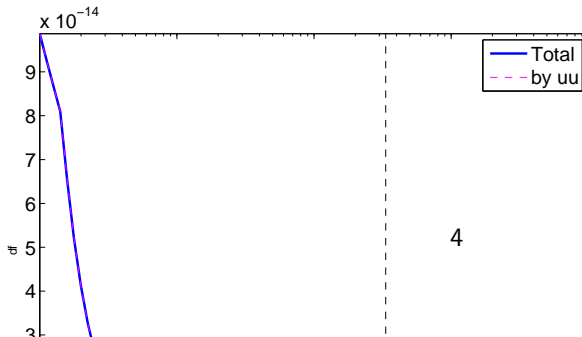
### Protein level and enzyme activity (mean and amplitude)



### Phase angles $[0, 2\pi]$



### Fitness change



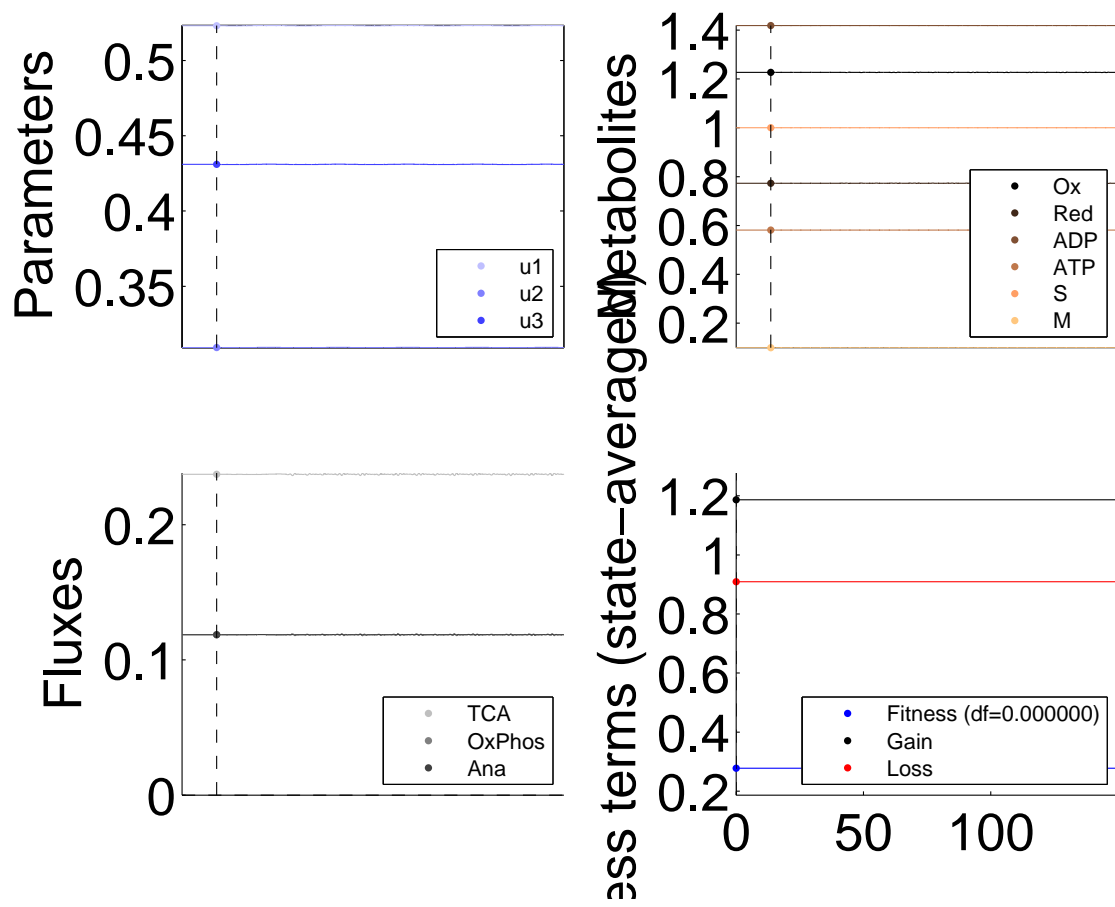
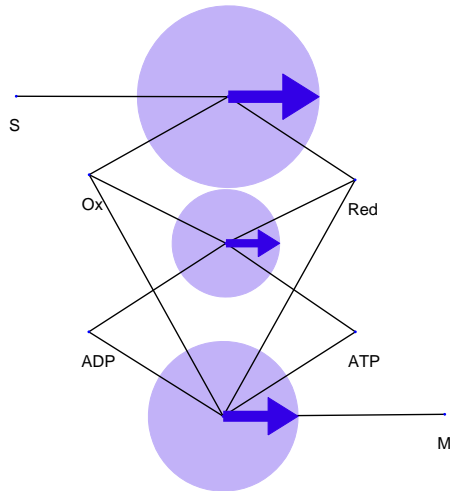
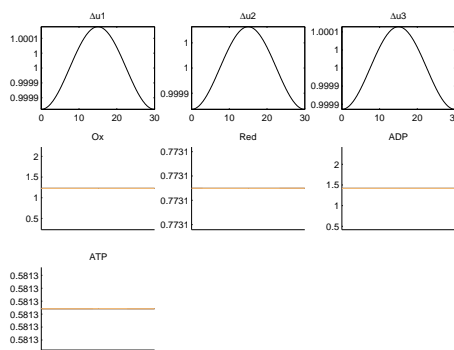
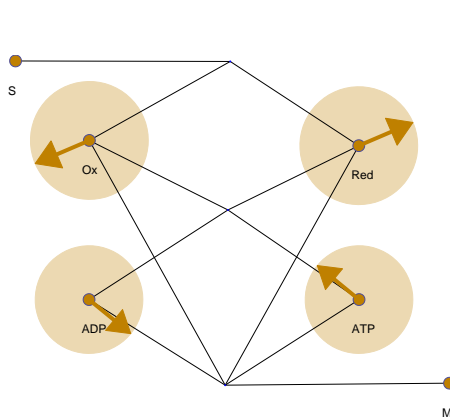


Figure 5: Numerical calculations: spontaneous oscillations. Perturbation frequency see first page.

### Enzyme rhythm



### Spontaneous oscillations (concentrations)



### Spontaneous oscillations (fluxes)

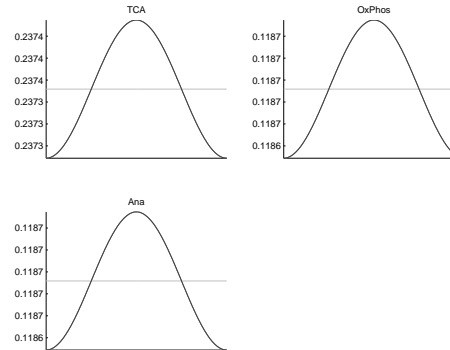
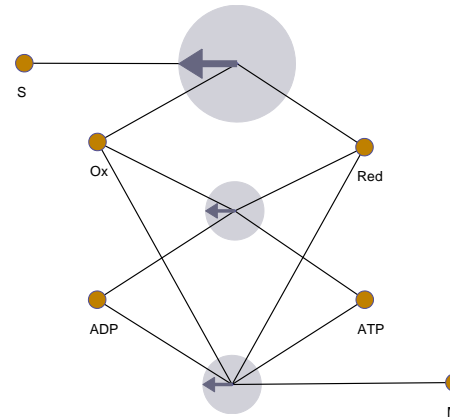


Figure 6: Spontaneous oscillations (local expansion; arrows: absolute changes). Perturbation frequency see first page.

Spontaneous oscillations

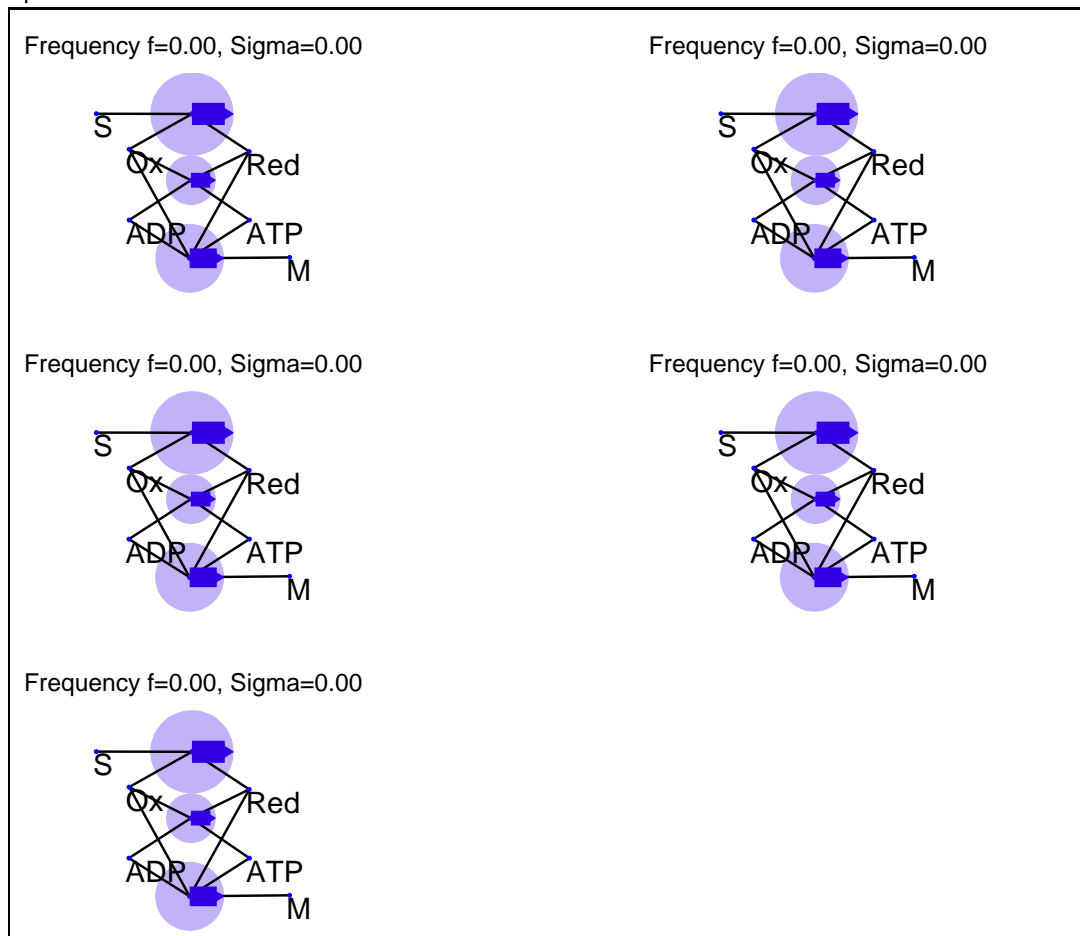


Figure 7: Spontaneous oscillations (or tendencies towards them) for various circular frequencies  $\omega$ . If the maximal fitness curvatures  $\lambda$  is positive, the rhythm is beneficial (local expansion; arrows: absolute changes).