

## Enzyme rhythms in model rainer\_1.speedy - spontaneous oscillations

Model name: rainer\_1

### o Optimisation problem

- Protein turnover time  $1 \text{ s} = 0.0167 \text{ min}$
- Perturbed parameter(s) :  $O_{2\text{ext}}$
- Perturbation frequency  $f$  :  $1/\text{s}$  (period 1 s)
- Scored quantity: BM dilution
- 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: 0
- spontaneous\_rhythm: 1
- spontaneous\_rhythm\_at\_omega: 1
- has\_spontaneous\_rhythm\_and\_inactive\_enzymes: 0

### o Beneficial self-induced oscillation found

- Maximum principal synergy found (in tested range) at frequency  $f = 1.78/\text{s}$  (period 0.562 s)
- Maximum fitness found (in tested range) at frequency  $f = 0.501/\text{s}$  (period 2 s)

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

- Change by perturbation alone (xx):  $-9.34\text{e-}07$

### o Self-induced oscillations?

- Maximally self-induced oscillations (in tested range) at  $f = 1.78$ , principal synergy 0.0195
- Beneficial self-induced oscillations found at frequency  $f = 1/\text{s}$  (principal synergy = 0.0155)
- Predicted fitness change (self-induced, 2nd order, amplitude below 1/2 of mean) at frequency  $f = 1$ :  $6.62\text{e-}05$
- Predicted maximal fitness change (self-induced, numeric opt, full amplitude constraints) at frequency  $f = 0.501$ :  $2.27\text{e-}07$

WARNING: an external rhythm is given and a self-induced rhythm has been found

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

- Fitness change (fitness-averaged):  $8.53\text{e-}05$
- Fitness change (state-averaged):  $8.53\text{e-}05$

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

- Fitness change (fitness-averaged) :  $4.71\text{e-}06$
- Fitness change (state-averaged):  $4.73\text{e-}06$

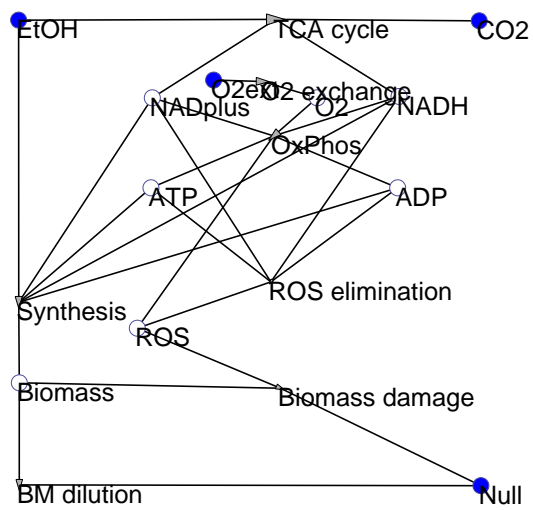


Figure 1: Network and reference flux

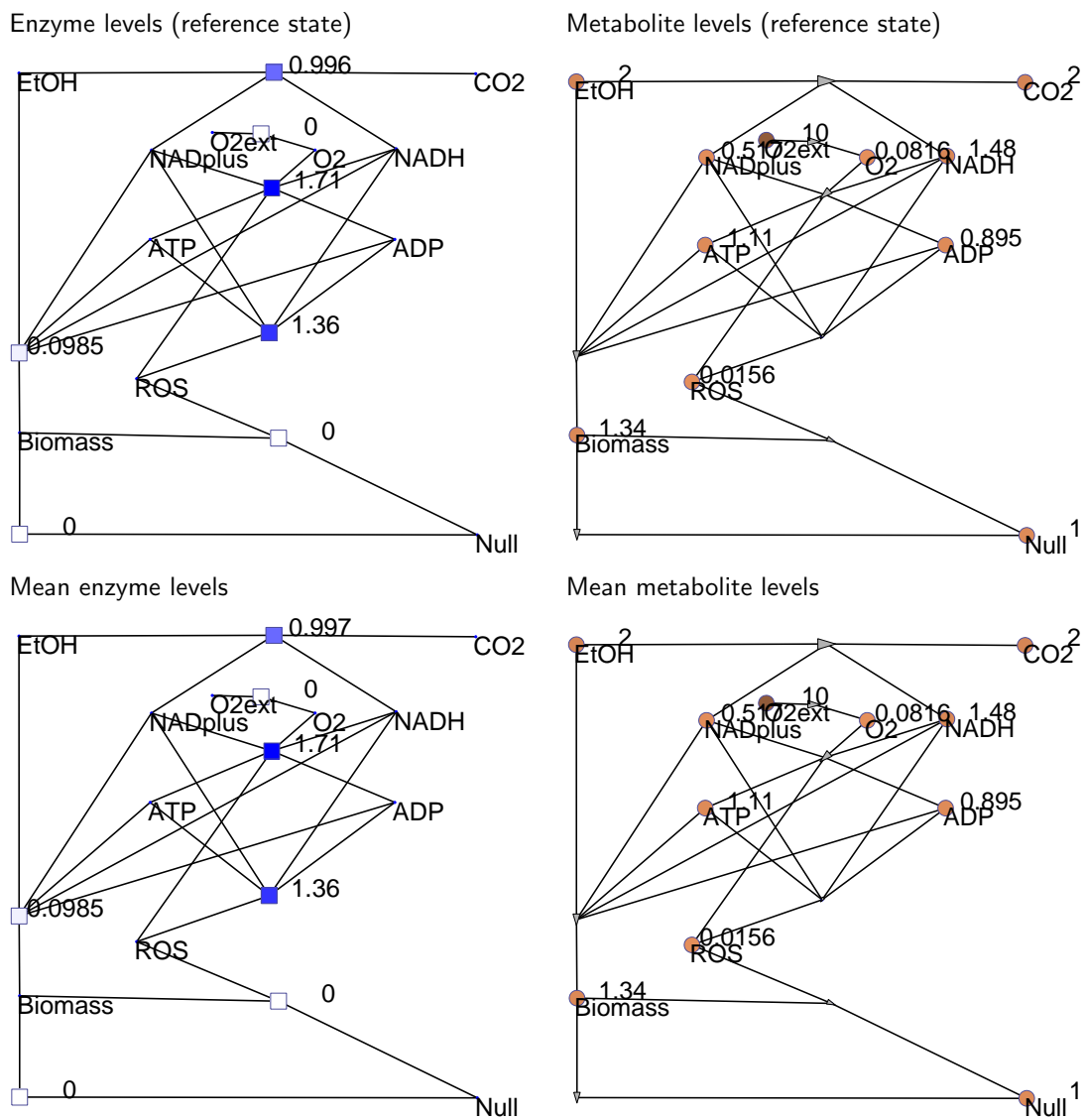


Figure 2: Reference state (top) and mean state during oscillation (bottom).

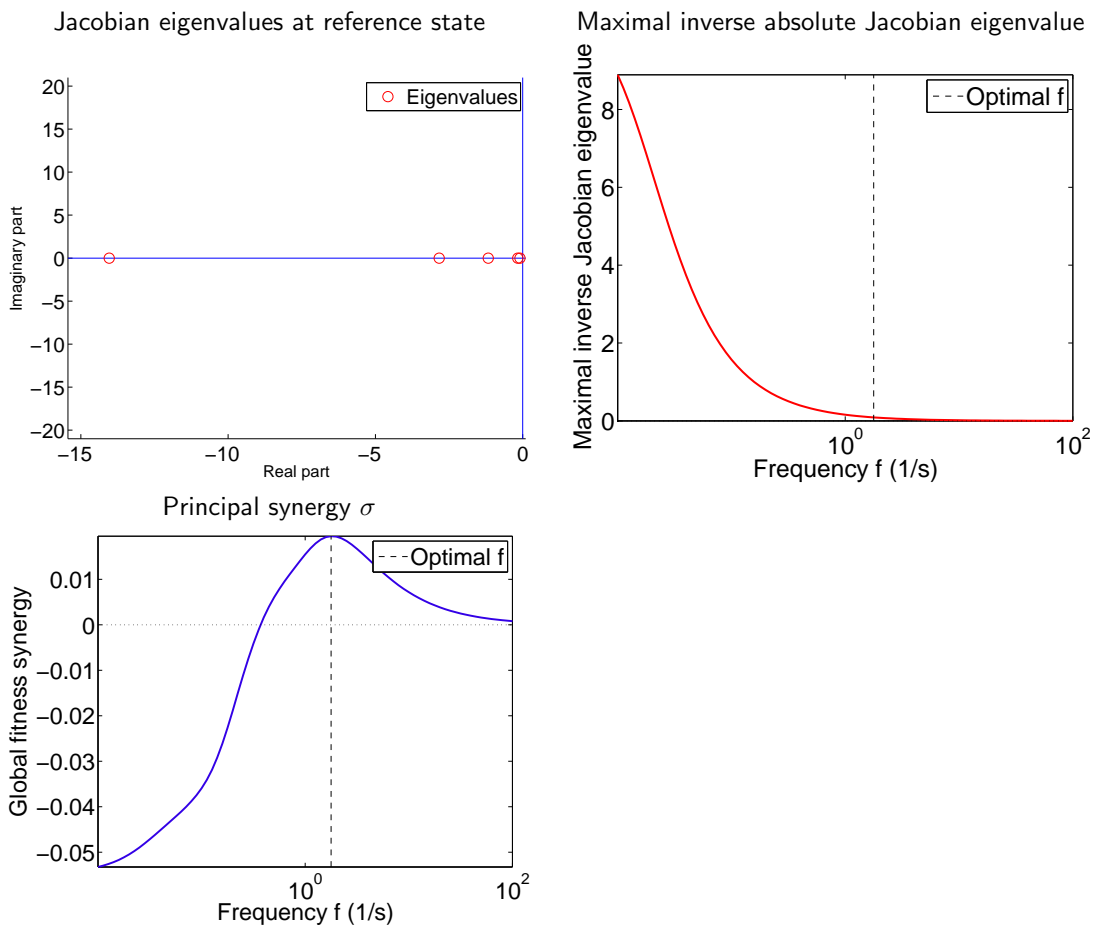
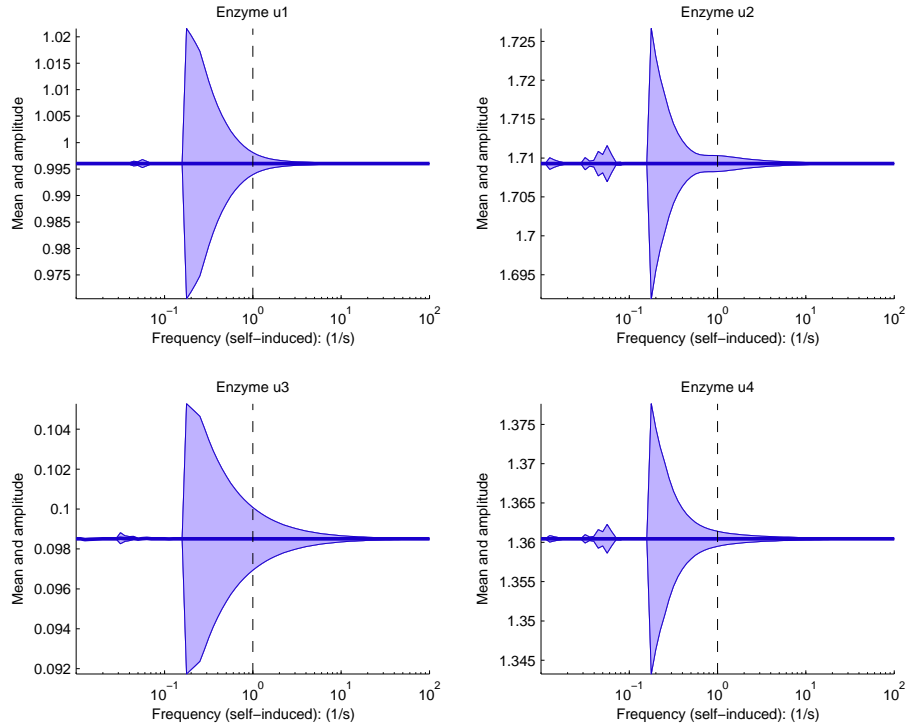
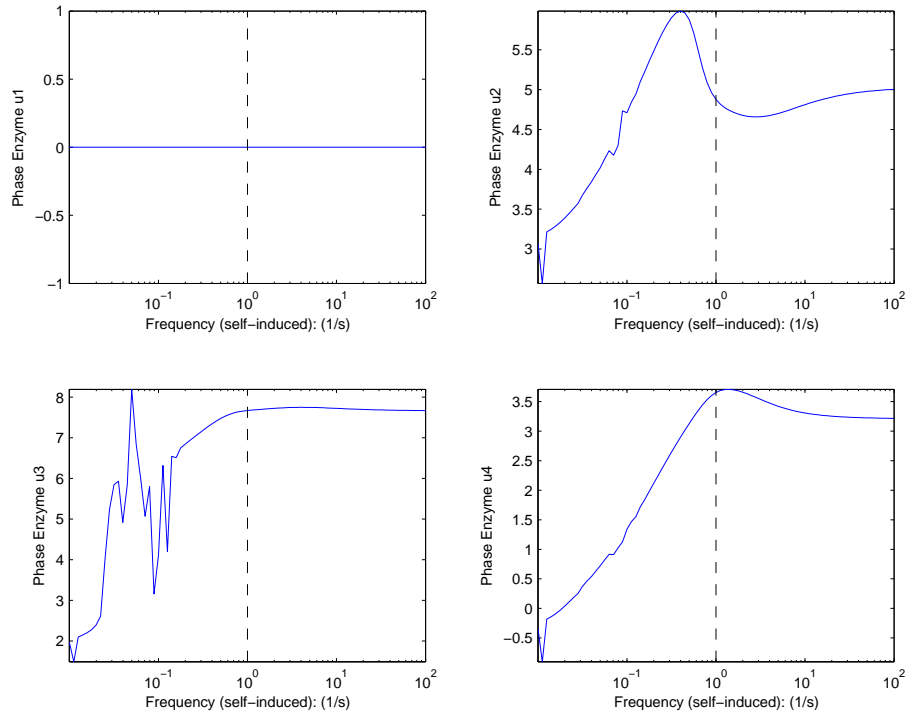


Figure 3: Control analysis: fitness curvatures. Left: Frequency-dependent fitness curvature eigenvalues. Right: relative sizes and phases of the individual enzyme levels (components of the leading fitness curvature eigenvector).

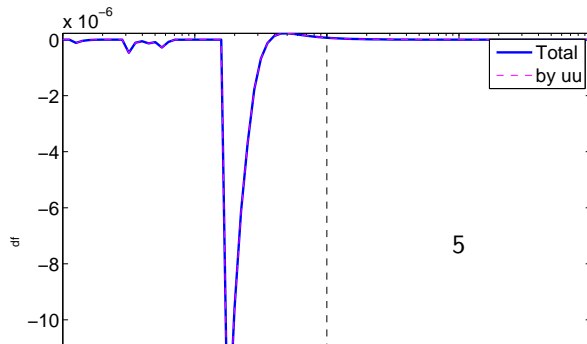
Protein level and enzyme activity (mean and amplitude)



Phase angles  $[0, 2\pi]$



Fitness change



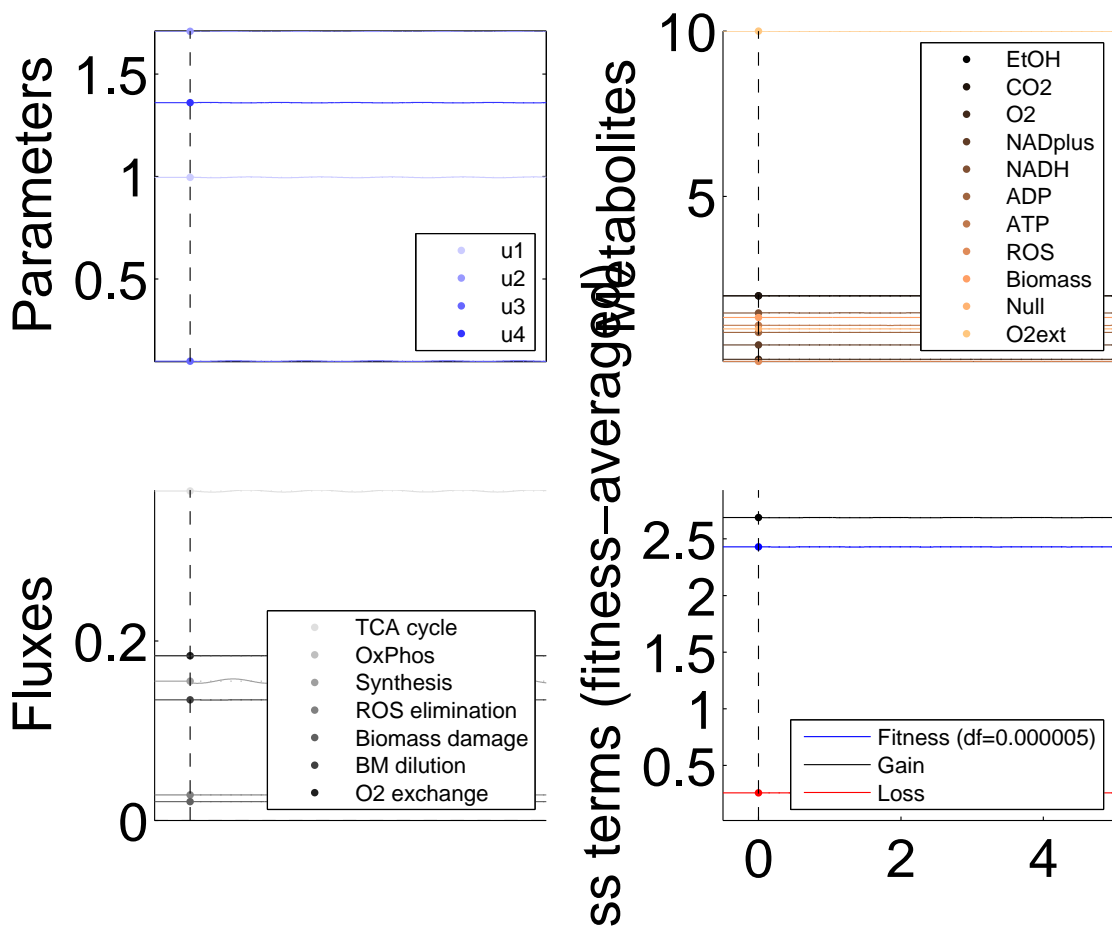
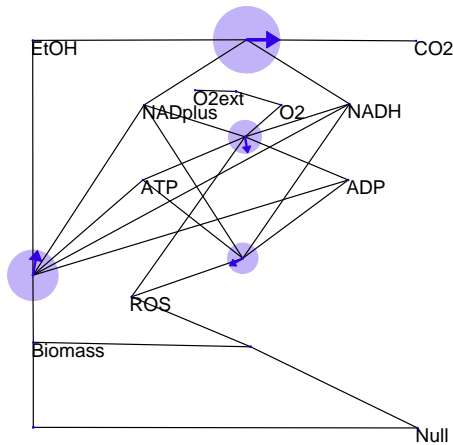
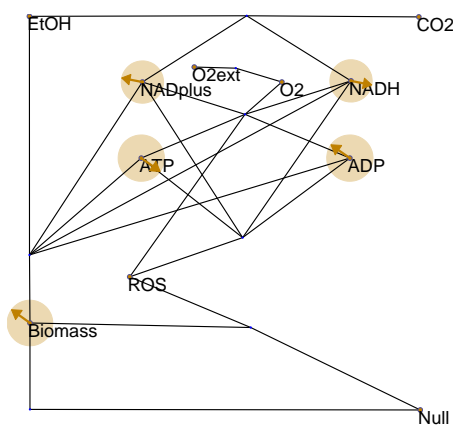


Figure 5: Numerical calculations: spontaneous oscillations. Perturbation frequency see first page.

### Enzyme rhythm



### Spontaneous oscillations (concentrations)



### Spontaneous oscillations (fluxes)

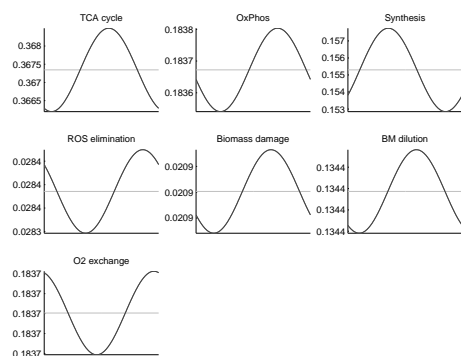
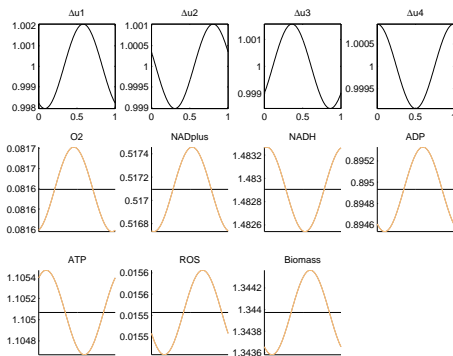
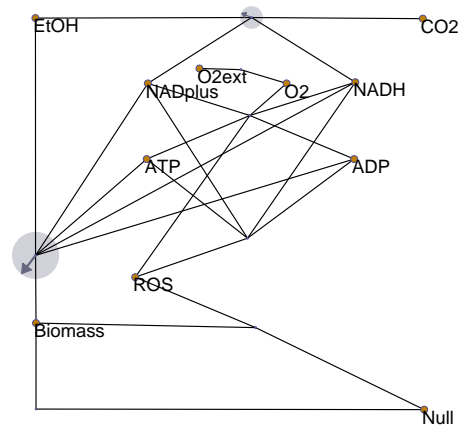


Figure 6: Spontaneous oscillations (local expansion; arrows: absolute changes). Perturbation frequency see first page.

Spontaneous oscillations

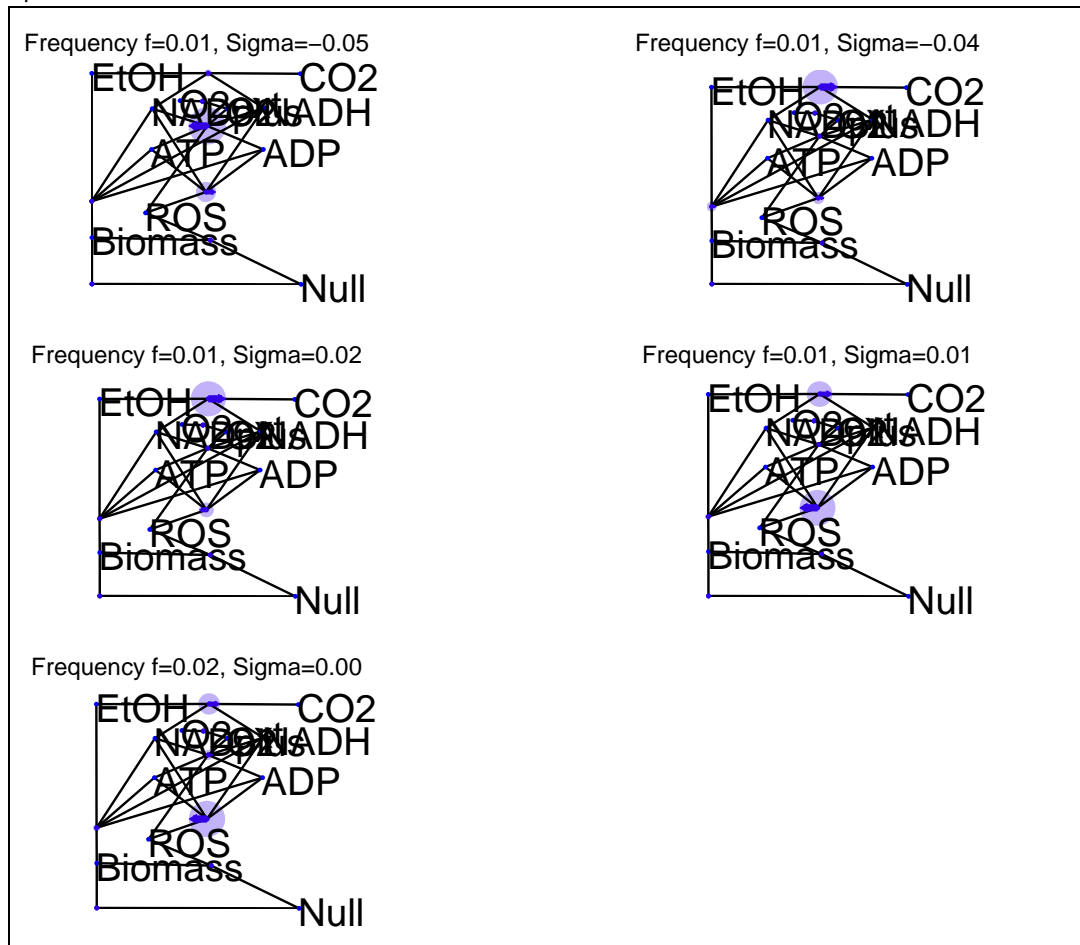


Figure 7: Spontaneous oscillations (or tendencies towards them) for various circular frequencies  $\omega$ . If the maximal fitness curvatures  $\lambda$  is positive, the rhythm is beneficial (local expansion; arrows: absolute changes).