

Enzyme rhythms in model ycm_cofactors.speedy

Model name: ycm_cofactors

o Optimisation problem

- Protein turnover time $1\text{ s} = 0.0167\text{ min}$
- Perturbed parameter(s) : $x_1\ x_2$
- Perturbation frequency f : $0.2/\text{s}$ (period 5 s)
- Scored quantity: R00200
- Scored quantity: R01512
- Scored quantity: R01600
- Scored quantity: R04779
- Scored quantity: R00235
- Scored quantity: GTP_irrev_ATP
- Scored quantity: Oxphos_Reduced_Acceptor_irrev_ATP
- Scored quantity: Oxphos_NADH_irrev_ATP
- Fitness-averaged fitness
- No posttranslational rhythms allowed
- Standard frequency considered f : $0.2/\text{s}$ (period 5 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

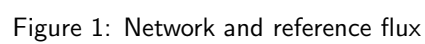
o No beneficial self-induced oscillation found

o Fitness changes after external perturbation at frequency $f=0.2/\text{s}$

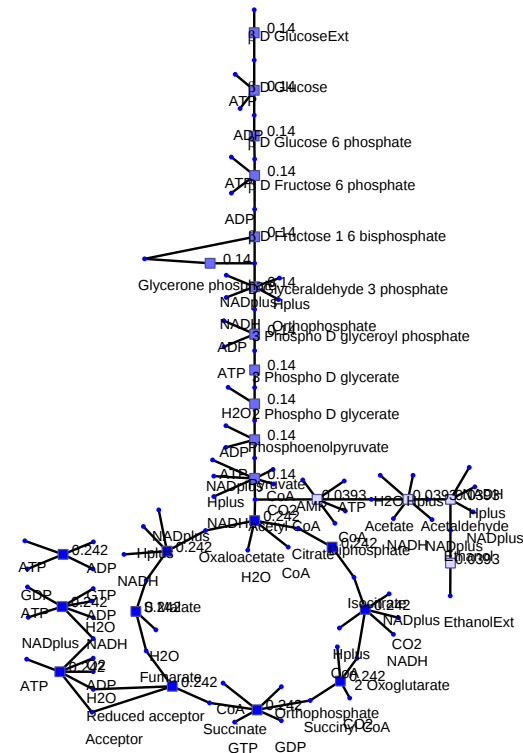
- Change by perturbation alone (xx): 0.00402
- Change by adaption synergies (xu): 3.99
- Change by periodic enzyme (uu): -0.901
- Change by enzyme mean shift (u): $-4.36\text{e-}09$
- Total fitness change : 3.09
- Fitness gain by adaption : 3.09
- Maximum adaptive fitness found (in tested range) at frequency $f=0.01/\text{s}$ (period 100 s)
- Predicted maximal fitness change (adaptive, numeric opt, full amplitude constraints) at frequency $f=0.01$: 4.15

o Self-induced oscillations?

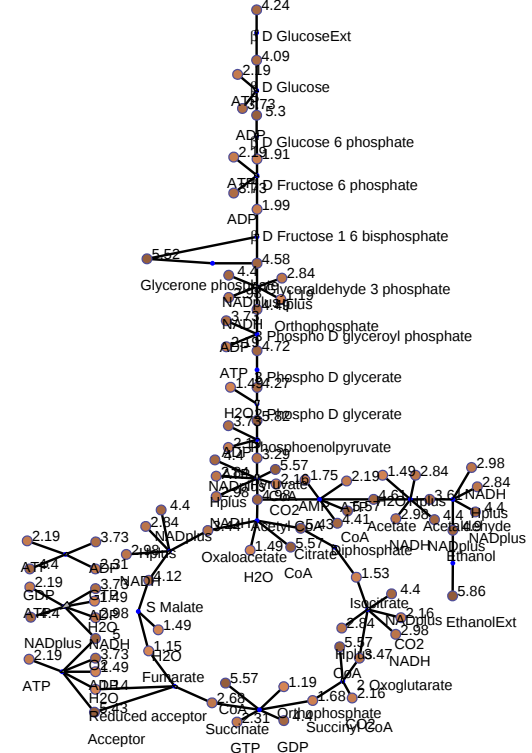
- No beneficial self-induced oscillations (2nd order, amplitude below 1/2 of mean) found at frequency $f=0.2/\text{s}$ (principal synergy = -0.636): Predicted fitness change -0.00083



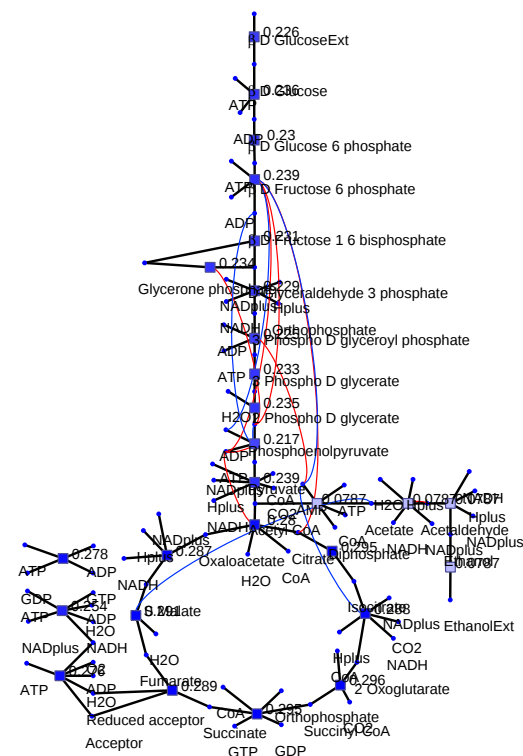
Enzyme levels (reference state)



Metabolite levels (reference state)



Mean enzyme levels



Mean metabolite levels

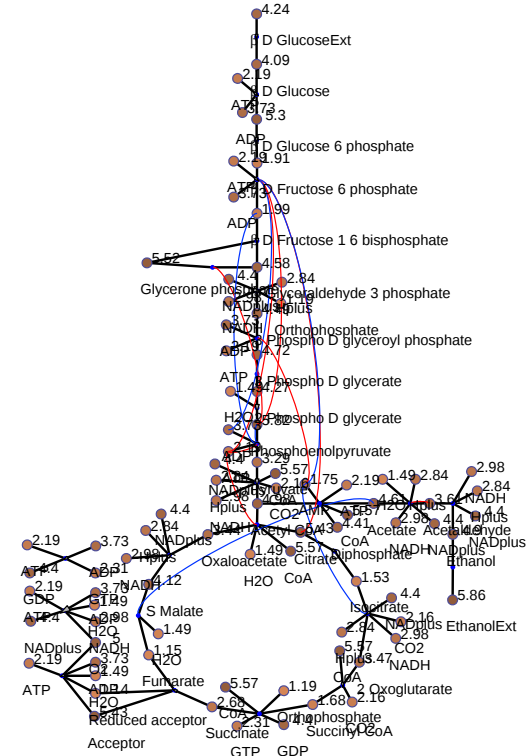
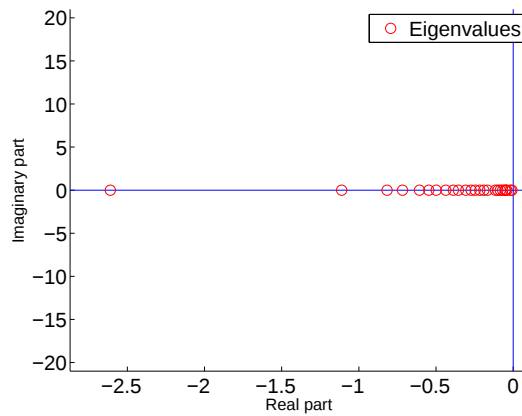
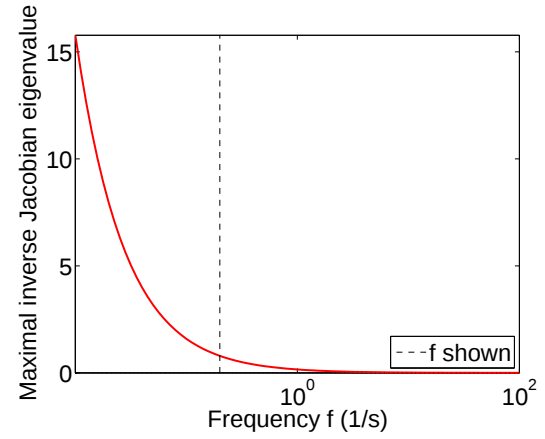


Figure 2: Reference state (top) and mean state during oscillation (bottom).

Jacobian eigenvalues at reference state



Maximal inverse absolute Jacobian eigenvalue



Principal synergy σ

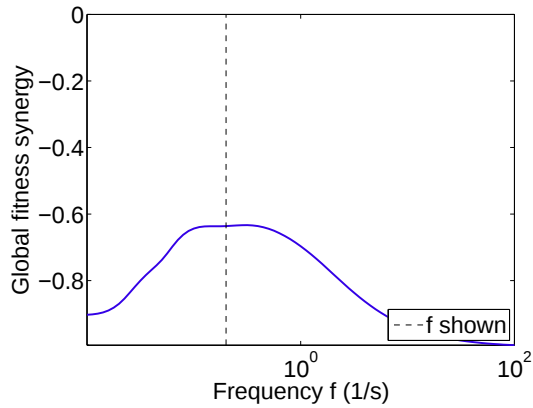
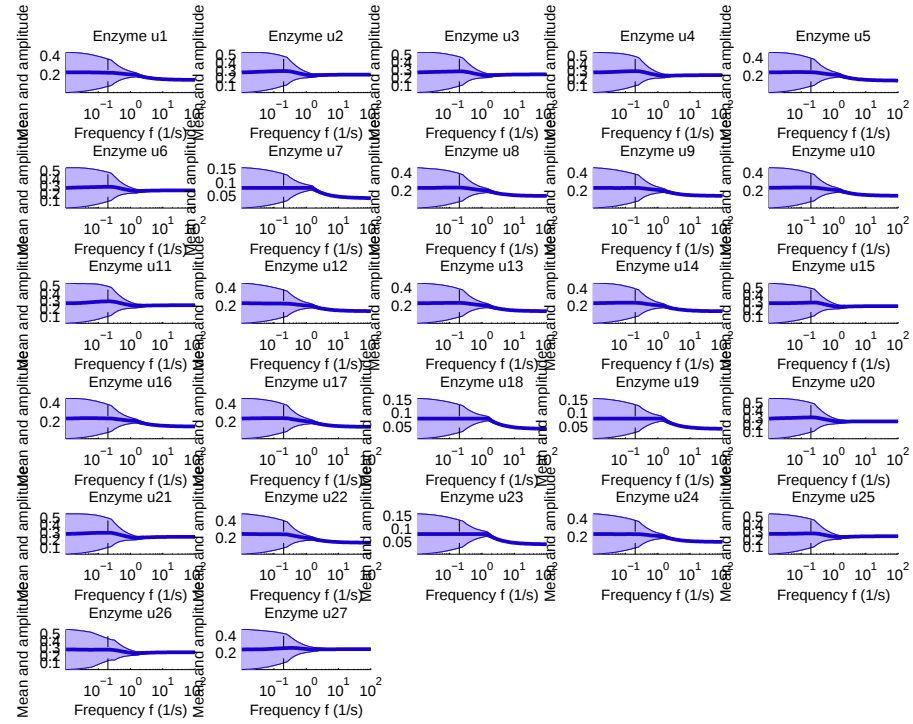
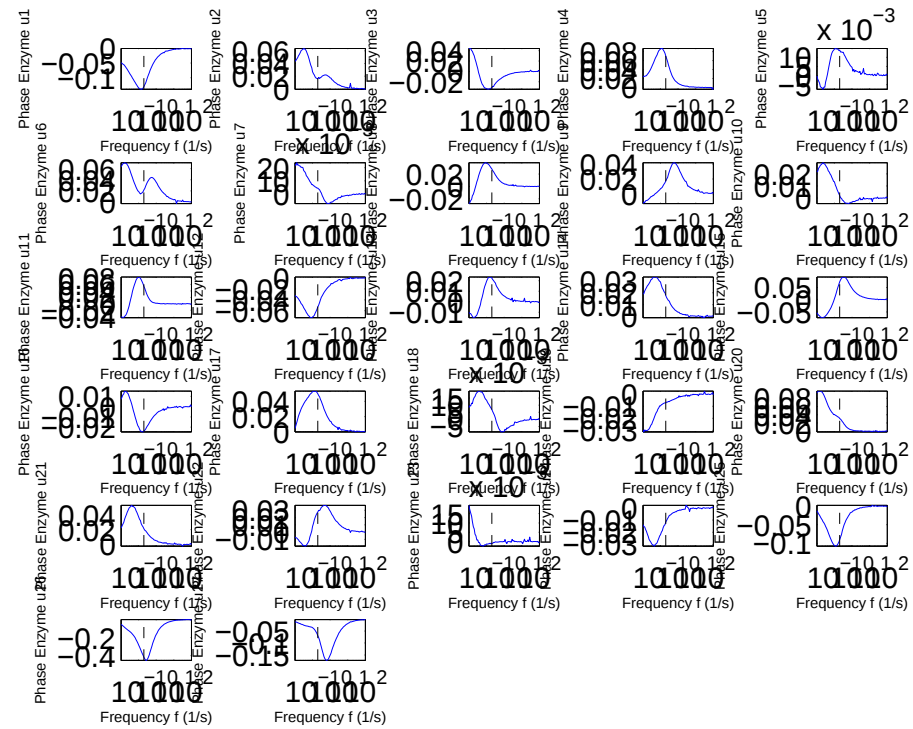


Figure 3: Control analysis. Left: Global fitness synergy (maximal fitness curvature eigenvalue), as a function of the frequency. Right: Relative amplitudes of individual enzymes for the least wasteful enzyme mode (components of the leading fitness curvature eigenvector).

Protein level and enzyme activity (mean and amplitude)



Phase angles $[0, 2\pi]$



Fitness change

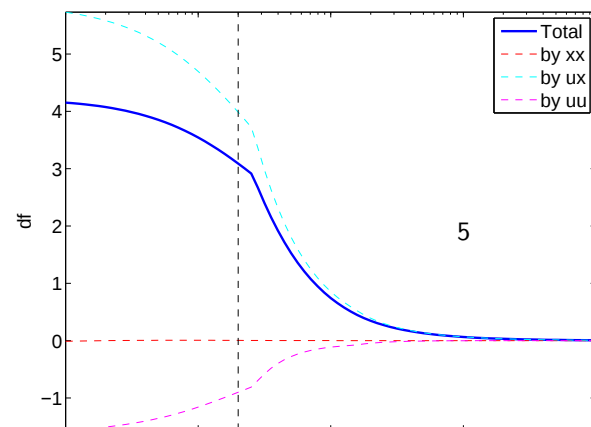
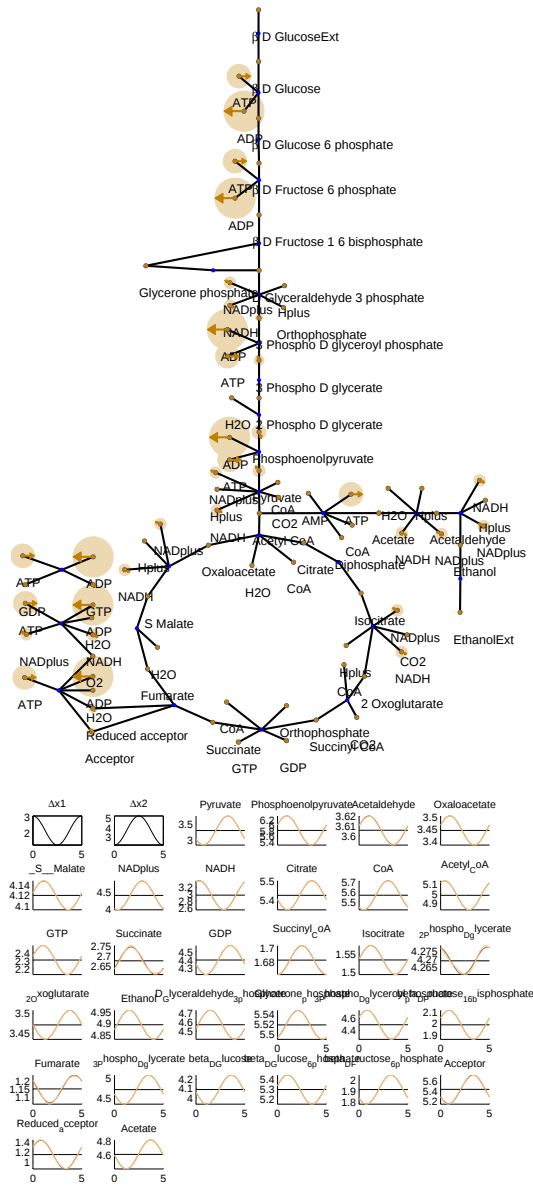


Figure 5: Numerical calculations: responsive oscillations (curves). Dynamic effects of oscillations. The panels show different types of variables: (i) Optimal periodic enzyme levels; (ii) internal metabolite levels; (iii) reaction fluxes; (iv) fitness, benefit, and cost. Perturbation frequency see first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

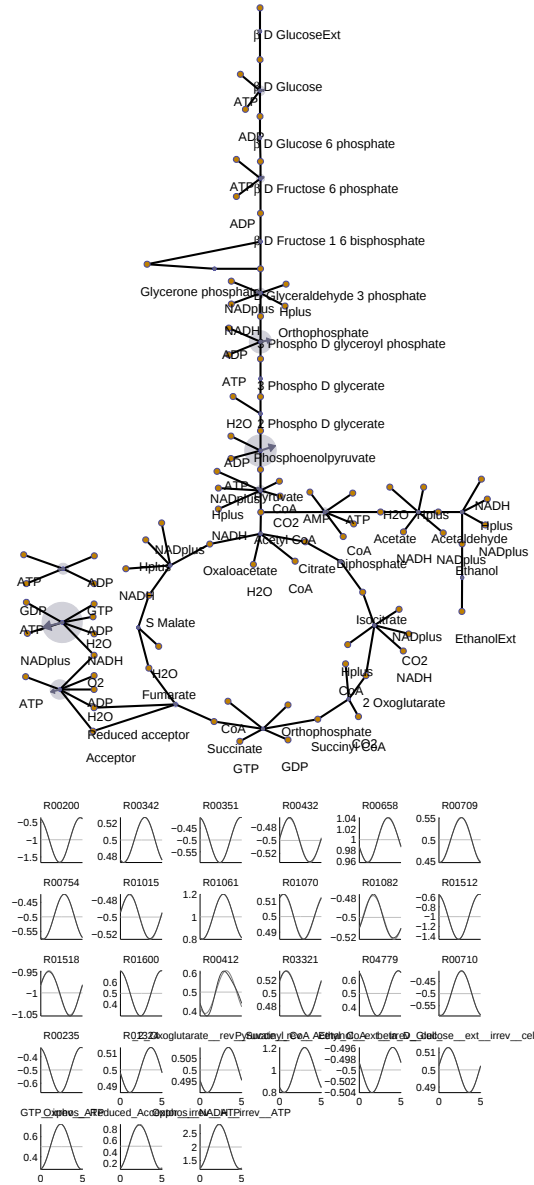
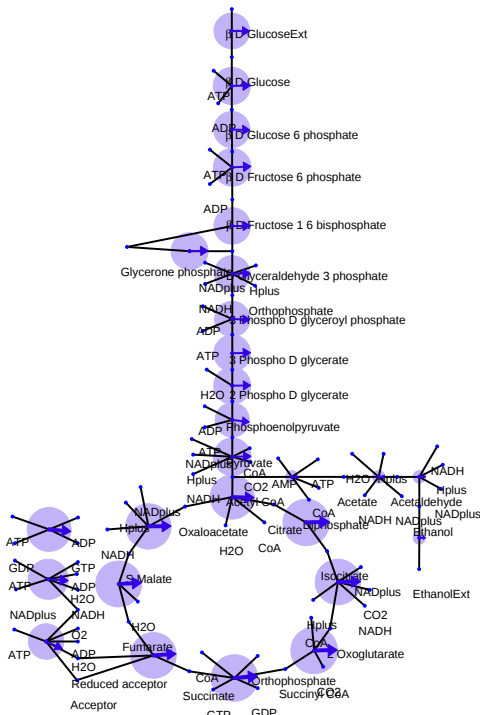
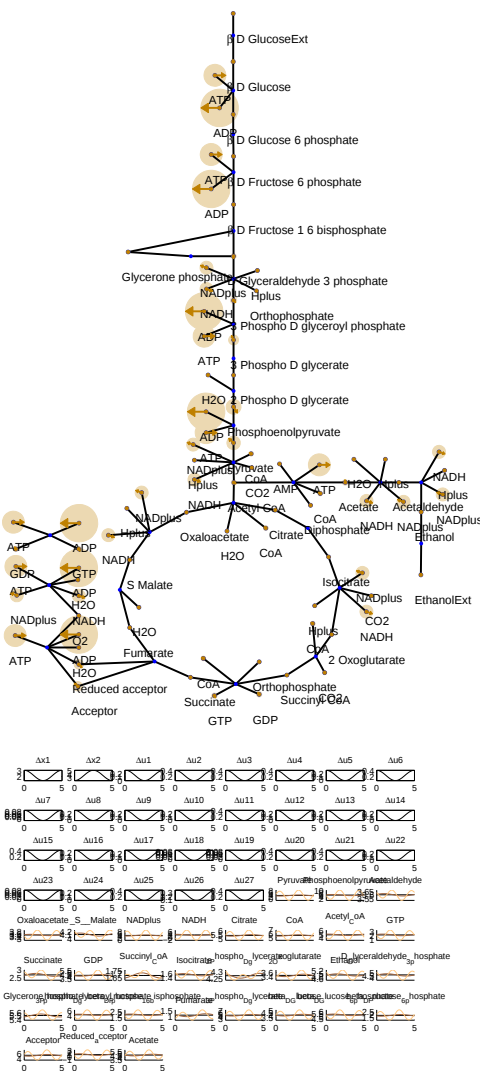


Figure 7: Responsive oscillations (local expansion; arrows: absolute changes) Perturbation frequency see first page.

Adaptive oscillations (enzymes)



Adaptive oscillations (metabolites)



Adaptive oscillations (fluxes)

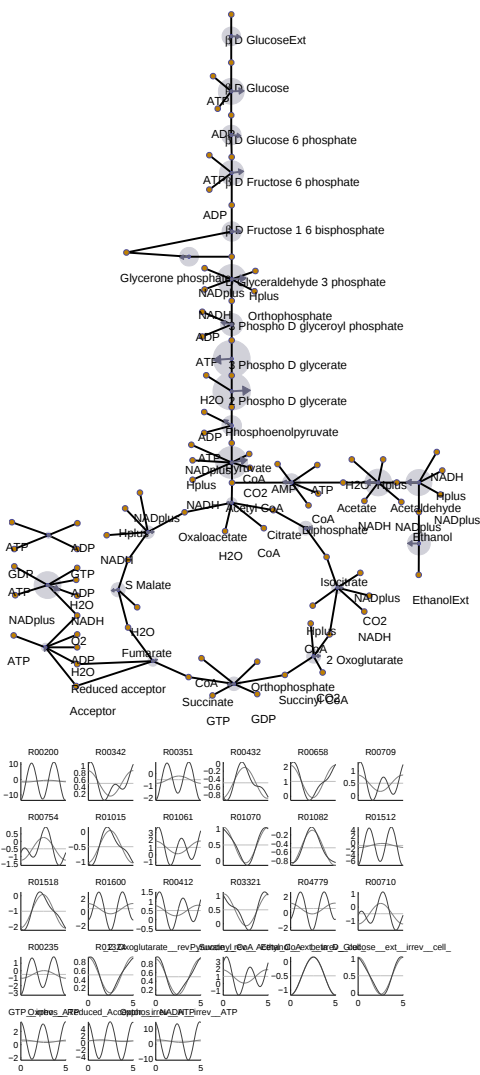
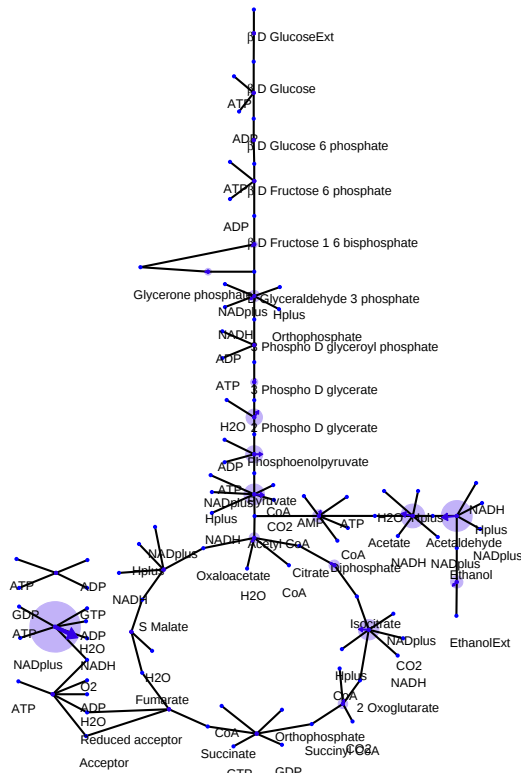


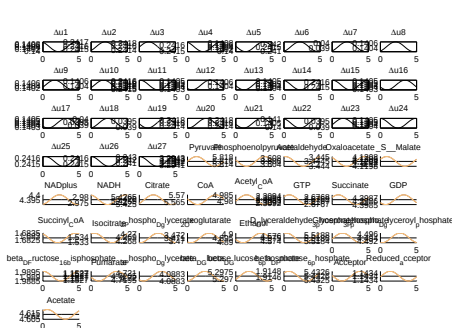
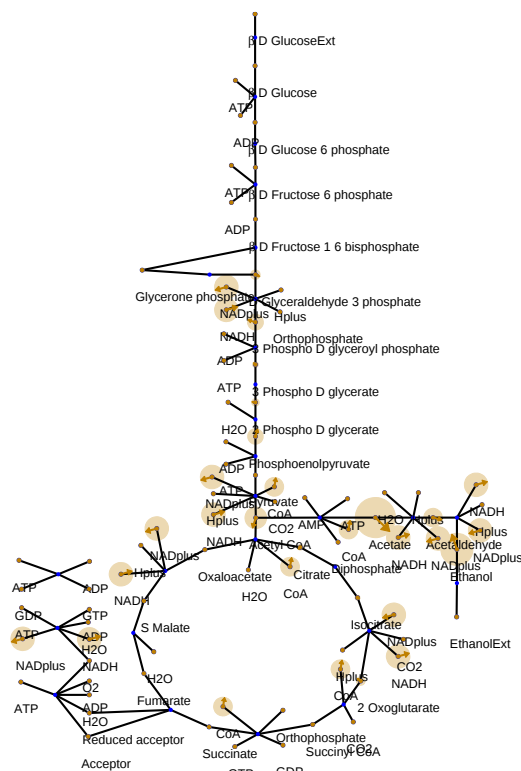
Figure 8: Adaption to forced oscillations (local expansion; arrows: absolute changes). Perturbation frequency see first page.

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

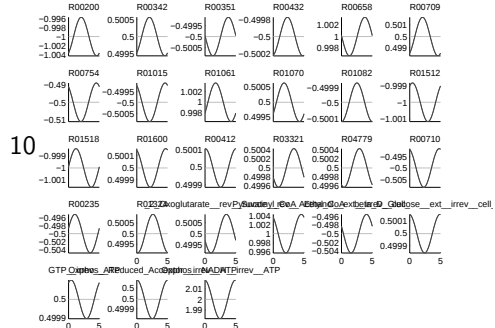
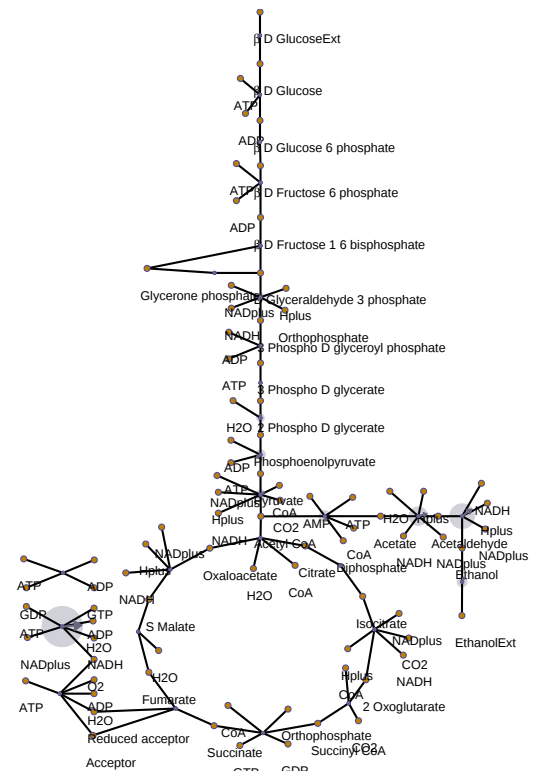
Enzyme rhythm



Spontaneous oscillations (concentrations)



Spontaneous oscillations (fluxes)



Adaptive

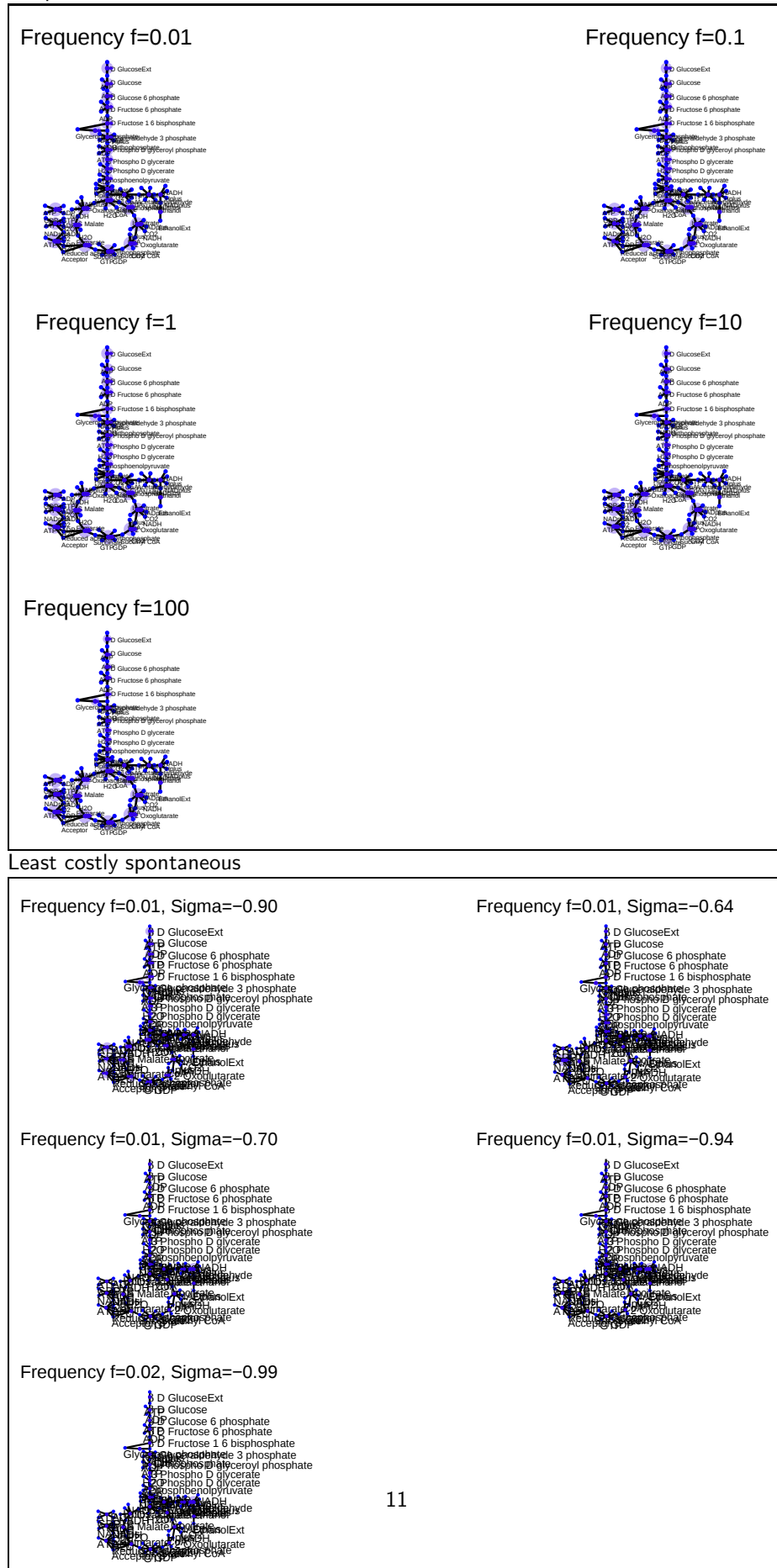


Figure 11: Potential oscillations at various frequencies (local expansion).