Enzyme rhythms in model ycm_oxygen.speedy

Model name: ycm_oxygen

o Optimisation problem
- Protein turnover time 1 s = 0.0167 min
- Perturbed parameter(s) : x11
- Perturbation frequency f : 0.2/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/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/s
- Change by perturbation alone (xx): 0.000117
- Change by adaption synergies (xu): 0.35
- Change by periodic enzyme (uu): -0.146
- Change by enzyme mean shift (u): -4.75e-10
- Total fitness change : 0.205
- Fitness gain by adaption : 0.205
- Maximum adaptive fitness found (in tested range) at frequency f =0.01/s (period 100 s)
- Predicted max. fitness change (adaptive, num. opt, full ampl. constraints) at frequency f =0.01: 0.242

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

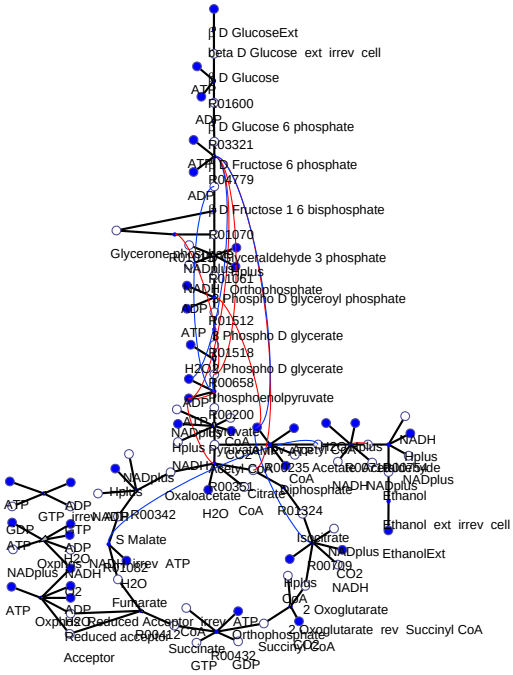
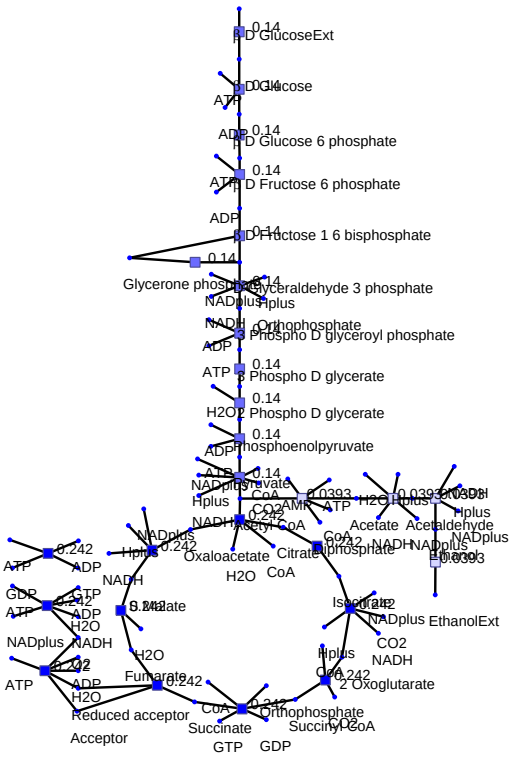
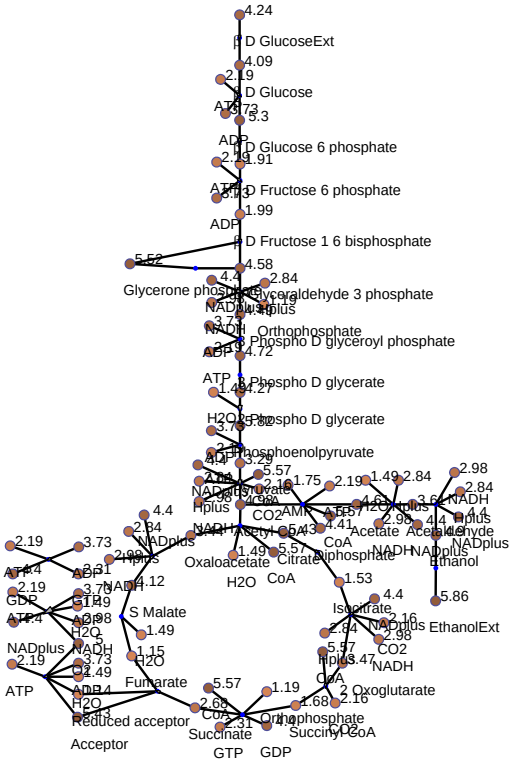


Figure 1: Network and reference flux

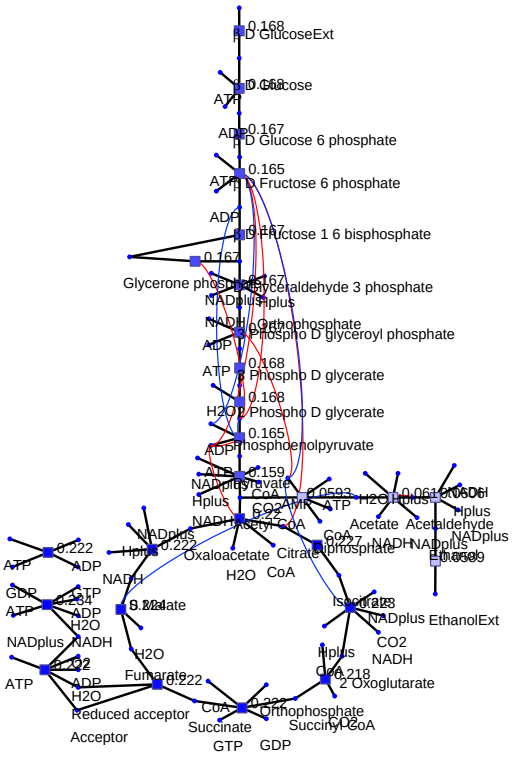
Enzyme levels (reference state)



Metabolite levels (reference state)



Mean enzyme levels



Mean metabolite levels

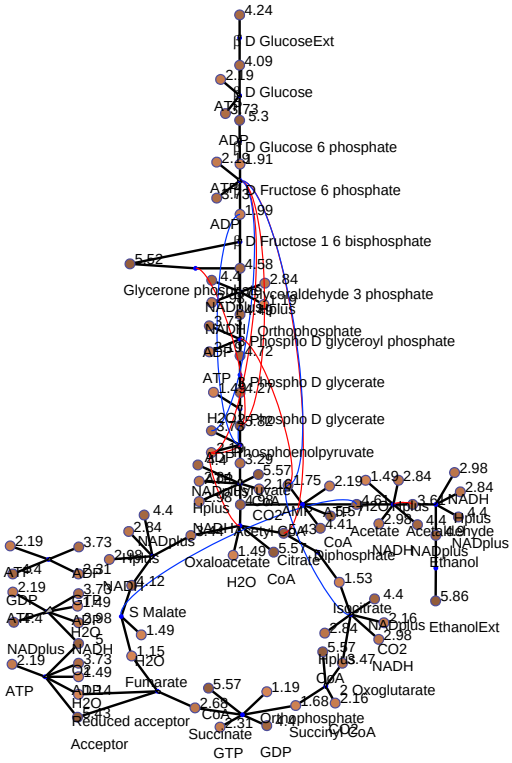


Figure 2: Reference state (top) and mean state during oscillation (bottom).

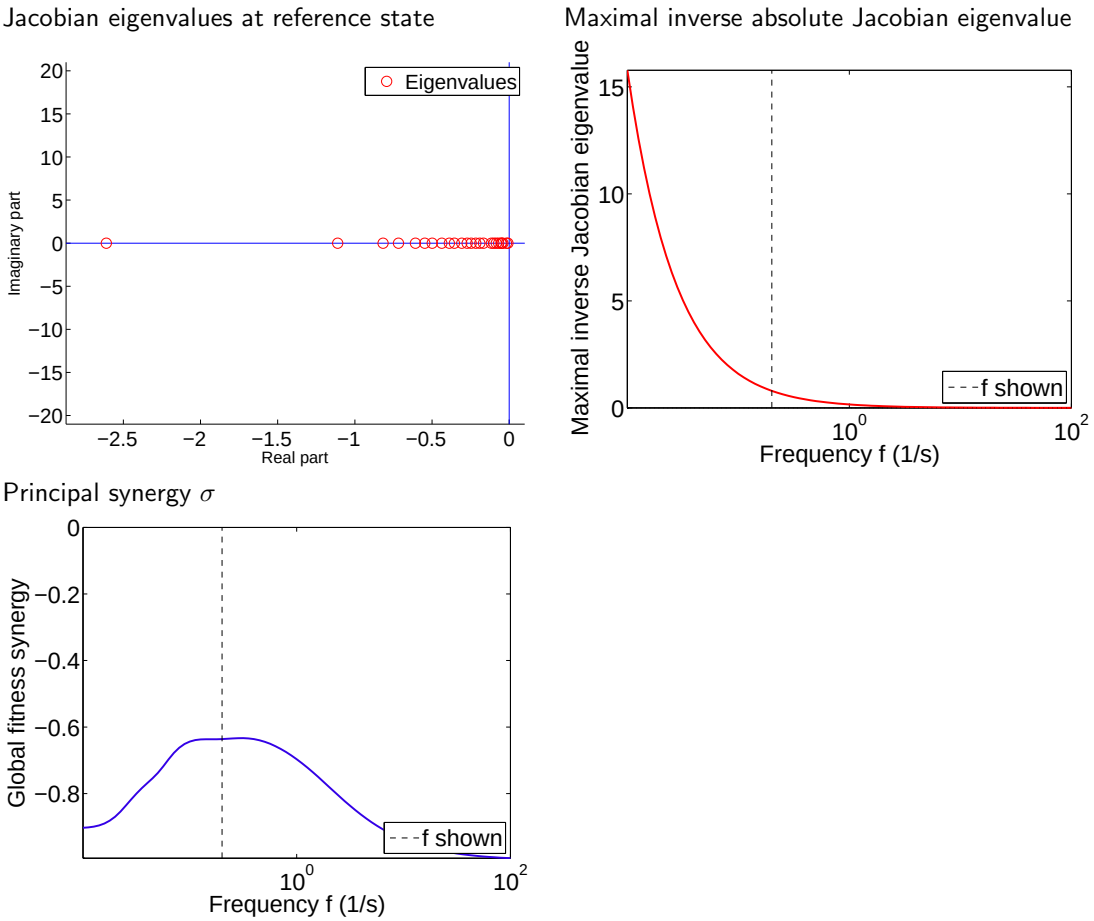
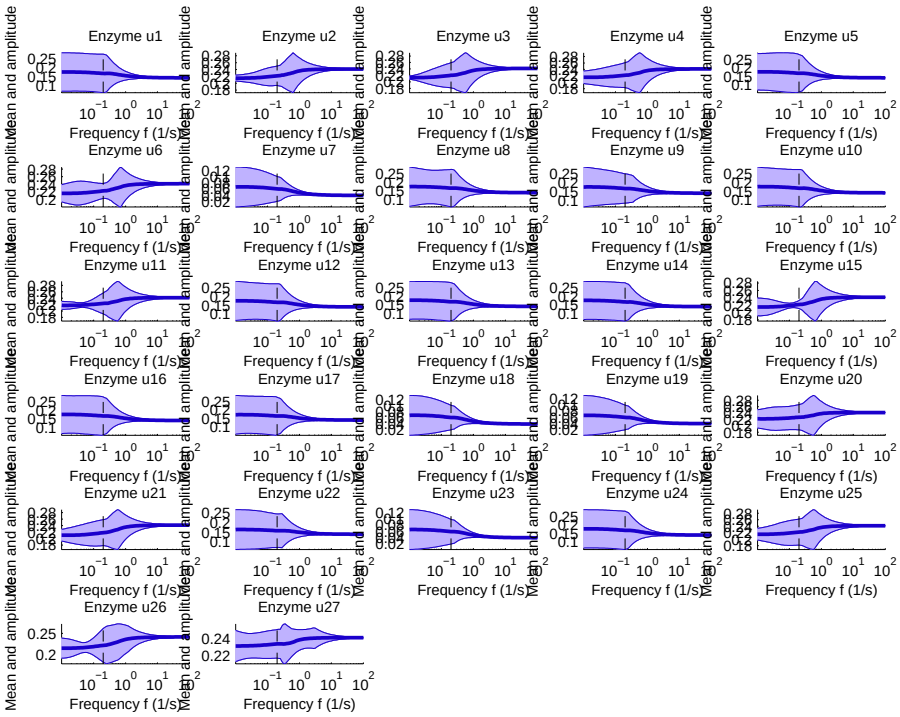
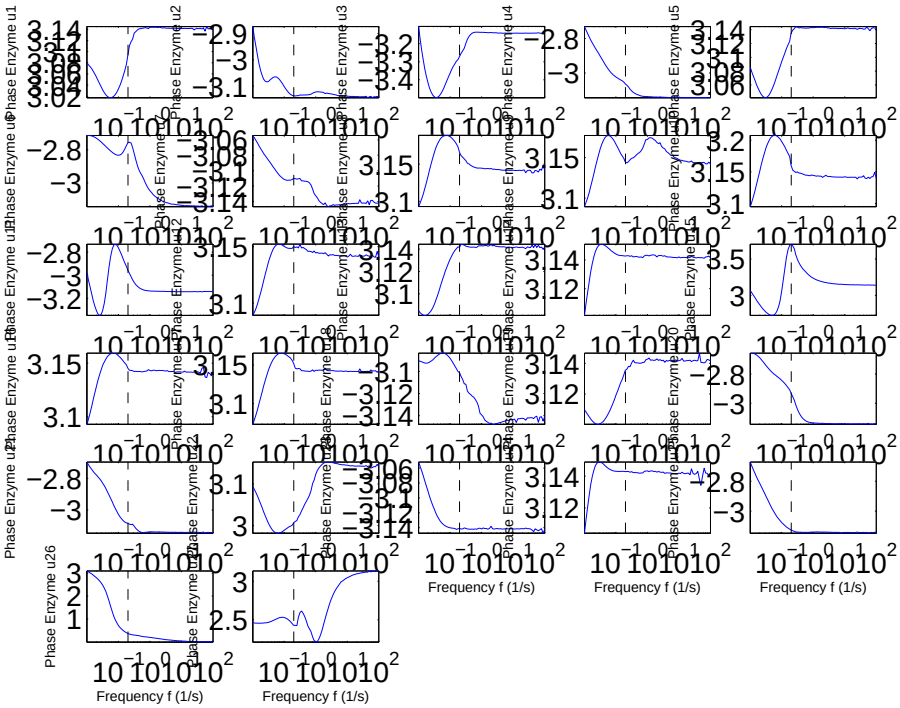


Figure 3: Control analysis. Left: Global fitness synergy (maximal fitness curvature eigenvalue), as a function of the frequency. Right: Relative amplitudes of individual enzymes for the least wasteful enzyme mode (components of the leading fitness curvature eigenvector).

Protein level and enzyme activity (mean and amplitude)



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



Fitness change

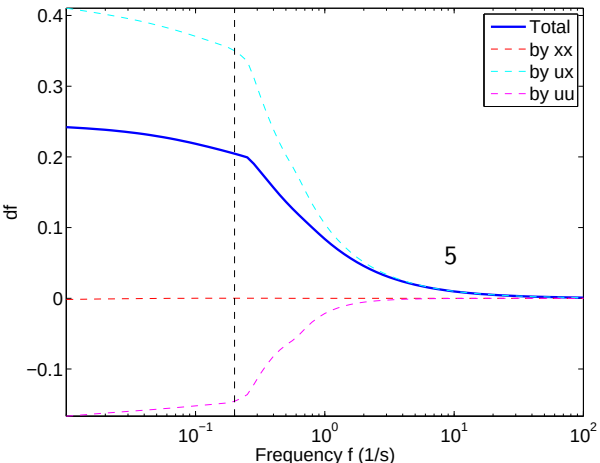


Figure 5: Numerical calculations: responsive oscillations (curves). Dynamic effects of oscillations. The panels show different types of variables: (i) Optimal periodic enzyme levels; (ii) internal metabolite levels; (iii) reaction fluxes; (iv) fitness, benefit, and cost. Perturbation frequency see first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

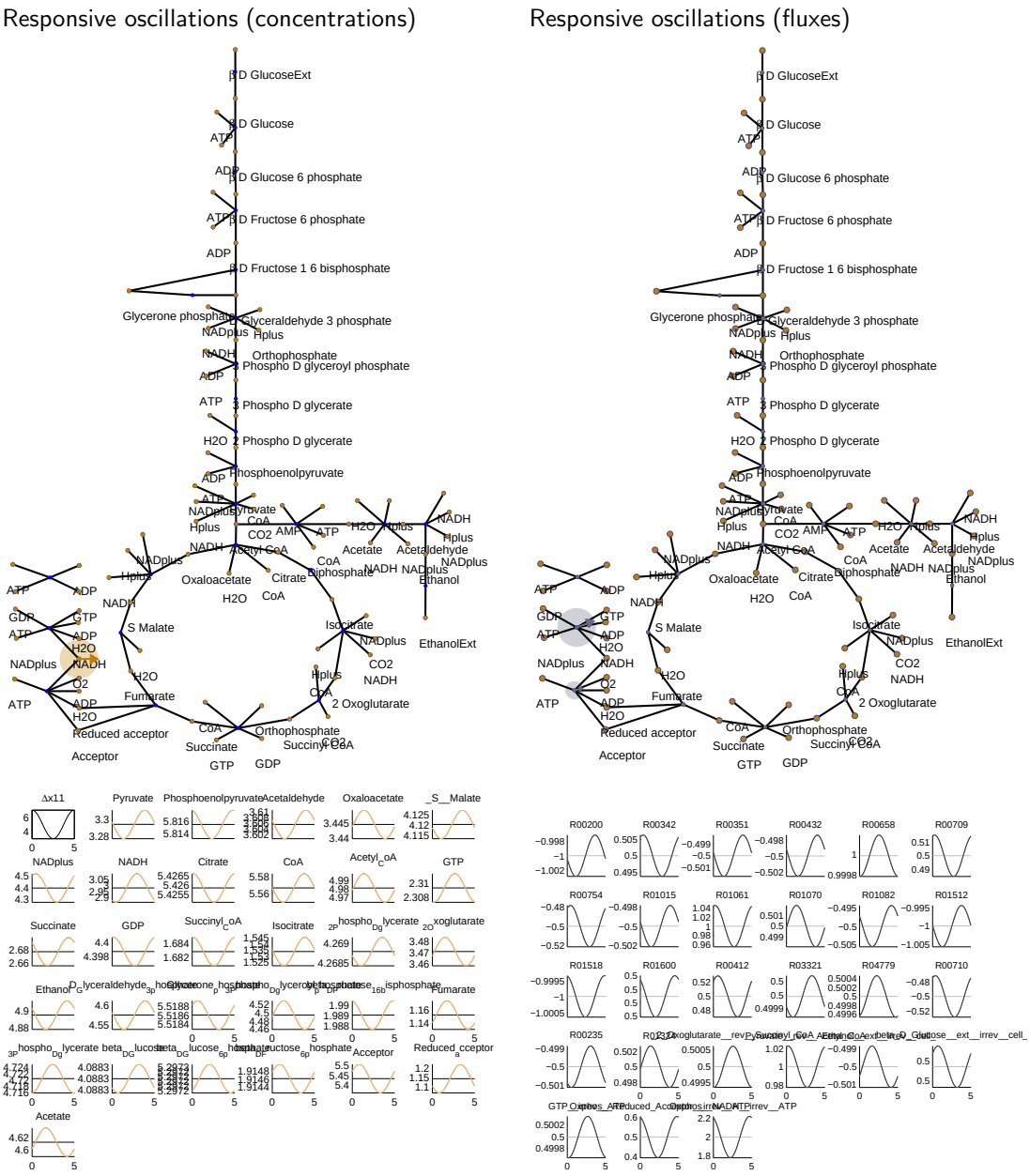
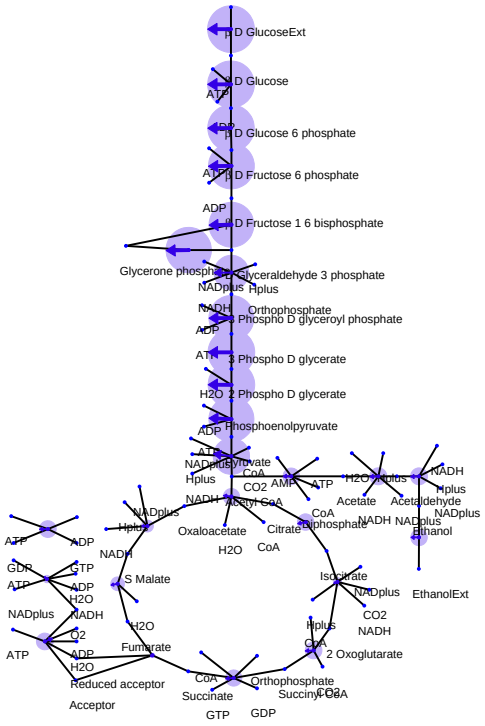
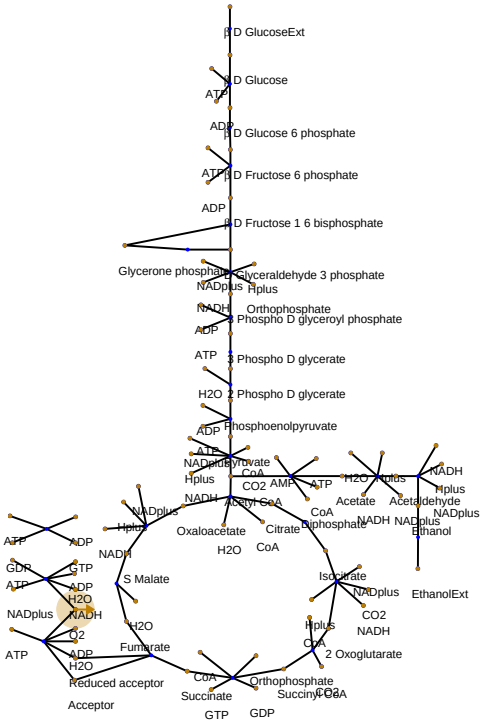


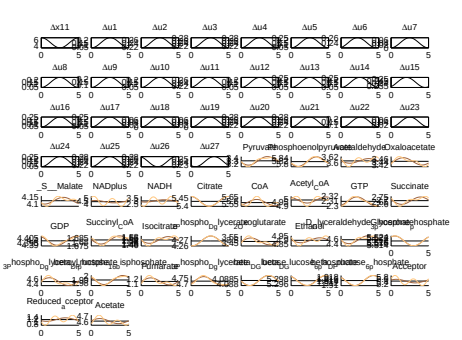
Figure 7: Responsive oscillations (local expansion; arrows: absolute changes) Perturbation frequency see first page.

Adaptive oscillations (enzymes)

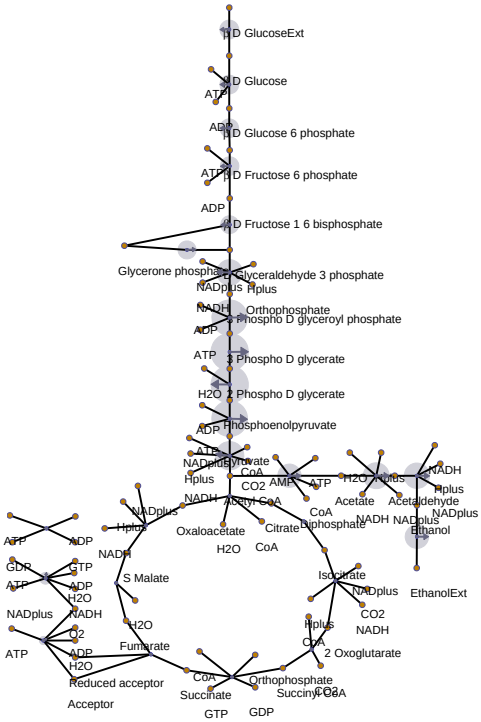


Adaptive oscillations (metabolites)





Adaptive oscillations (fluxes)



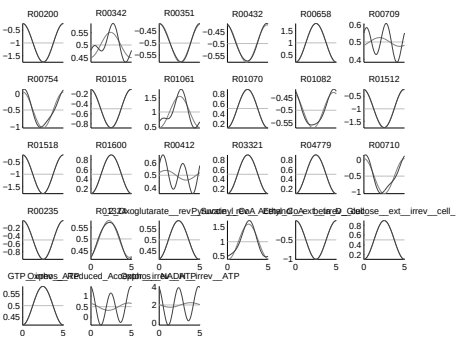
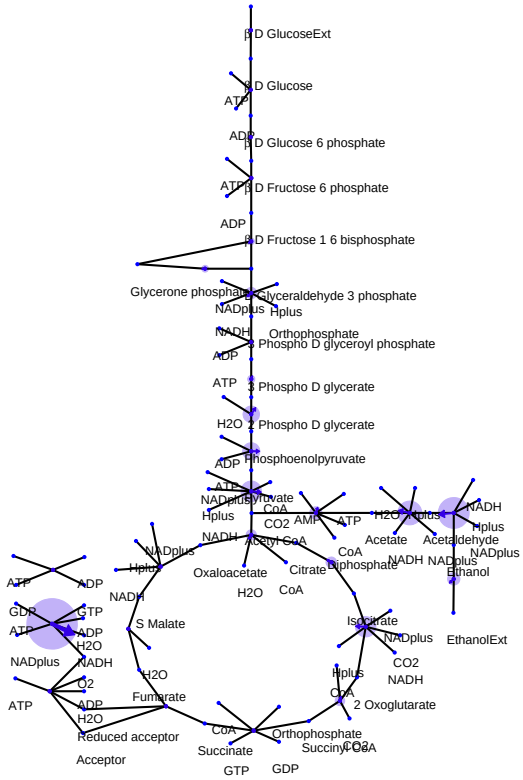


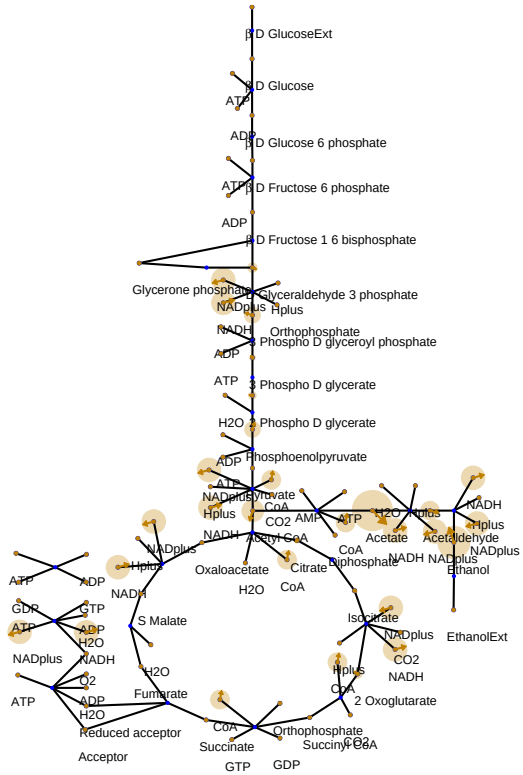
Figure 8: Adaption to forced oscillations (local expansion; arrows: absolute changes). Perturbation frequency see first page.

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

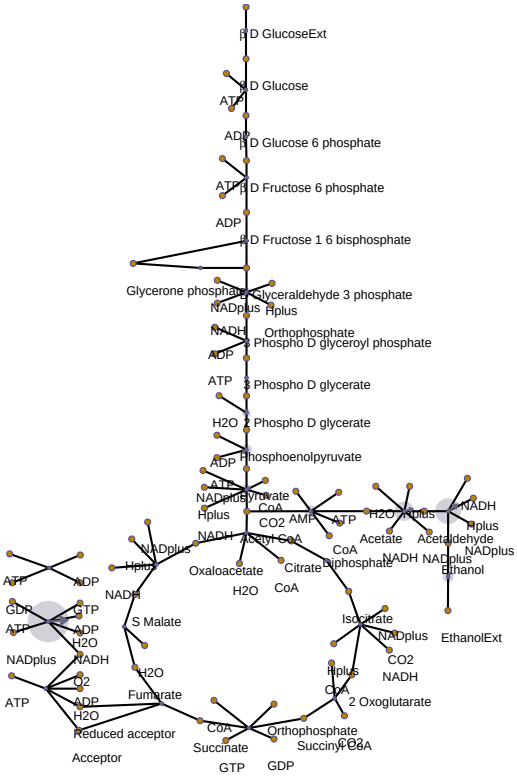
Enzyme rhythm

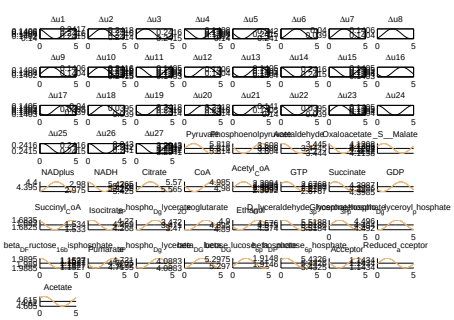


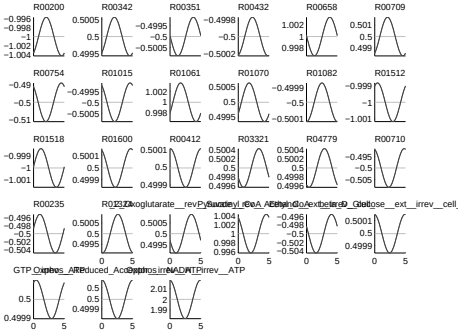
Spontaneous oscillations (concentrations)



Spontaneous oscillations (fluxes)

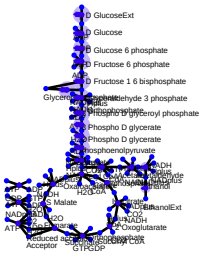




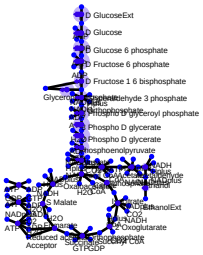


Adaptive

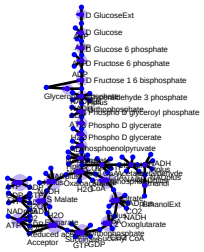
Frequency f=0.01



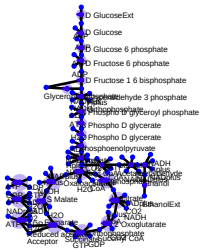
Frequency f=0.1



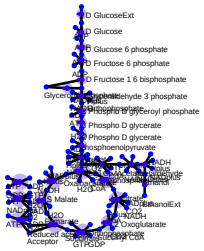
Frequency f=1



Frequency f=10

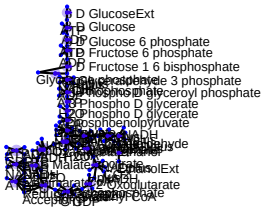


Frequency f=100

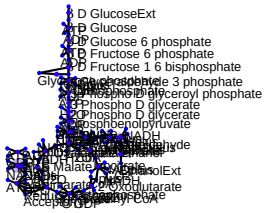


Least costly spontaneous

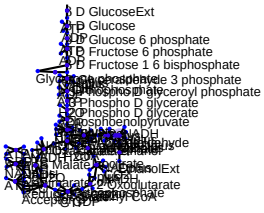
Frequency f=0.01, Sigma=−0.90



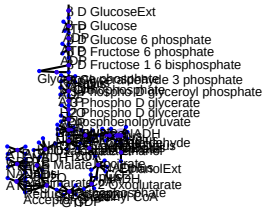
Frequency f=0.01, Sigma=−0.64



Frequency f=0.01, Sigma=−0.70



Frequency f=0.01, Sigma=−0.94



Frequency f=0.02, Sigma=−0.99

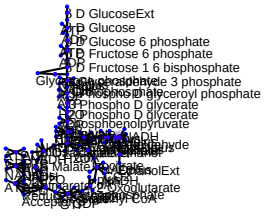


Figure 11: Potential oscillations at various frequencies (local expansion).