

## Enzyme rhythms in model one\_reaction.speedy

Model name: one\_reaction

### o Optimisation problem

- Protein turnover time  $1 \text{ s} = 0.0167 \text{ min}$
- Perturbed parameter(s) : S1
- Perturbation frequency  $f$  :  $0.1/\text{s}$  (period 10 s)
- Scored quantity: v1
- Fitness-averaged fitness
- No posttranslational rhythms allowed
- Standard frequency considered  $f$  :  $0.1/\text{s}$  (period 10 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 $f=0.1/\text{s}$

- Change by perturbation alone (xx):  $7.21\text{e-}08$
- Change by adaption synergies (xu): 0.118
- Change by periodic enzyme (uu):  $-0.0471$
- Change by enzyme mean shift (u):  $3.45\text{e-}13$
- Total fitness change : 0.0708
- Fitness gain by adaption : 0.0708
- Maximum adaptive fitness found (in tested range) at frequency  $f = 0.01/\text{s}$  (period 100 s)
- Predicted max. fitness change (adaptive, num. opt, full ampl. constraints) at frequency  $f = 0.01$ : 0.0749

### o Self-induced oscillations?

- No beneficial self-induced oscillations (2nd order, amplitude below 1/2 of mean) found at frequency  $f = 0.1/\text{s}$  (principal synergy =  $-0.5$ ): Predicted fitness change  $-0.0156$

### o Numerical calculation (responsive, $f=0.1$ )

- Fitness change (fitness-averaged):  $-3.61\text{e-}16$
- Fitness change (state-averaged):  $1.78\text{e-}15$

### o Numerical calculation (adaptive, $f=0.1$ )

- Fitness change (fitness-averaged): 0.072
- Fitness change (state-averaged): 0.118

### o Numerical calculation (self-induced rhythm, amplitude below 1/2 of mean, $f=0.1$ )

- Fitness change (fitness-averaged) : 0
- Fitness change (state-averaged):  $1.78\text{e-}15$

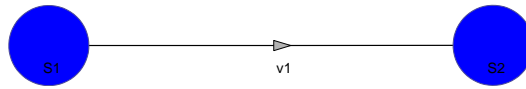


Figure 1: Network and reference flux

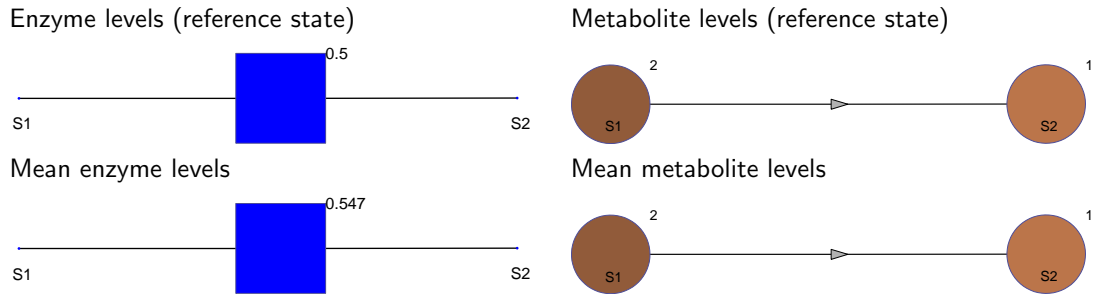


Figure 2: Reference state (top) and mean state during oscillation (bottom).

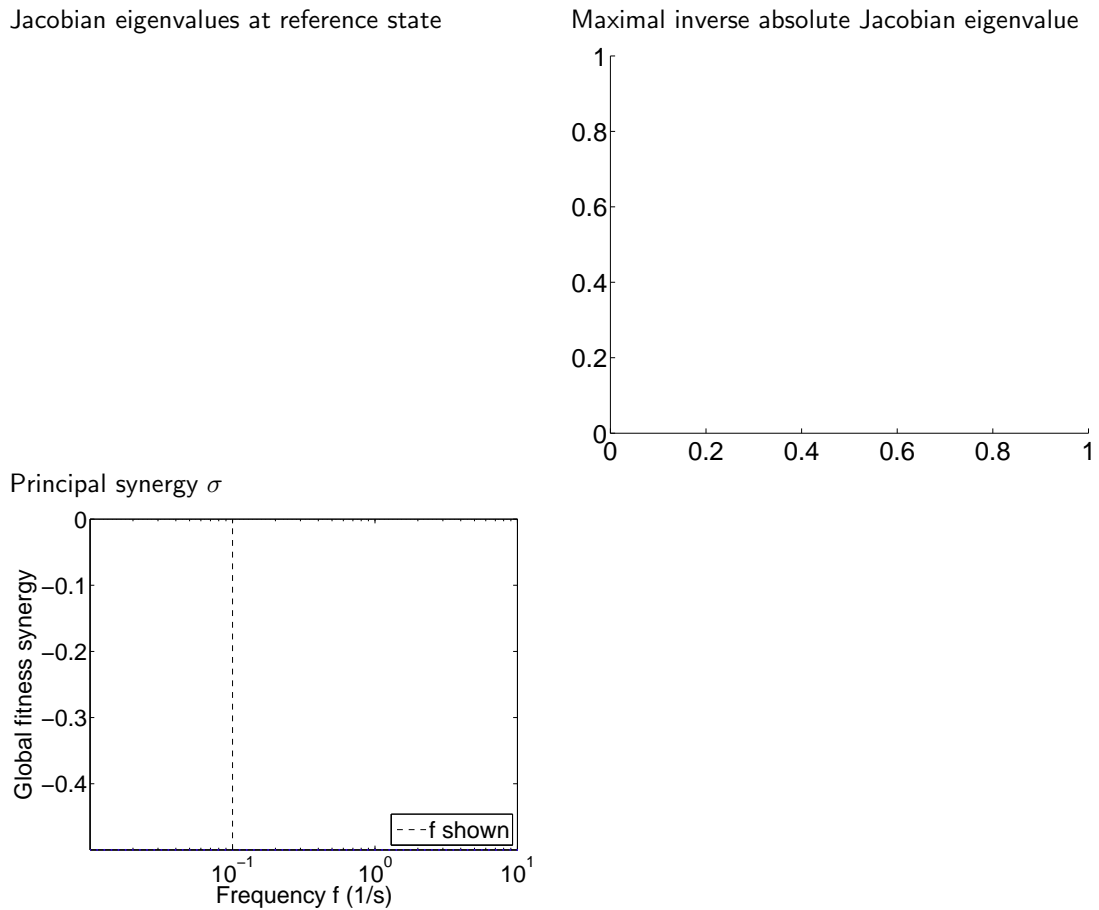
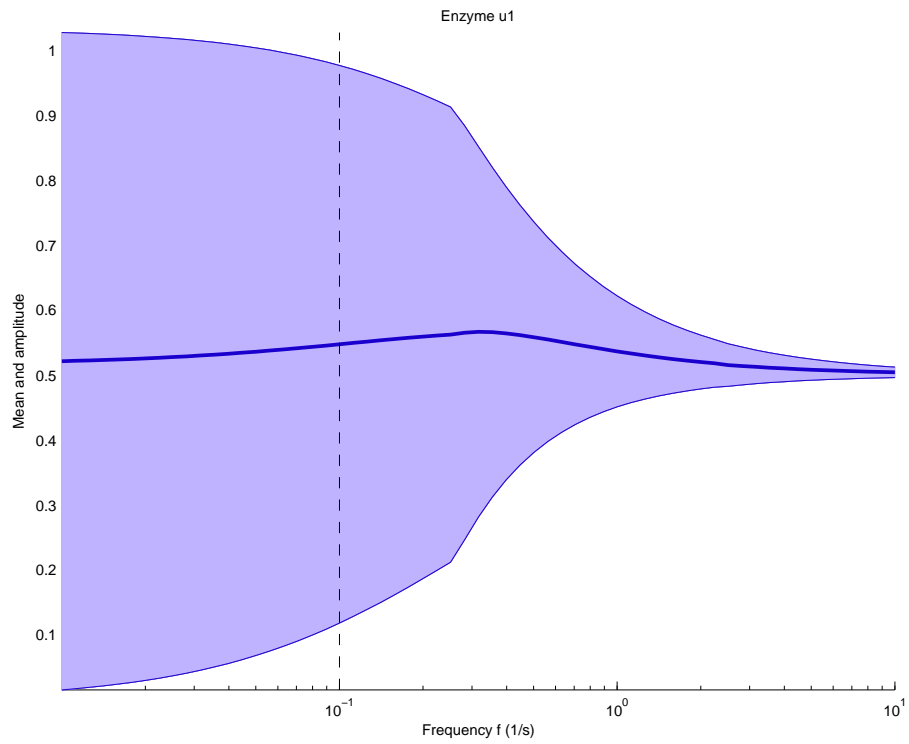
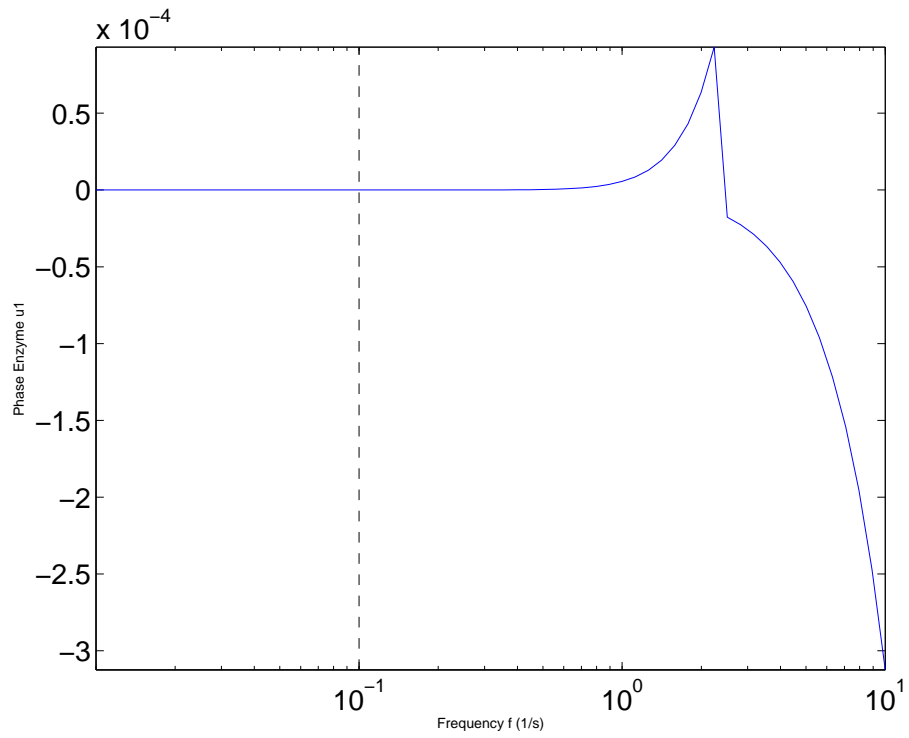


Figure 3: Control analysis. Left: Global fitness synergy (maximal fitness curvature eigenvalue), as a function of the frequency. Right: Relative amplitudes of individual enzymes for the least wasteful enzyme mode (components of the leading fitness curvature eigenvector).

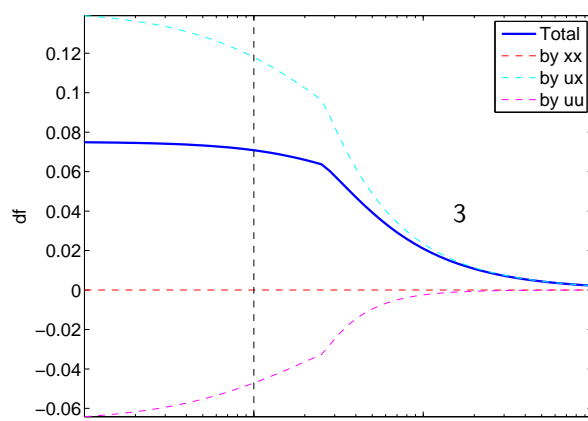
### Protein level and enzyme activity (mean and amplitude)



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



### Fitness change



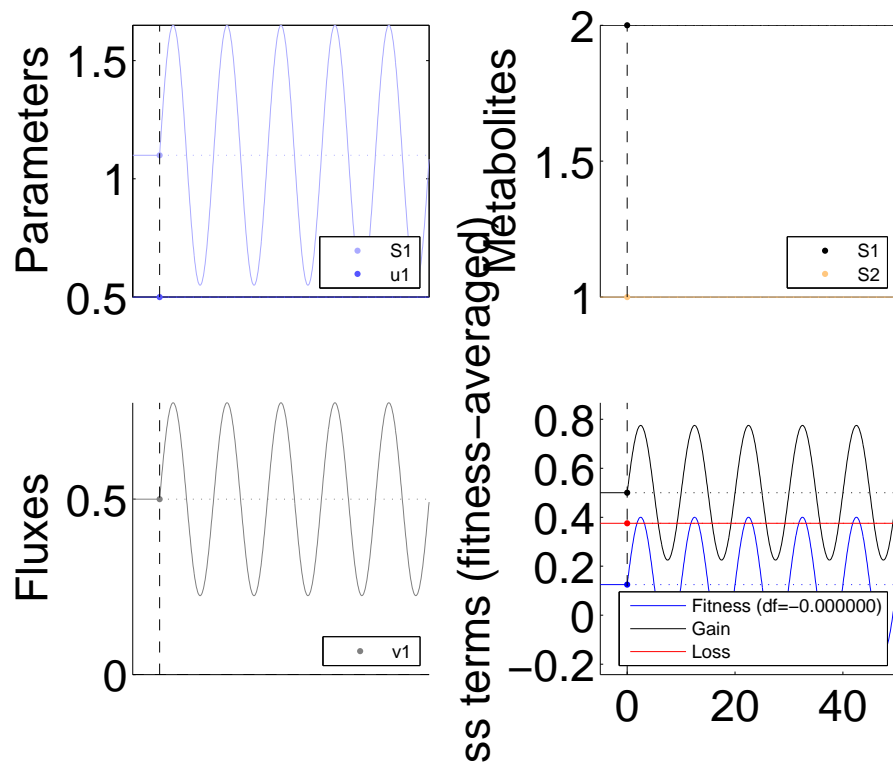


Figure 5: Numerical calculations: responsive oscillations (curves). Dynamic effects of oscillations. The panels show different types of variables: (i) Optimal periodic enzyme levels; (ii) internal metabolite levels; (iii) reaction fluxes; (iv) fitness, benefit, and cost. Perturbation frequency see first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

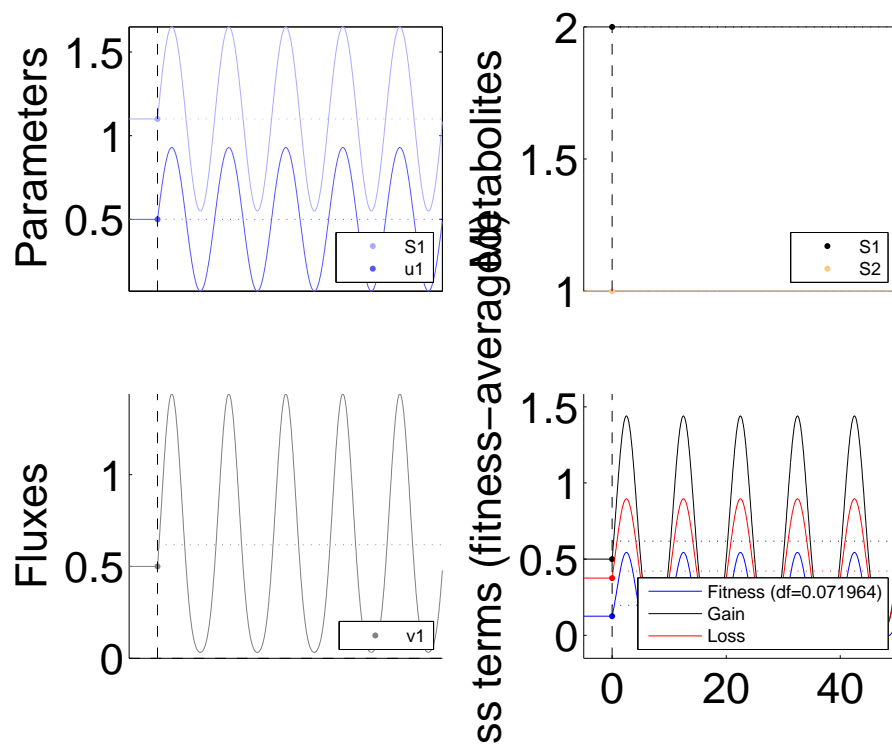


Figure 6: Numerical calculations: adaptive oscillations (curves). Dynamic effects of oscillations. The panels show different types of variables: (i) Optimal periodic enzyme levels; (ii) internal metabolite levels; (iii) reaction fluxes; (iv) fitness, benefit, and cost. Perturbation frequency see first page.

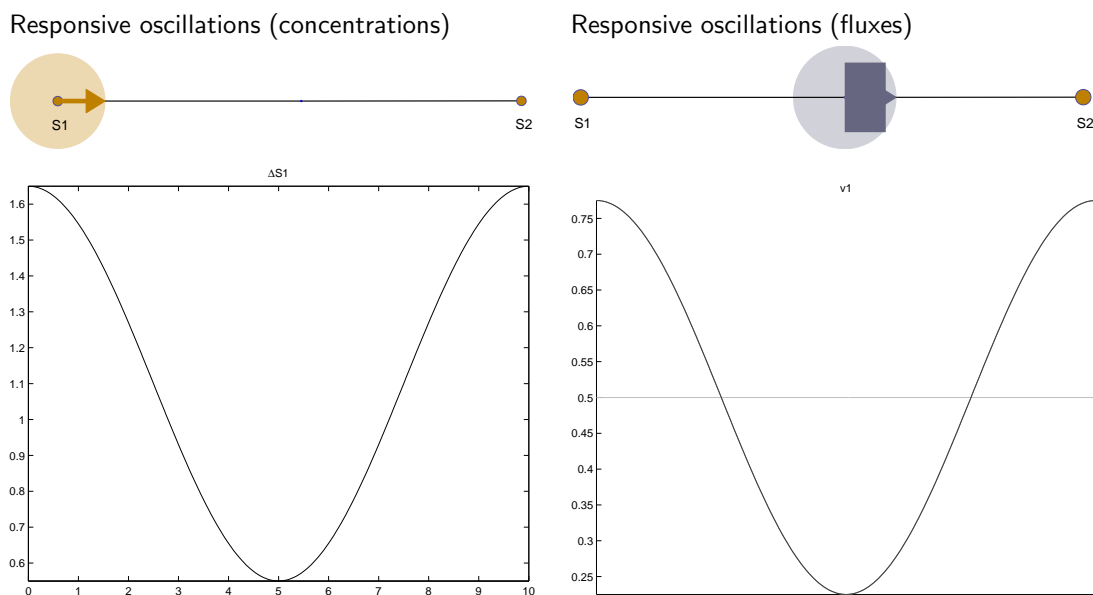
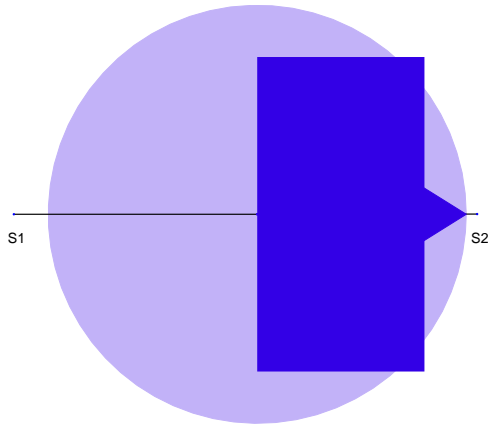
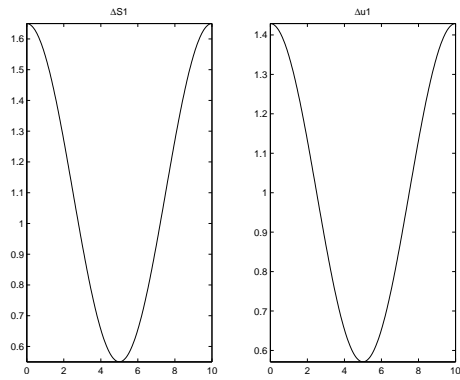


Figure 7: Responsive oscillations (local expansion; arrows: absolute changes) Perturbation frequency see first page.

Adaptive oscillations (enzymes)



Adaptive oscillations (metabolites)



Adaptive oscillations (fluxes)

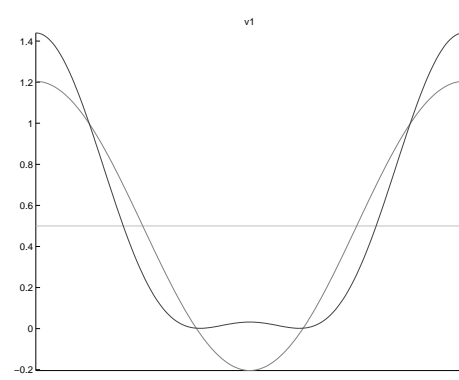


Figure 8: Adaption to forced oscillations (local expansion; arrows: absolute changes). Perturbation frequency see first page.

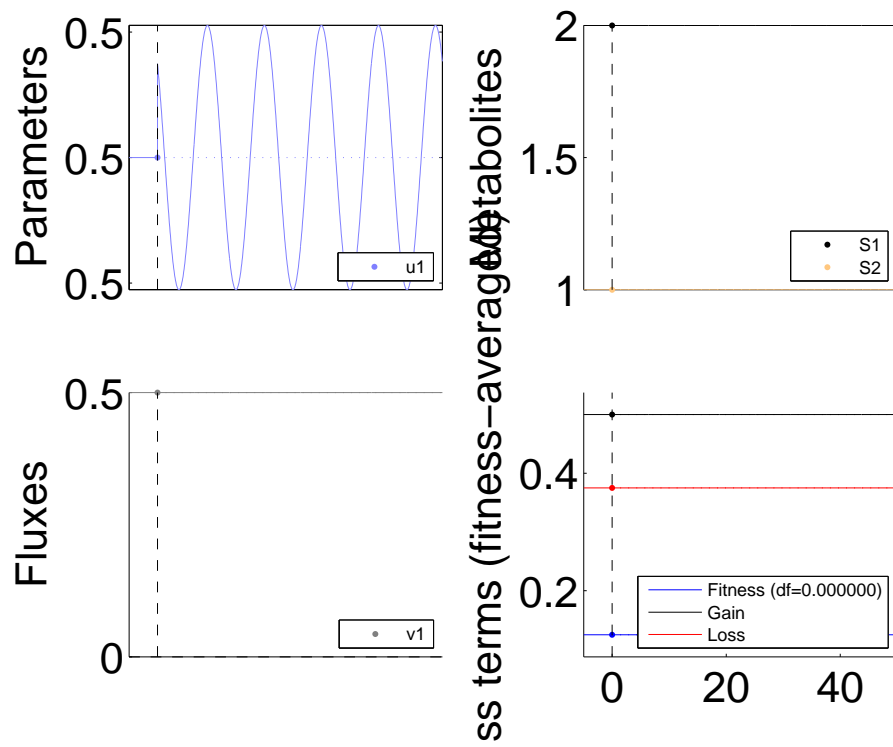
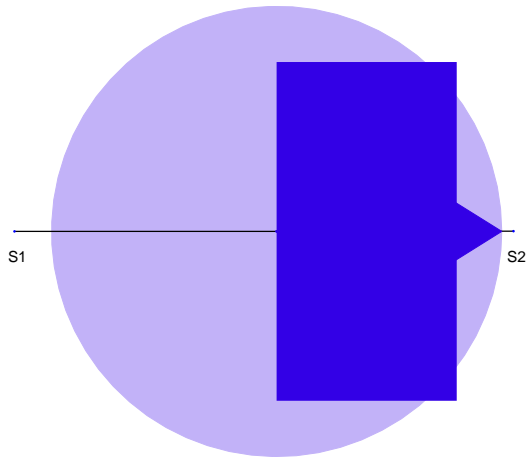
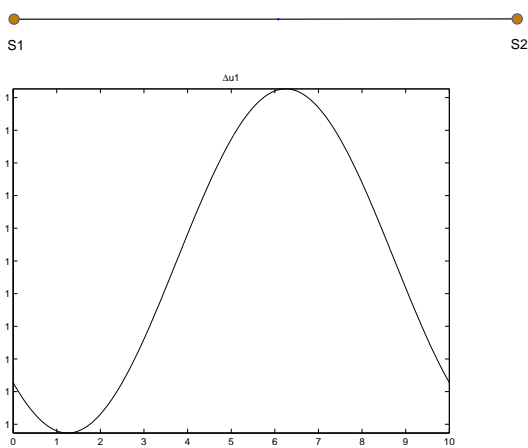


Figure 9: Tentative spontaneous oscillations. Perturbation frequency see first page.

### Enzyme rhythm



### Spontaneous oscillations (concentrations)



### Spontaneous oscillations (fluxes)

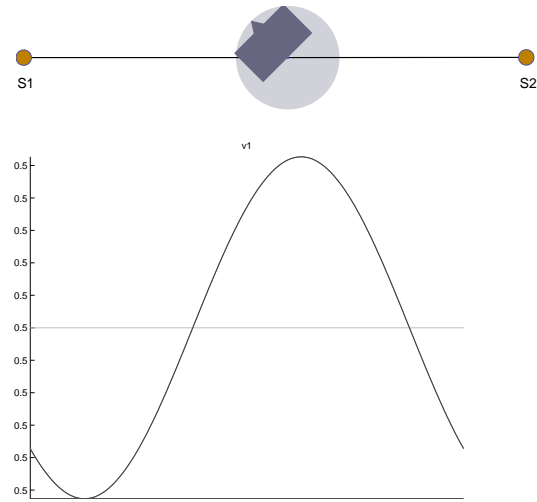
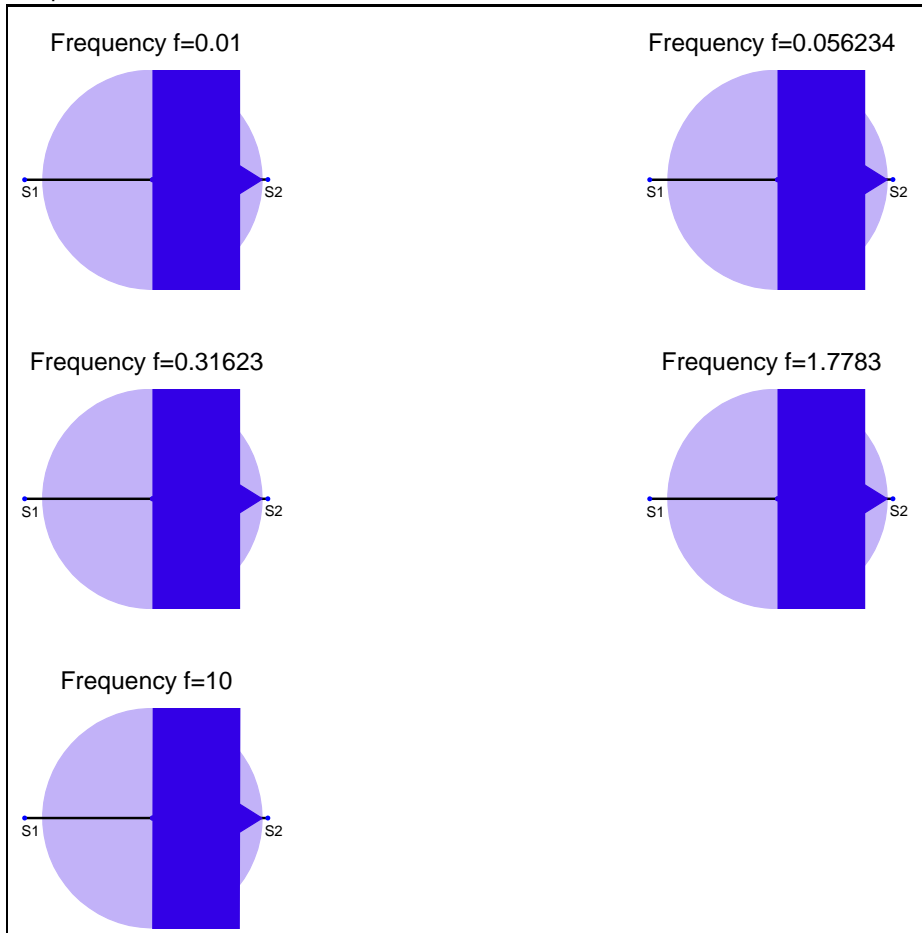


Figure 10: Tentative spontaneous oscillations (local expansion; arrows: absolute changes). Perturbation frequency see first page.



Adaptive



Least costly spontaneous

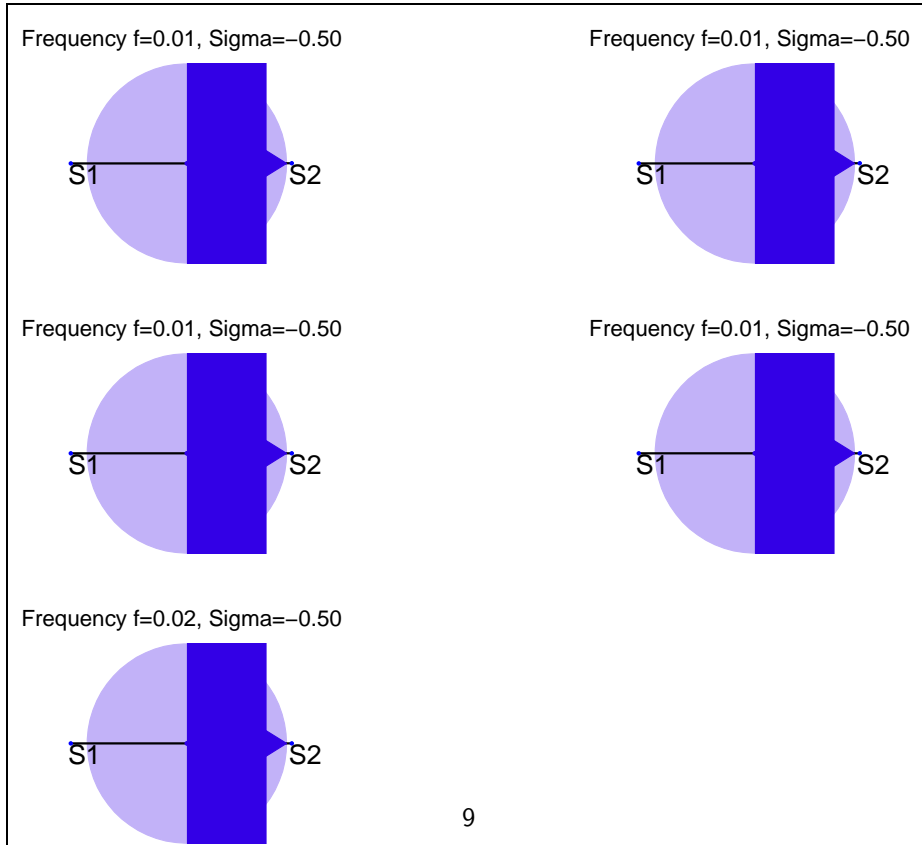


Figure 11: Potential oscillations at various frequencies (local expansion).