

## Enzyme rhythms in model time\_gap2.speedy - spontaneous oscillations

Model name: time\_gap2

### o Optimisation problem

- Protein turnover time  $1\text{ s} = 0.0167\text{ min}$
- Perturbed parameter(s) : X0
- Perturbation frequency  $f$  :  $0.1/\text{s}$  (period 10 s)
- Scored quantity: v4
- 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: 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  $f = 0.794/\text{s}$  (period 1.26 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 $f=0.1/\text{s}$

- Change by perturbation alone (xx): 0.00206
- Change by adaption synergies (xu): 0.0194
- Change by periodic enzyme (uu): -0.00969
- Change by enzyme mean shift (u): 0
- Total fitness change : 0.0118
- Fitness gain by adaption : 0.00969
- Maximum adaptive fitness found (in tested range) at frequency  $f = 0.224/\text{s}$  (period 4.47 s)
- Predicted maximal fitness change (adaptive, numeric opt, full amplitude constraints) at frequency  $f = 0.224$ : 0.0133

### 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 = -0.00706): Predicted fitness change -0.00418

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

- Fitness change (fitness-averaged): 0.00208
- Fitness change (state-averaged): 0.0021

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

- Fitness change (fitness-averaged): 0.0113
- Fitness change (state-averaged): 0.0158

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

- Fitness change (fitness-averaged) :  $-3.8\text{e-}07$
- Fitness change (state-averaged):  $-3.8\text{e-}07$

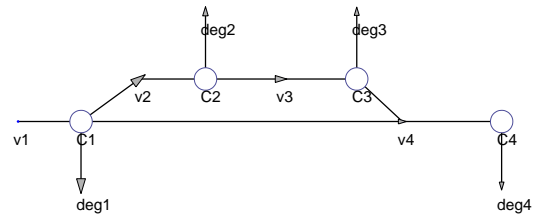


Figure 1: Network and reference flux

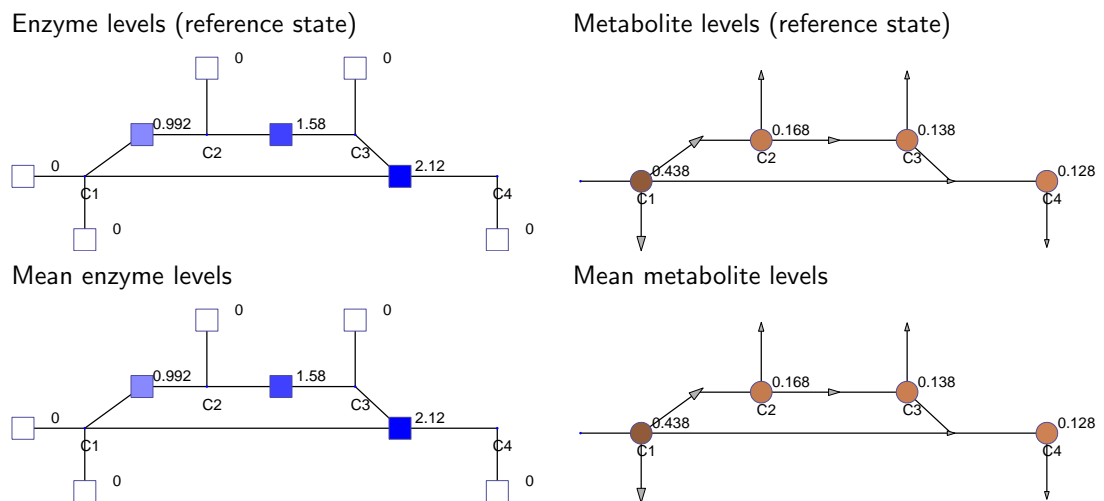


Figure 2: Reference state (top) and mean state during oscillation (bottom).

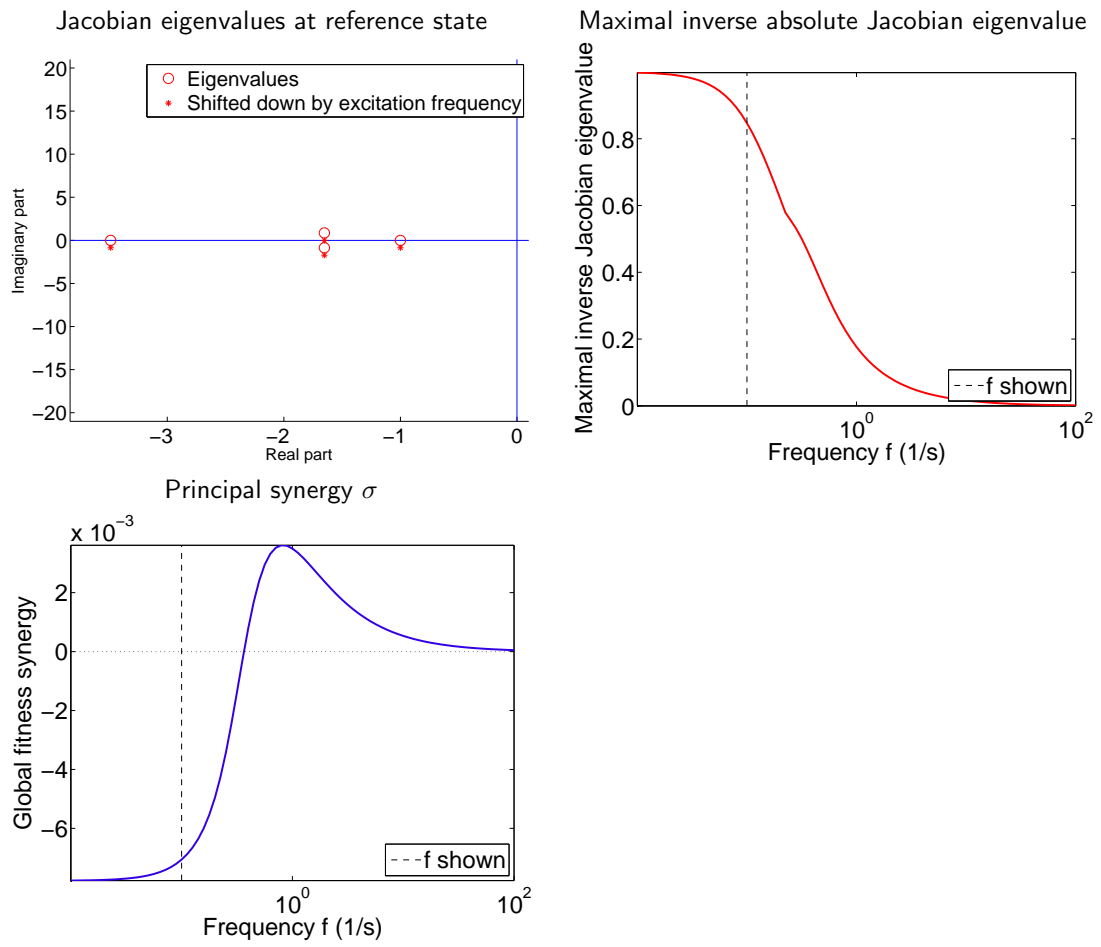
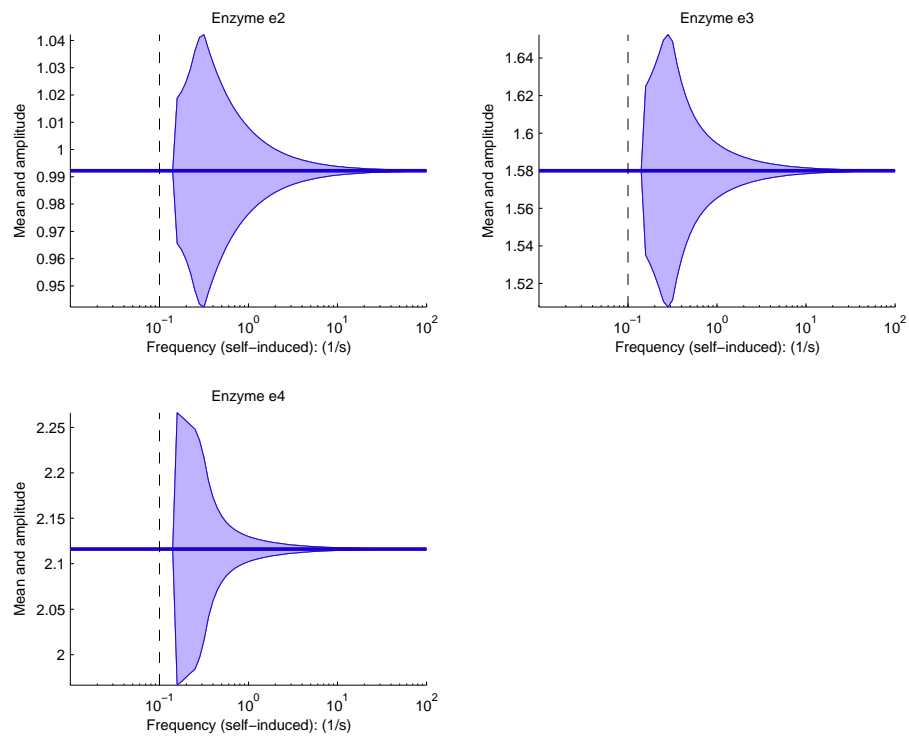
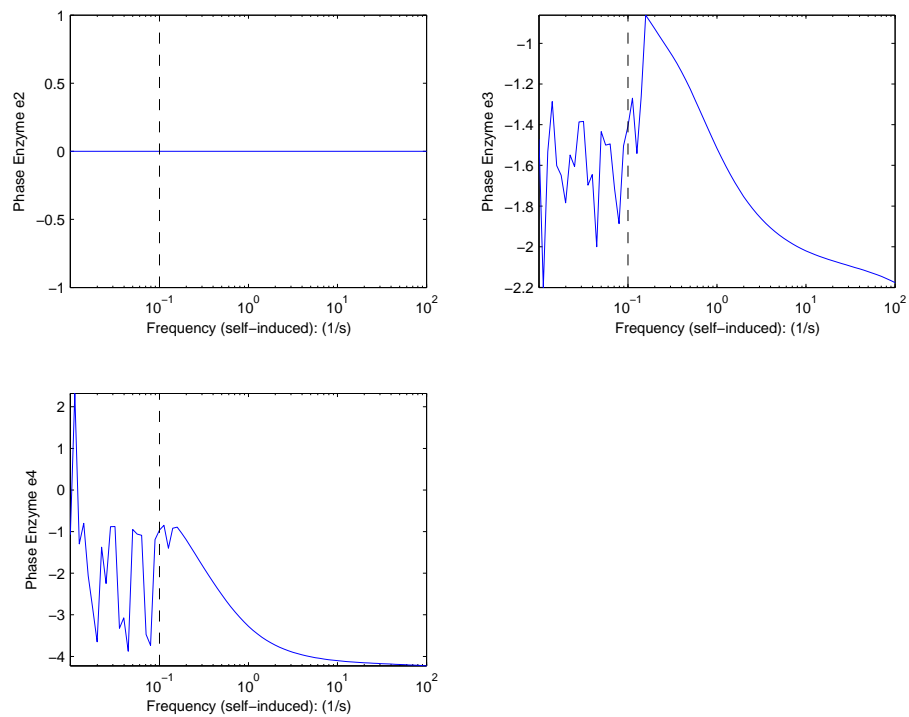


Figure 3: Control analysis: fitness curvatures. Left: Frequency-dependent fitness curvature eigenvalues. Right: relative sizes and phases of the individual enzyme levels (components of the leading fitness curvature eigenvector).

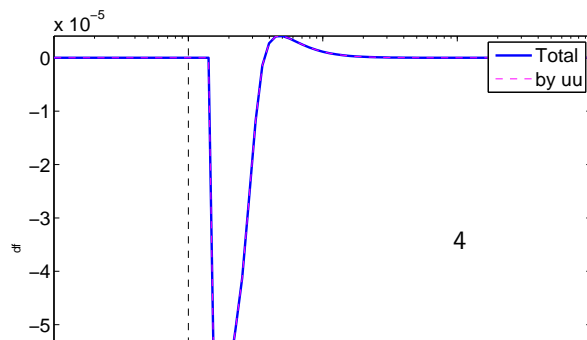
## Protein level and enzyme activity (mean and amplitude)



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



## Fitness change



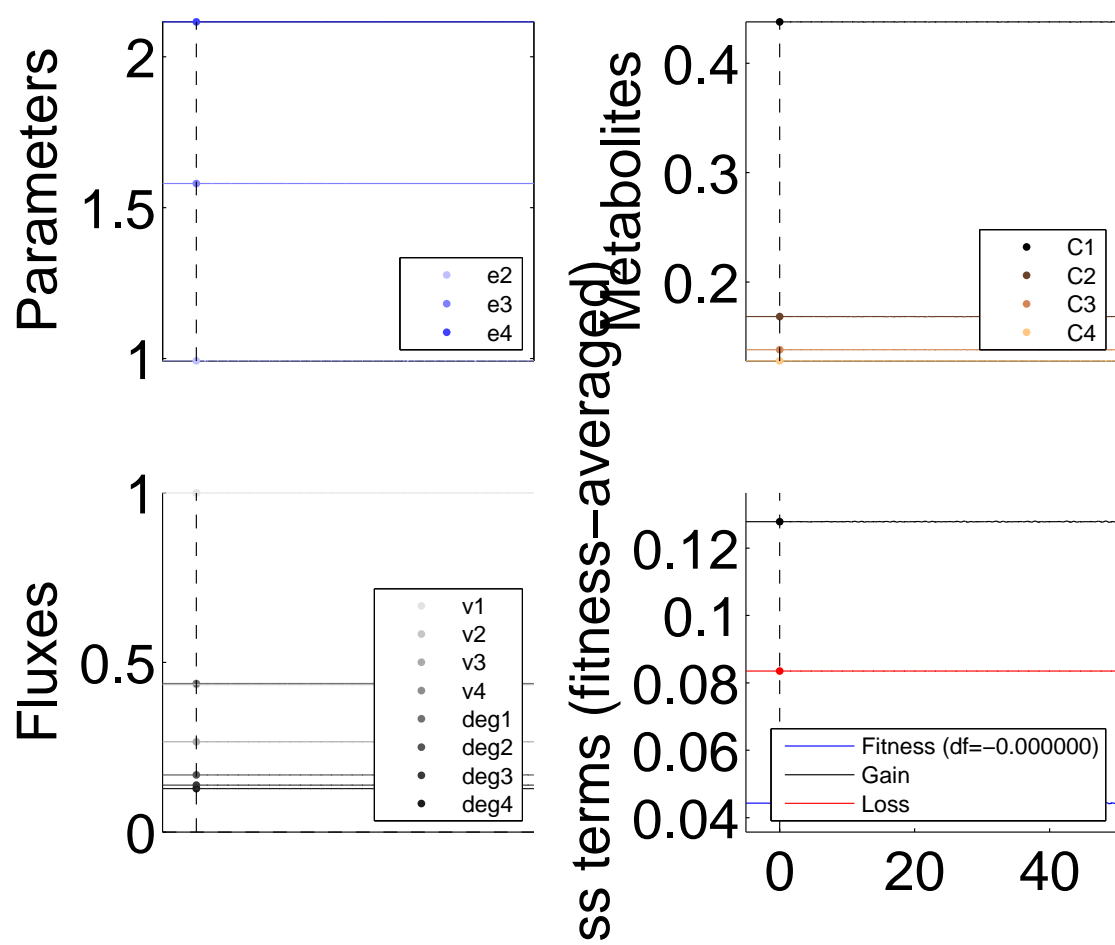
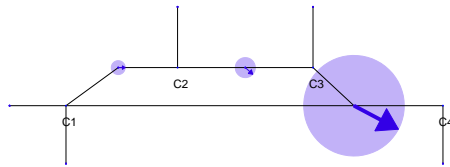
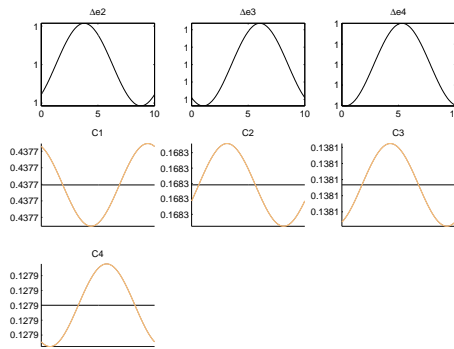
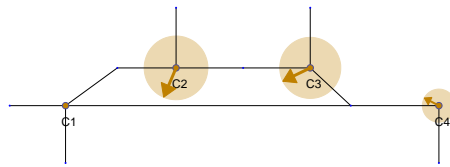


Figure 5: Numerical calculations: spontaneous oscillations. Perturbation frequency see first page.

### Enzyme rhythm



### Spontaneous oscillations (concentrations)



### Spontaneous oscillations (fluxes)

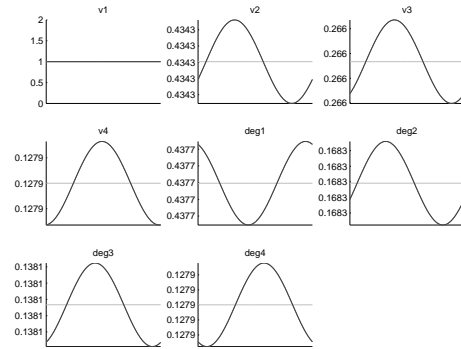
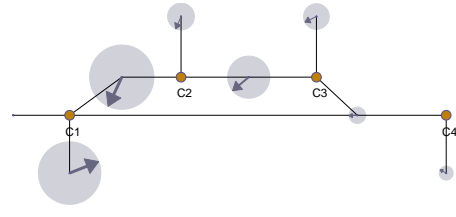


Figure 6: Spontaneous oscillations (local expansion; arrows: absolute changes). Perturbation frequency see first page.

### Spontaneous oscillations

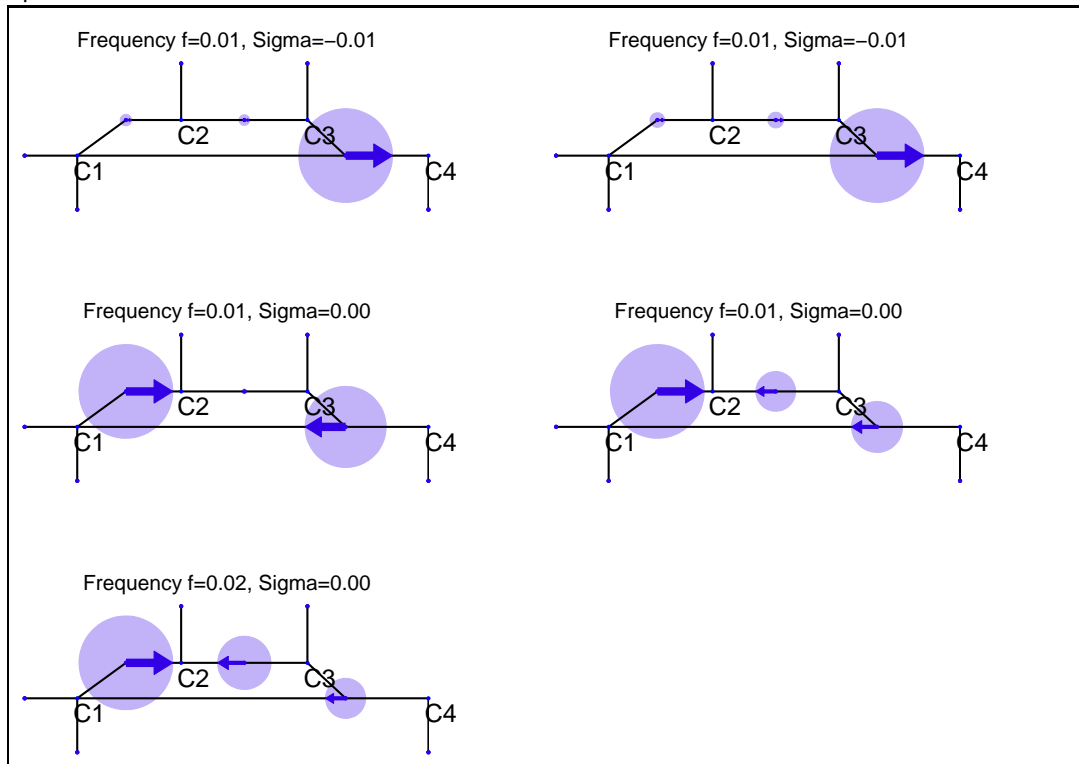


Figure 7: Spontaneous oscillations (or tendencies towards them) for various circular frequencies  $\omega$ . If the maximal fitness curvatures  $\lambda$  is positive, the rhythm is beneficial (local expansion; arrows: absolute changes).