

Enzyme rhythms in model repressilator.speedy - spontaneous oscillations

Model name: repressilator

o Optimisation problem

- Protein turnover time $1 \text{ s} = 0.0167 \text{ min}$
- No external perturbation considered
- Scored quantity: v1
- Scored quantity: v2
- Scored quantity: v3
- State-averaged fitness
- No posttranslational rhythms allowed
- Standard frequency considered $f : 0.0167/\text{s}$ (period 60 s)

o Model properties:

- inactive_enzymes: 0
- balanced_reference_state: 1
- consider_external_rhythm: 0
- 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 $f = 0.112/\text{s}$ (period 8.91 s)
- Maximum fitness found (in tested range) at frequency $f = 0.0891/\text{s}$ (period 11.2 s)

o Self-induced oscillations?

- Maximally self-induced oscillations (in tested range) at $f = 0.112$, principal synergy 0.663
- Beneficial self-induced oscillations found at frequency $f = 0.0167/\text{s}$ (principal synergy = 0.447)
- Predicted fitness change (self-induced, 2nd order, amplitude below 1/2 of mean) at frequency $f = 0.0167$: 0.0285
- Predicted maximal fitness change (self-induced, numeric opt, full amplitude constraints) at frequency $f = 0.0891$: 0.144

o Numerical calculation (self-induced rhythm, amplitude below 1/2 of mean, $f=0.0167$)

- Fitness change (fitness-averaged) : -0.0384
- Fitness change (state-averaged): 0.127

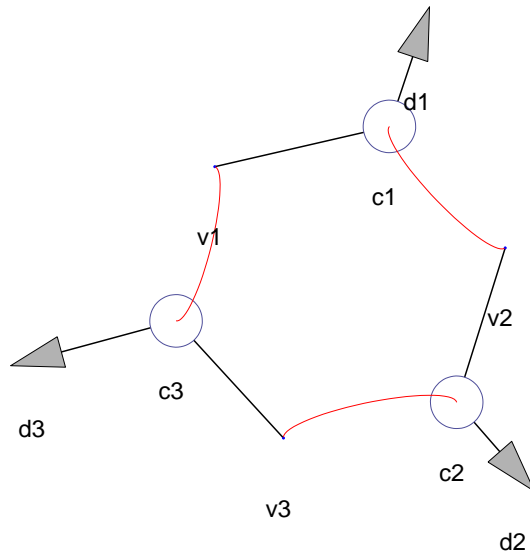


Figure 1: Network and reference flux

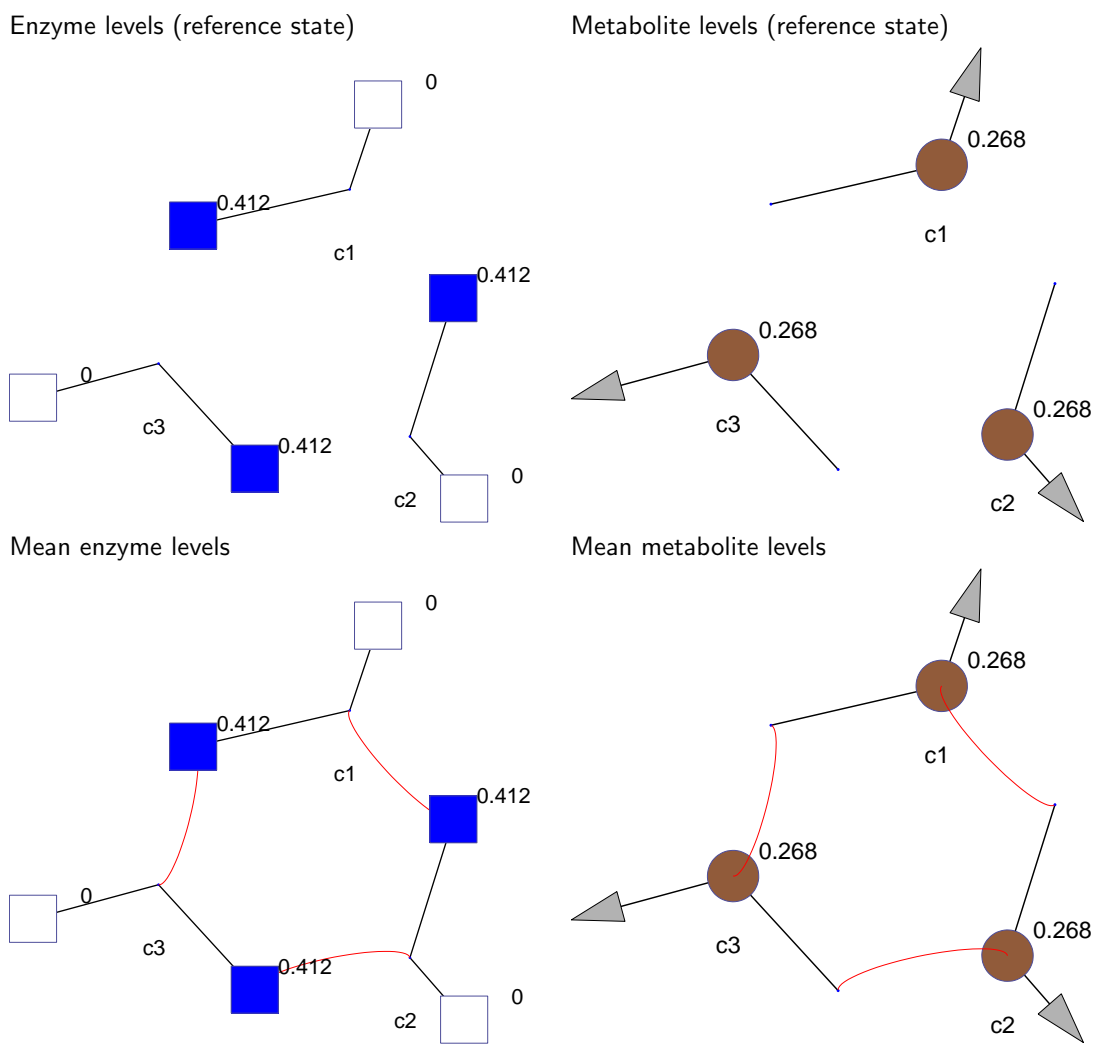


Figure 2: Reference state (top) and mean state during oscillation (bottom).

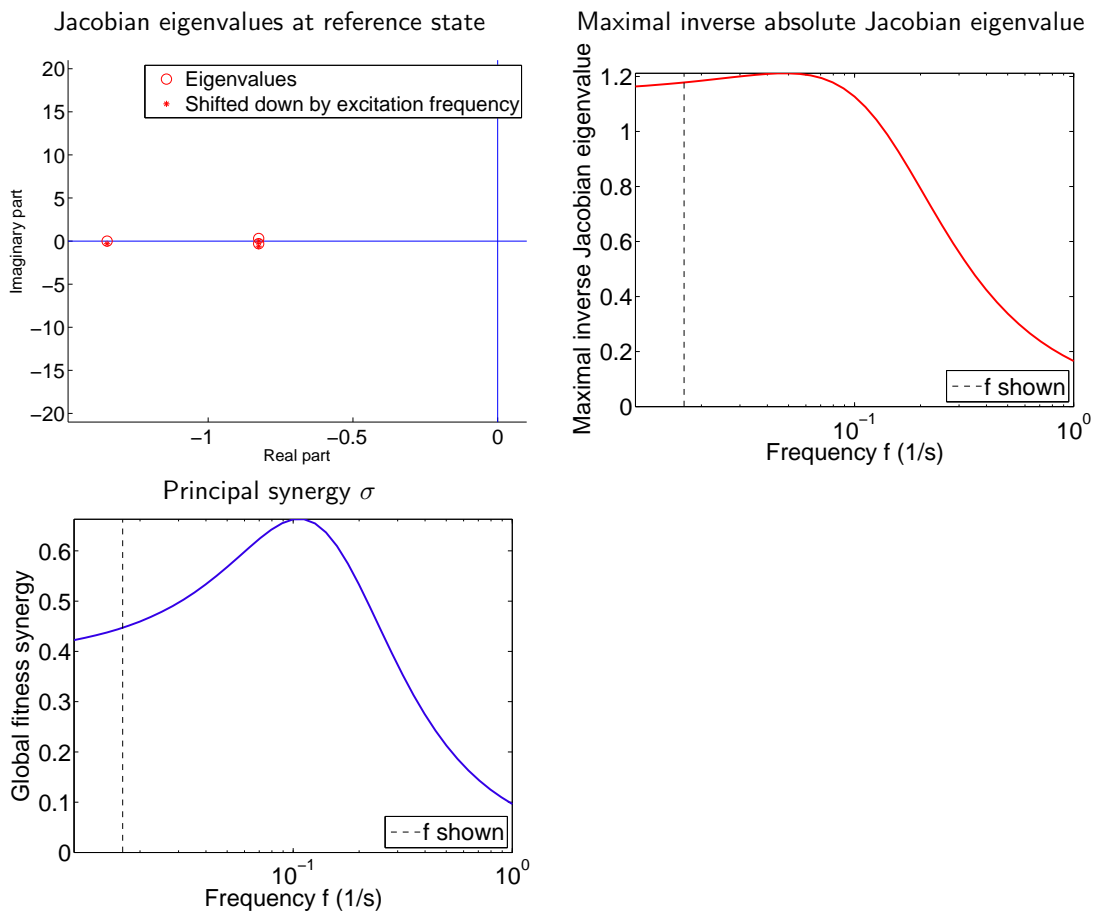
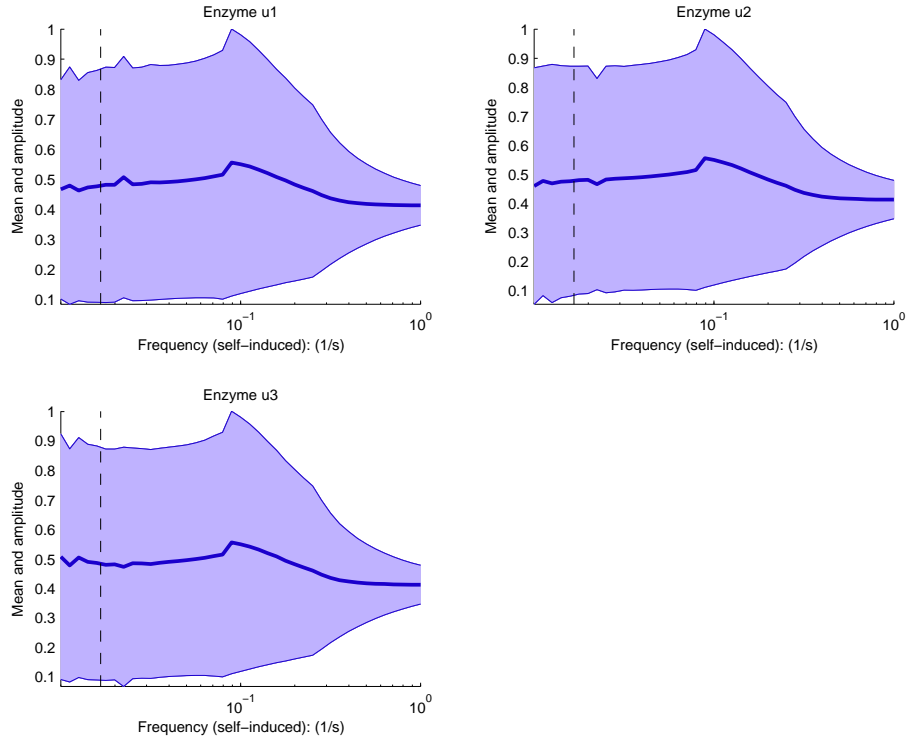
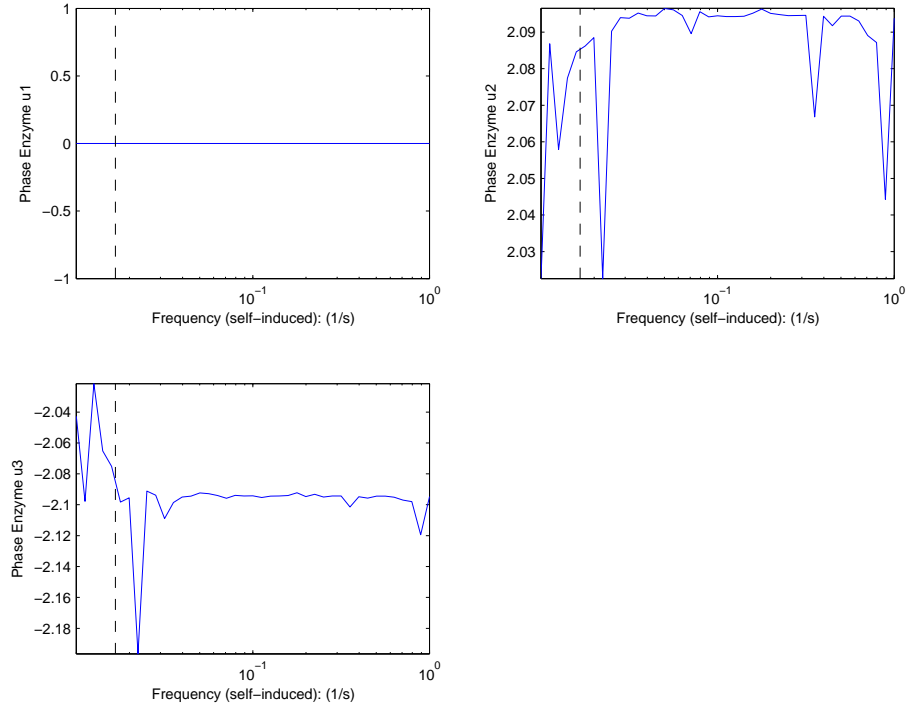


Figure 3: Control analysis: fitness curvatures. Left: Frequency-dependent fitness curvature eigenvalues. Right: relative sizes and phases of the individual enzyme levels (components of the leading fitness curvature eigenvector).

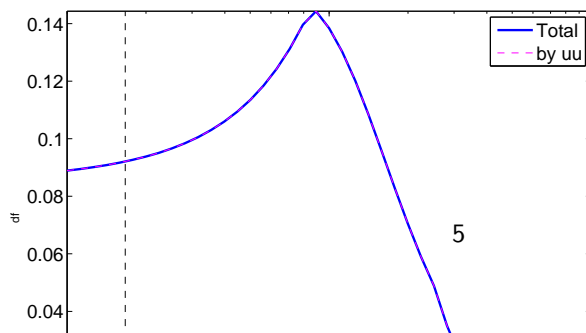
Protein level and enzyme activity (mean and amplitude)



Phase angles $[0, 2\pi]$



Fitness change



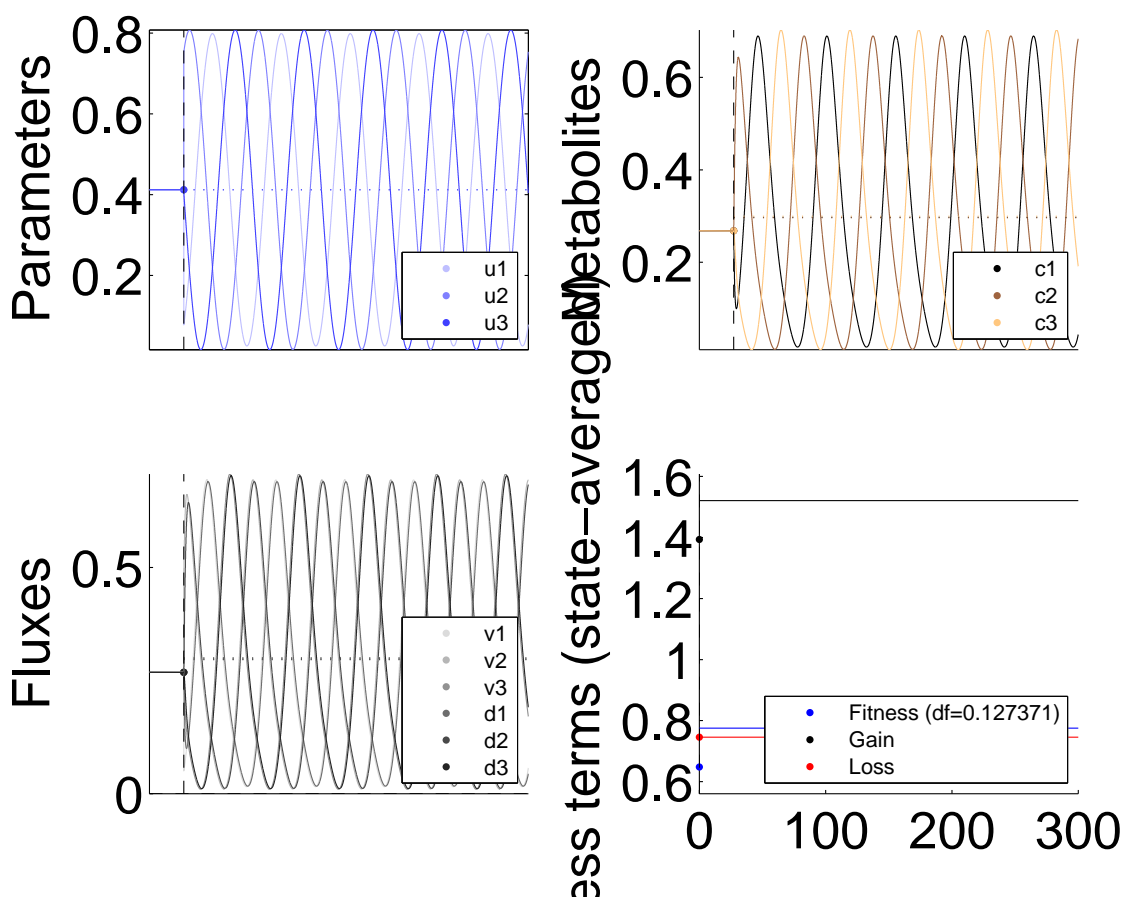
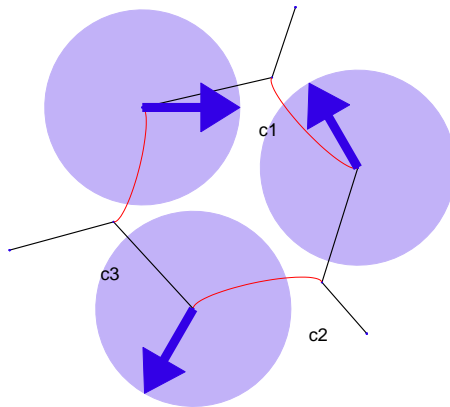
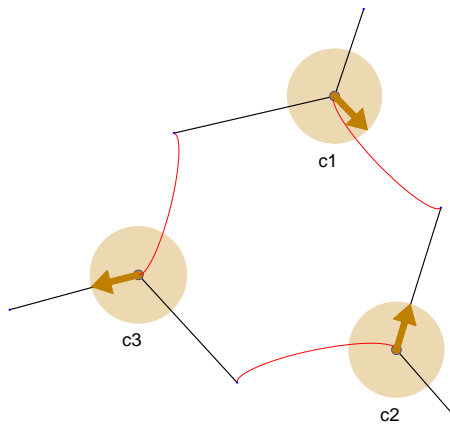


Figure 5: Numerical calculations: spontaneous oscillations. Perturbation frequency see first page.

Enzyme rhythm



Spontaneous oscillations (concentrations)



Spontaneous oscillations (fluxes)

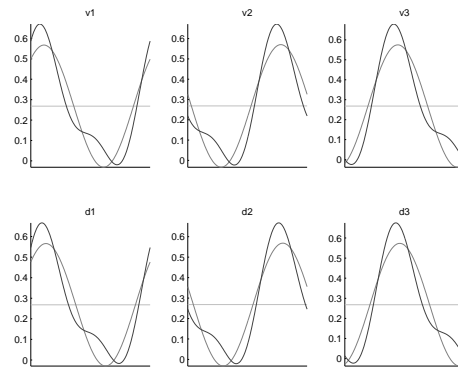
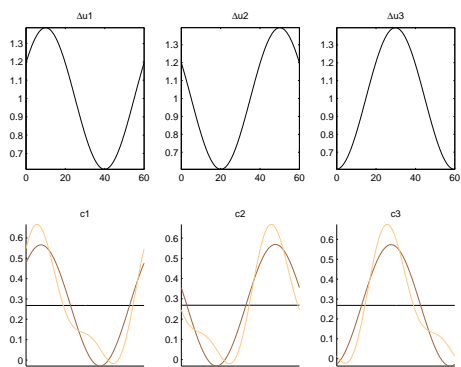
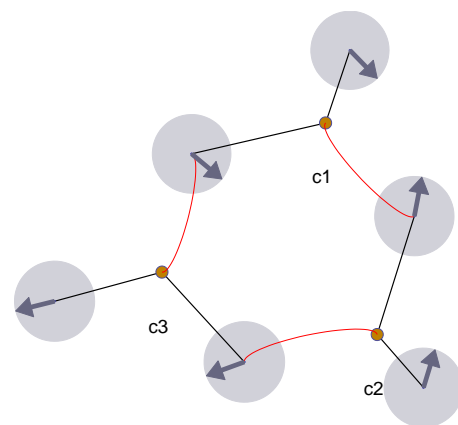


Figure 6: Spontaneous oscillations (local expansion; arrows: absolute changes). Perturbation frequency see first page.

Spontaneous oscillations

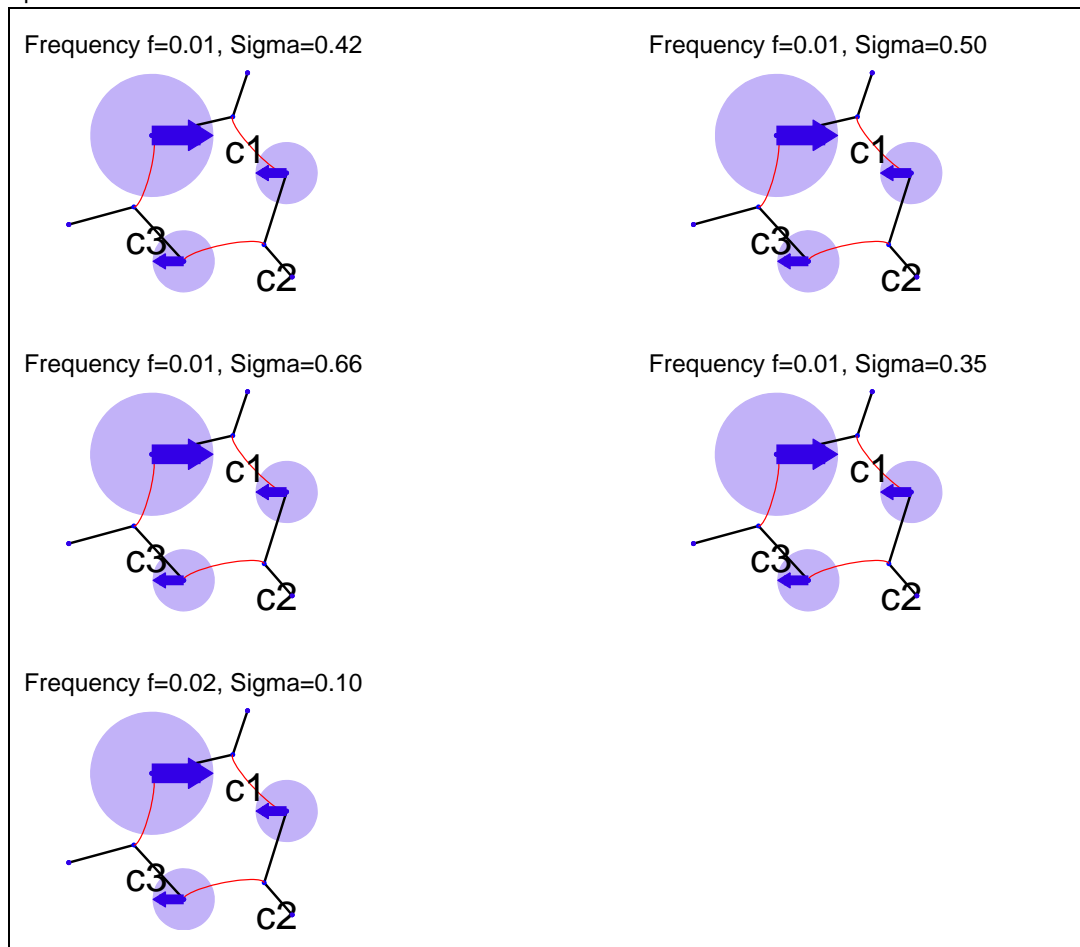


Figure 7: Spontaneous oscillations (or tendencies towards them) for various circular frequencies ω . If the maximal fitness curvatures λ is positive, the rhythm is beneficial (local expansion; arrows: absolute changes).