Tau-Leaping - Speeding Stochastic Simulation

Applied Numerics in Systems Biology Seminar

Balduin Laubisch

Freie Universität Berlin

Tau-Leaping Method

- simulate stochastic models faster
- simulate complex stochastic models in feasible time

Freie Universität Berlin

SSA vs. Tau-Leaping vs. ODE

SSA

$$X_t = X_0 + \sum_j s_{\cdot,j} \, \mathcal{P}\left(\int_0^t a_j(X_s) \, ds \right)$$

Tau-Leaping

$$X_{t+\Delta t} \approx X_t + \sum_j s_{\cdot,j} \, \mathcal{P}\left(a_j(X_t) \Delta t \right)$$

ODE

$$\frac{dX_t}{dt} = \sum_j s_{\cdot,j} \cdot a_j(X_t)$$

Tau-Leaping Implementation

Freie Universität Berlin

```
def tau_leap_simulate(model, T, h):
    # population
    x = [model[0]]
    # propensity functions
    r = model[2]
    # stoichiometric matrix
    s = np.array(model[1])
    # time
    t = [0]
    while (t[-1] < T):
        # calculate reaction rates
        ai = r(x[-1])

        if (t[-1] + h > T):
            # last time step size
            h = T - t[-1]

        # change in x according to current propensity and tau leap condition
        k = np.random.poisson(np.array(ai) * h)
        dx = s.dot(k)

        # update time and population
        t.append(t[-1] + h)
        x.append(np.add(dx, x[-1]))

    return x, t
```

Experimental Setup

Assess Tau-Leaping method on different models and reproduce dynamics

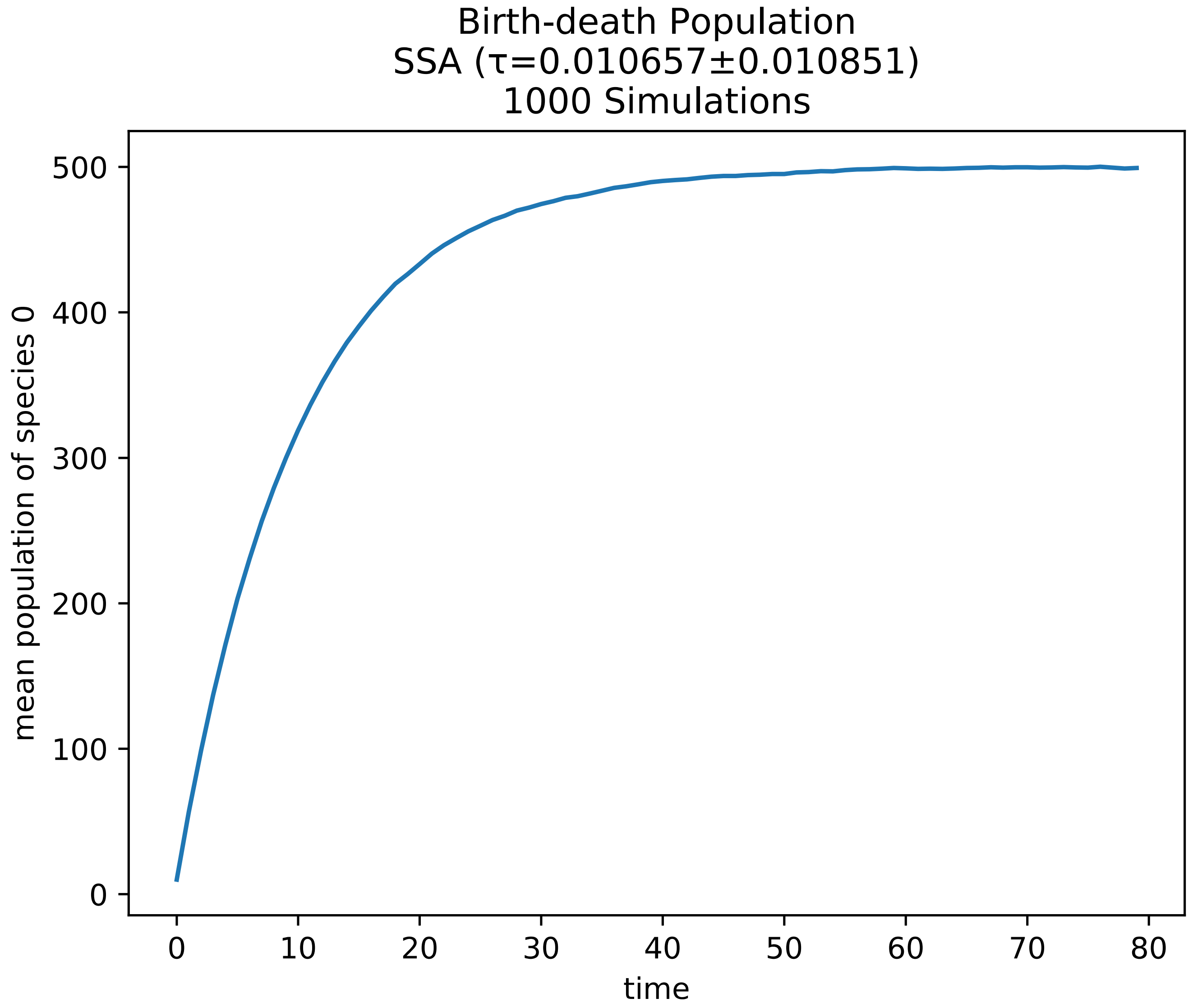
- Birth-death process
- Banana / Boomerang model
- Schlögl model

Birth-death process

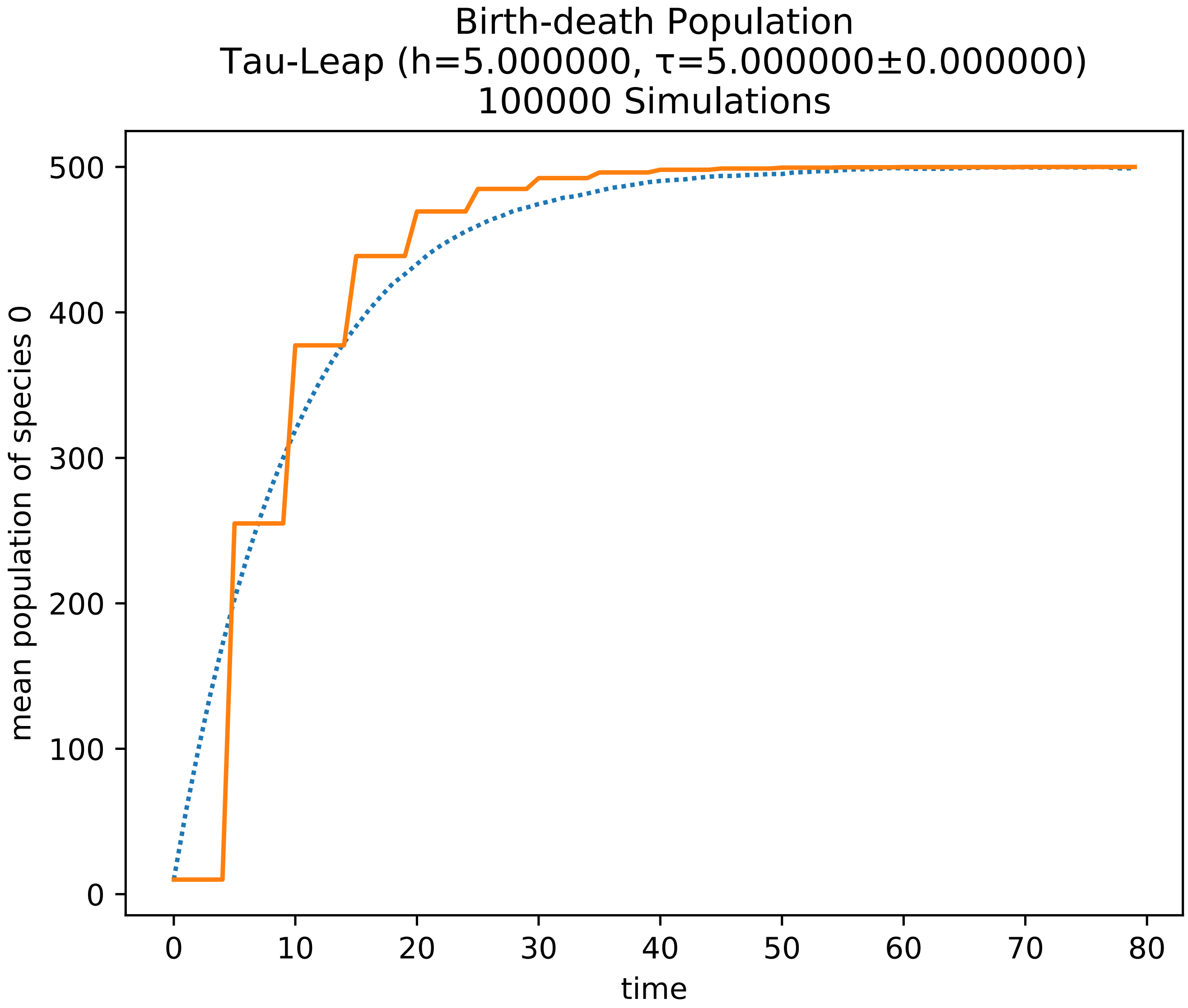
$$\emptyset \xrightarrow{\lambda=50} X \xrightarrow{\beta=0.1} \emptyset$$

- $X(0) = 10$
- stationary distribution at $\lambda/\beta = 500$

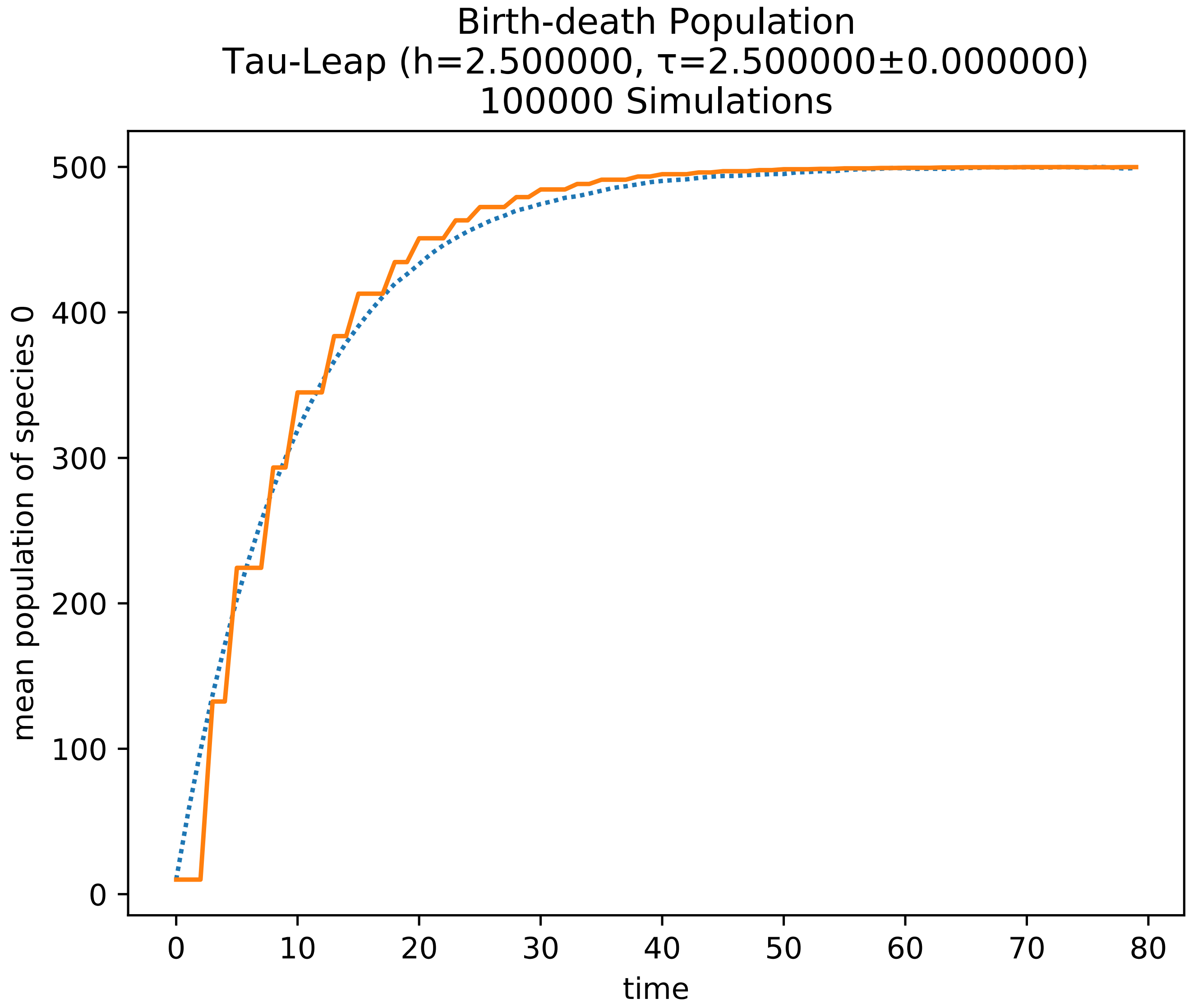
Birth-death stationary distribution



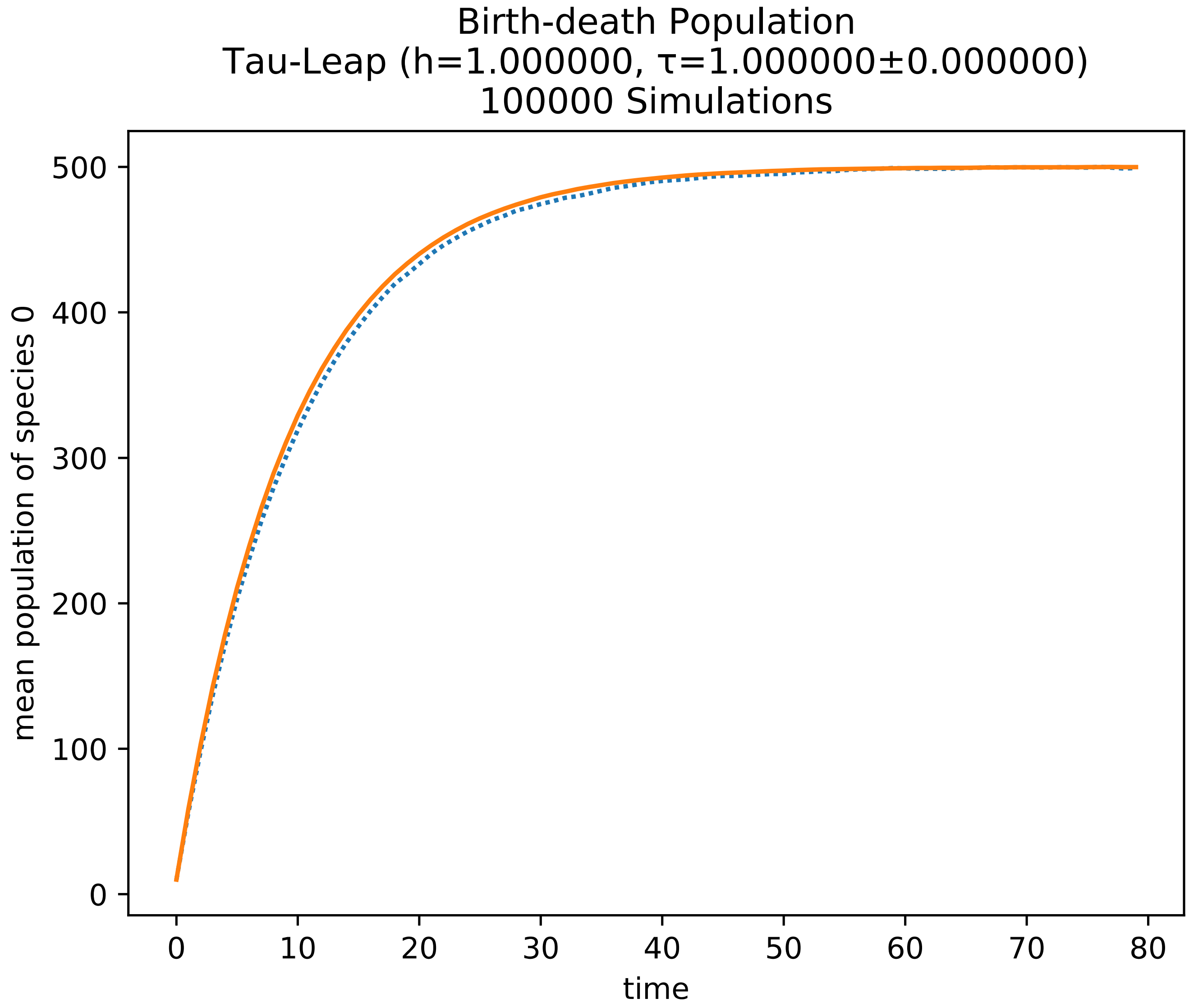
Birth-death stationary distribution



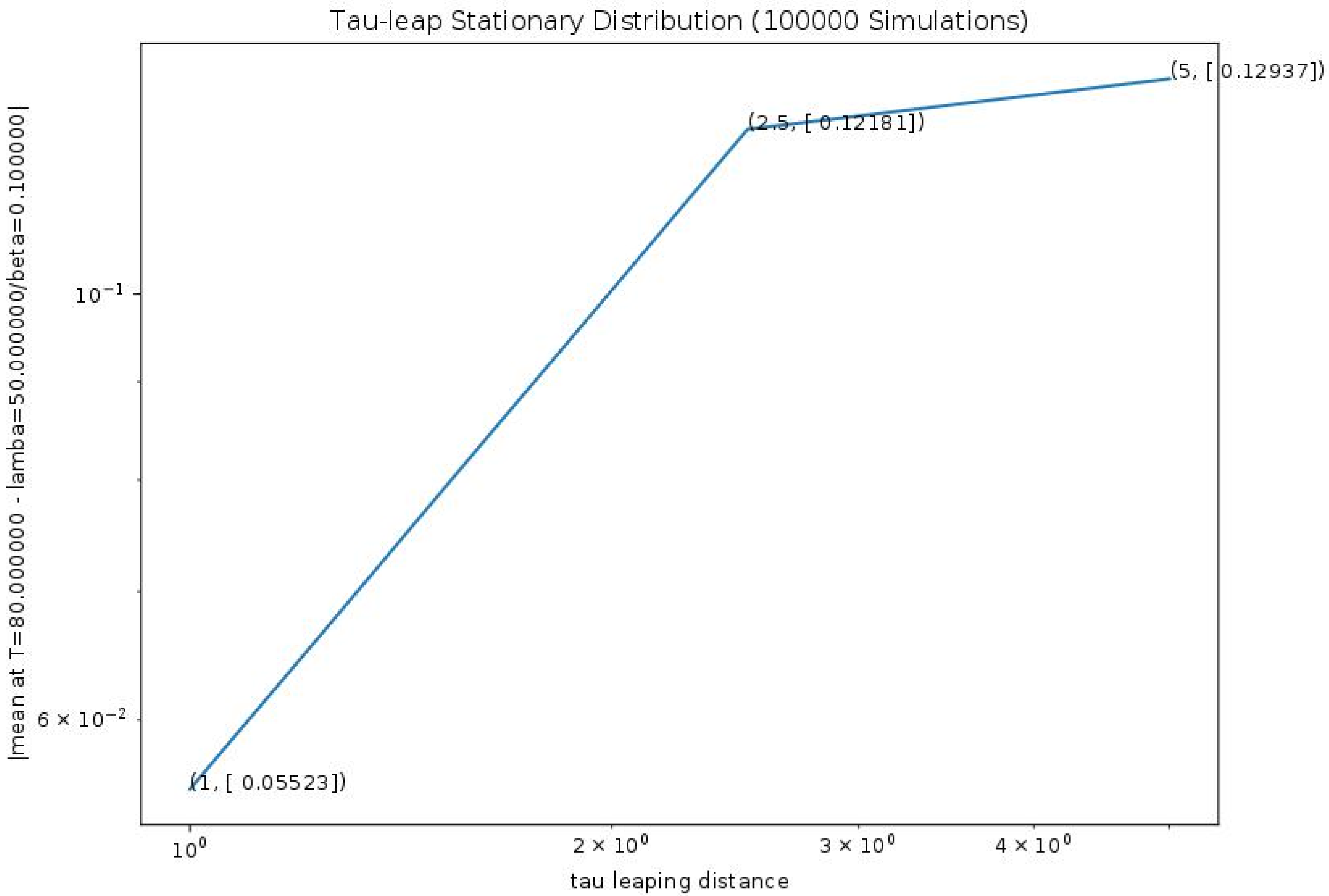
Birth-death stationary distribution



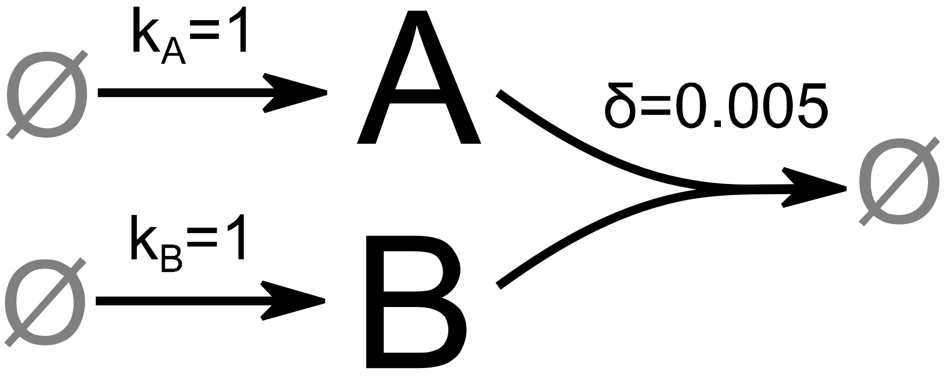
Birth-death stationary distribution



Birth-death stationary distribution



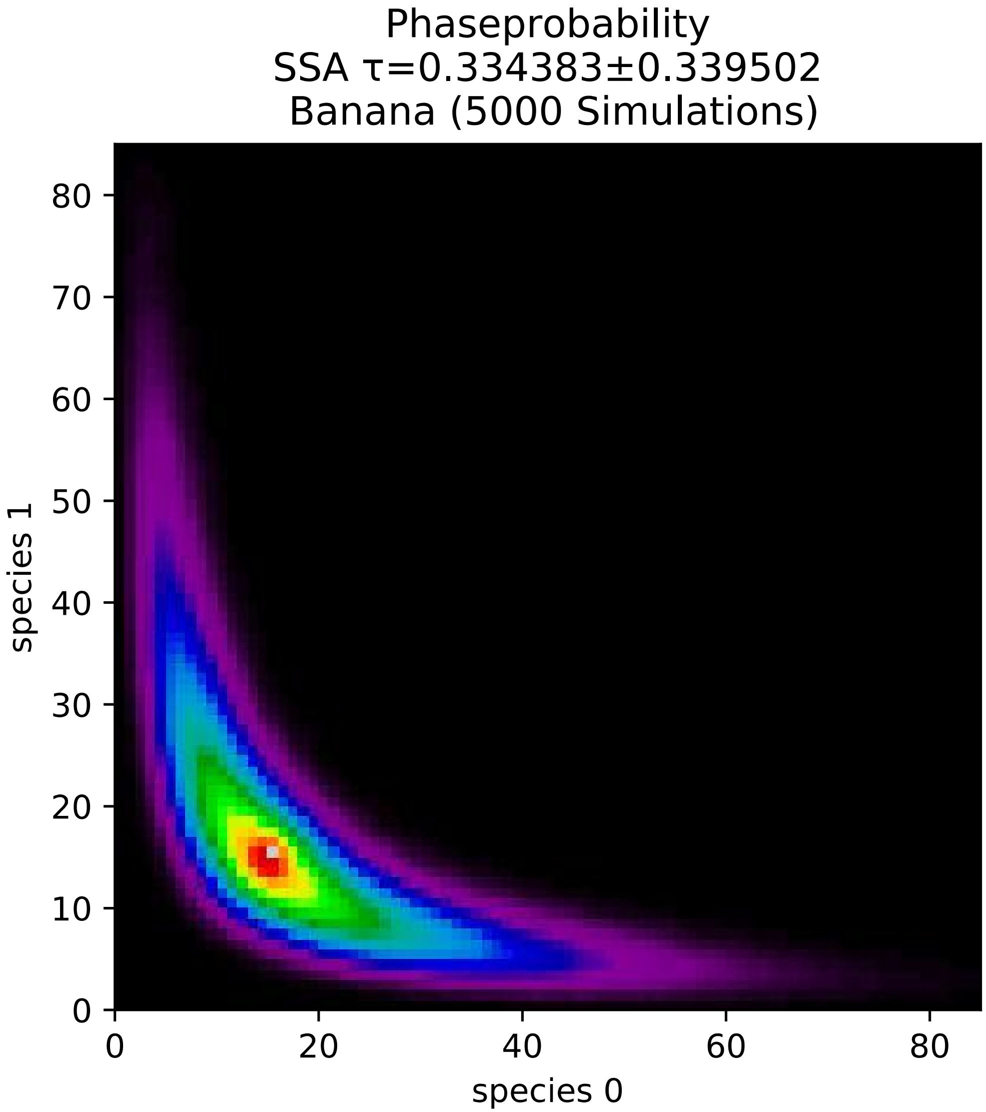
Banana / Boomerang model



- A(0) = B(0) = 10
- increasing population for A or B only mutually exclusive

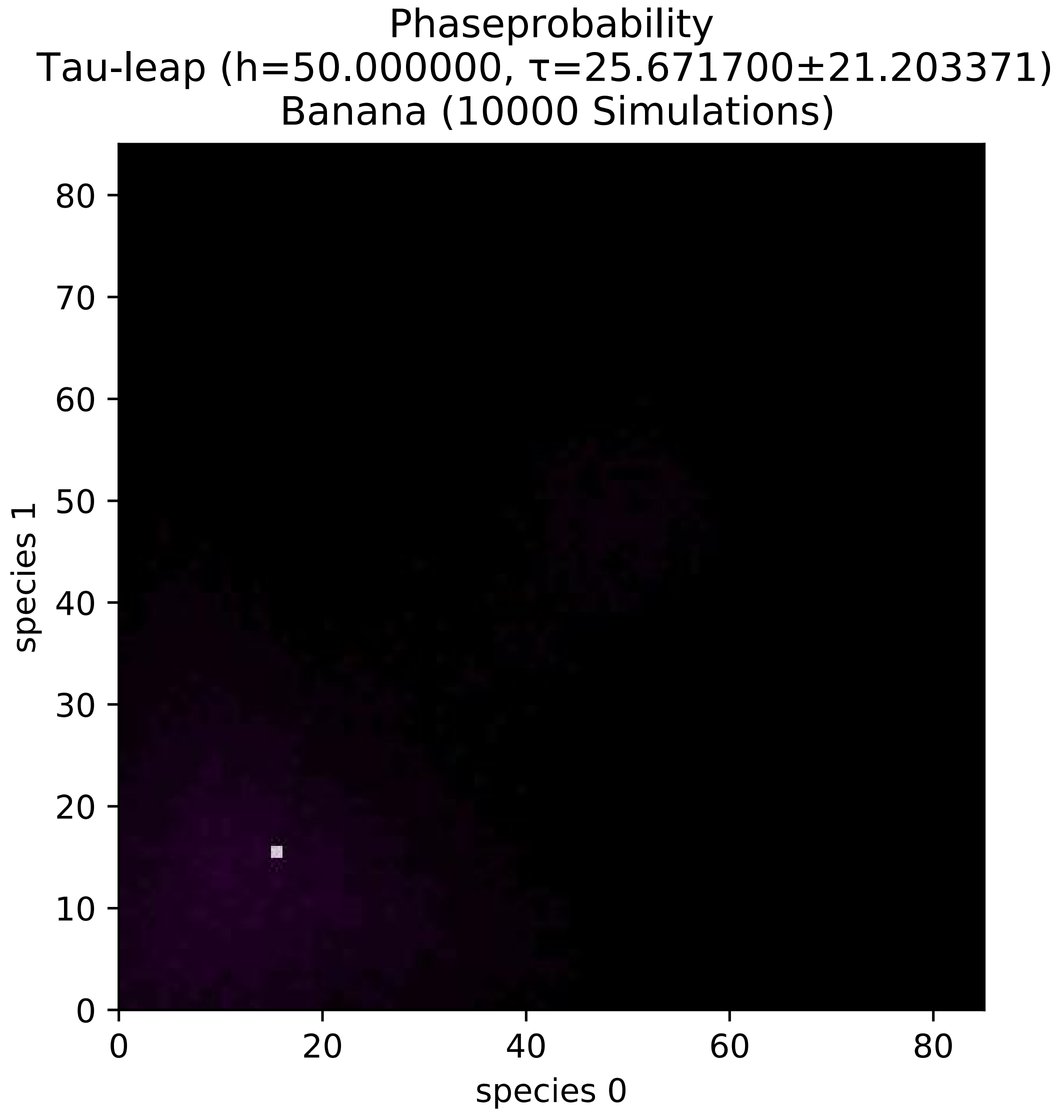
Bending the Banana

Freie Universität Berlin

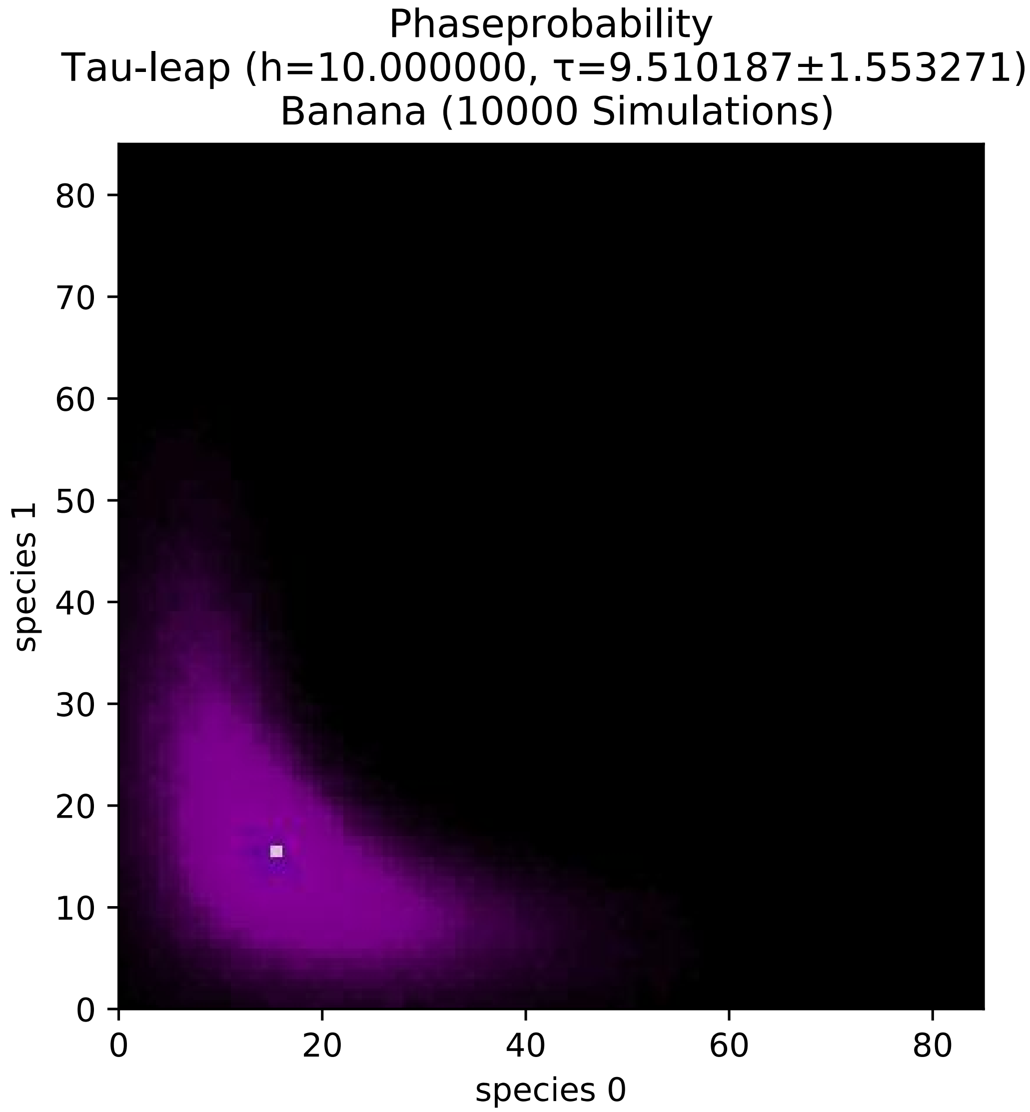


Bending the Banana

Freie Universität Berlin

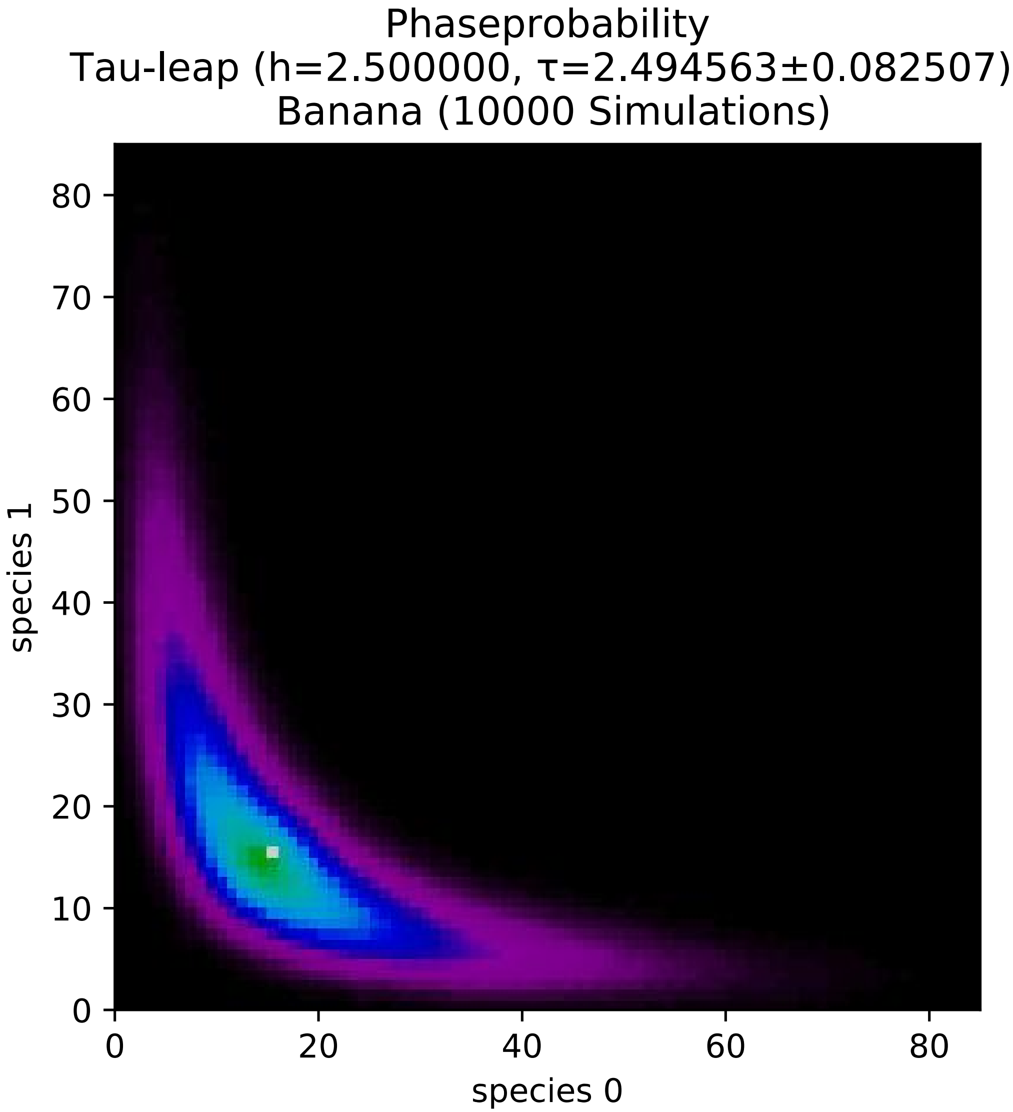


Bending the Banana



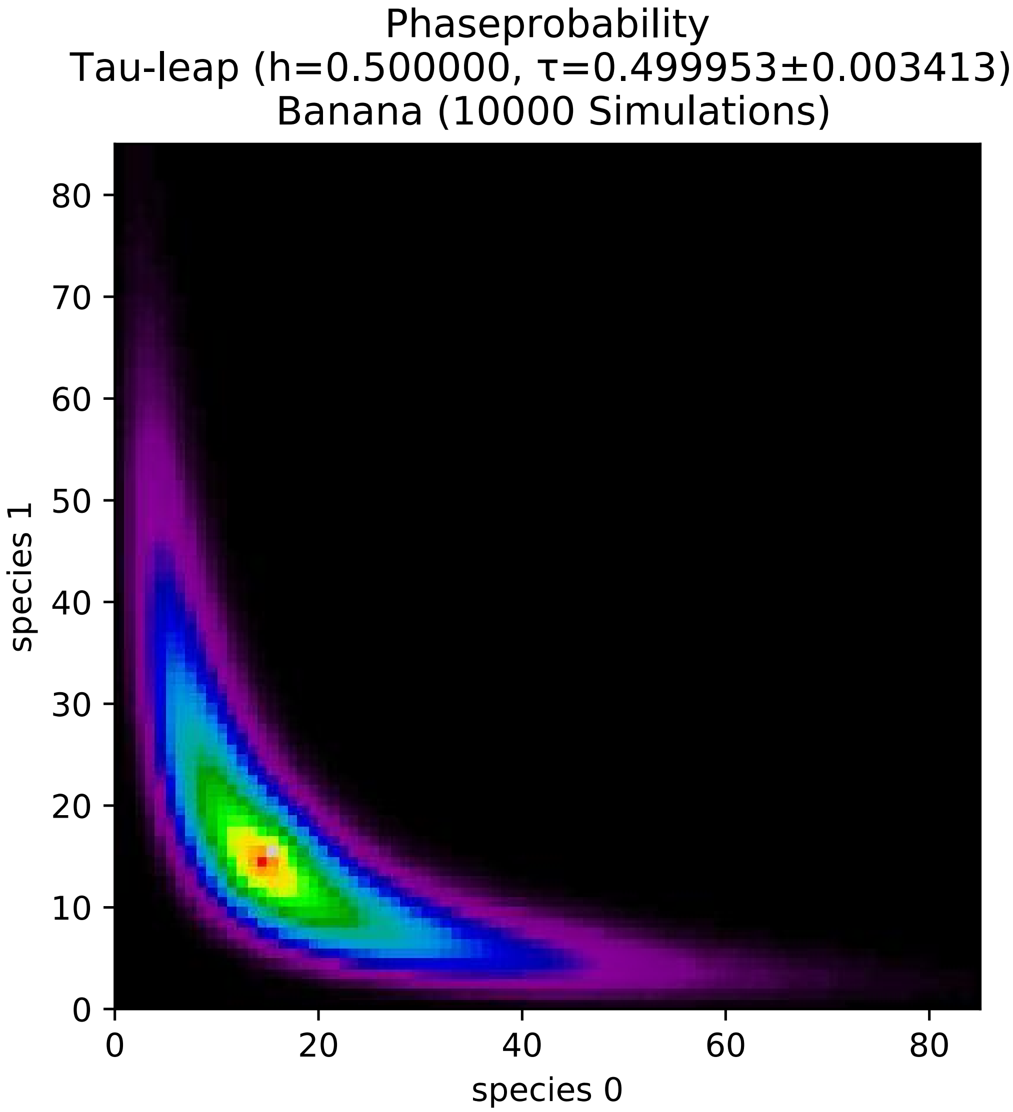
Bending the Banana

Freie Universität Berlin

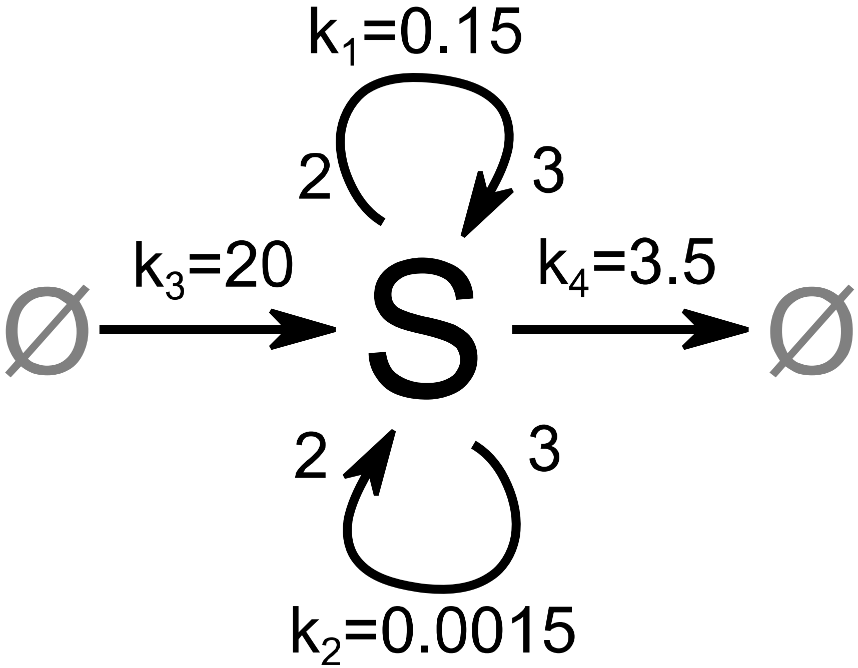


Bending the Banana

Freie Universität Berlin



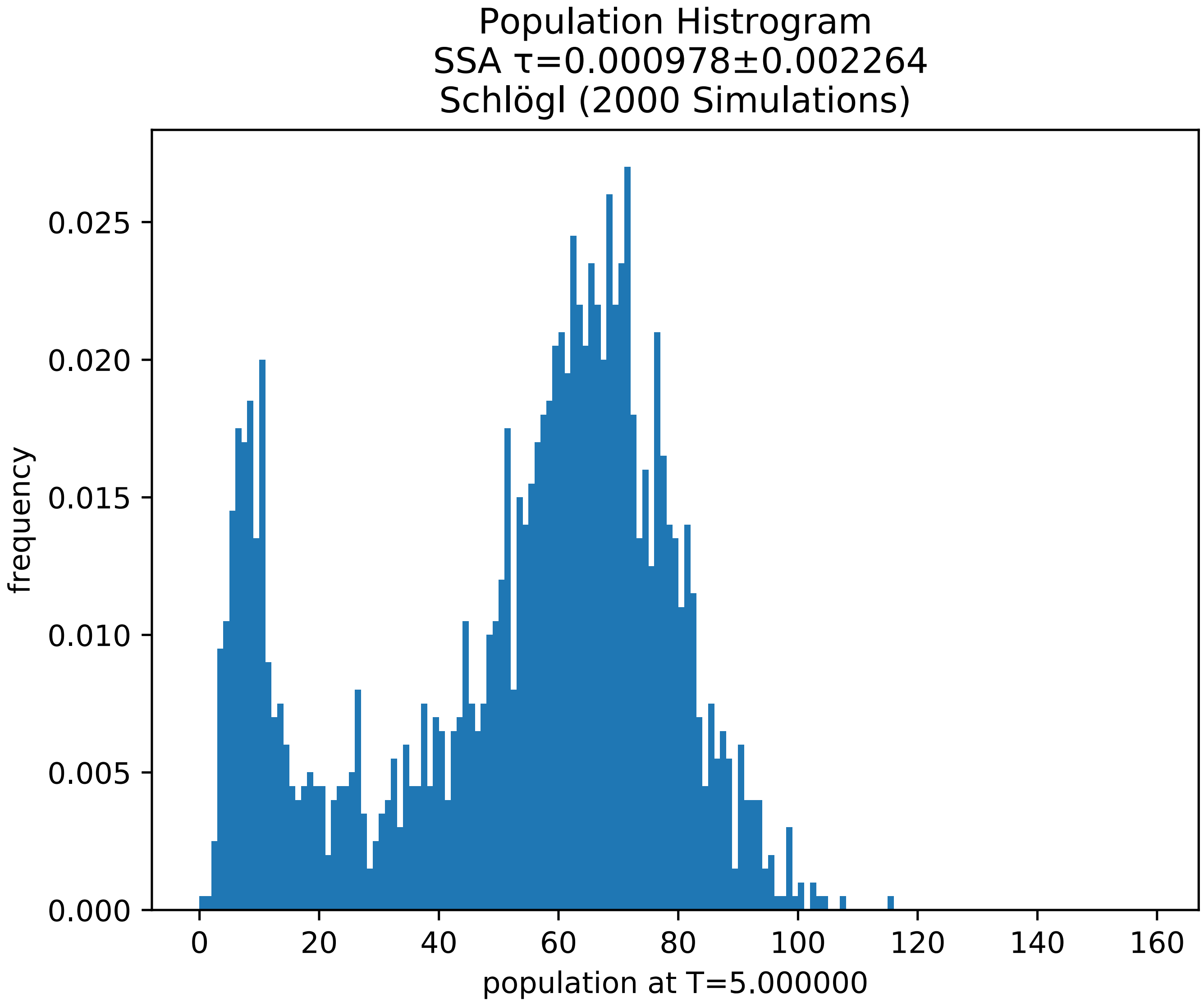
Schlögl model



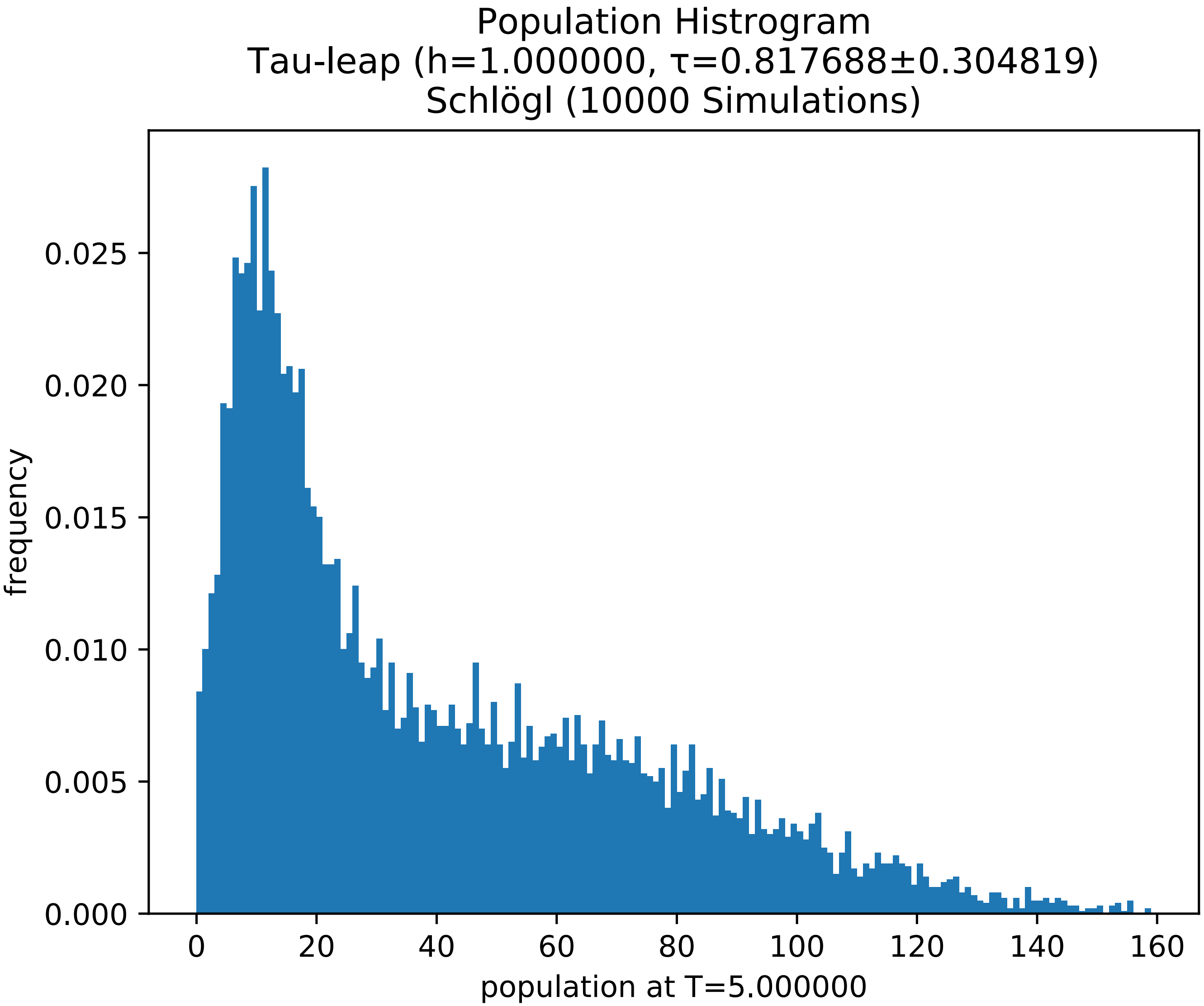
- S(0) = 40
- bistability in time

Schlögl Bistability

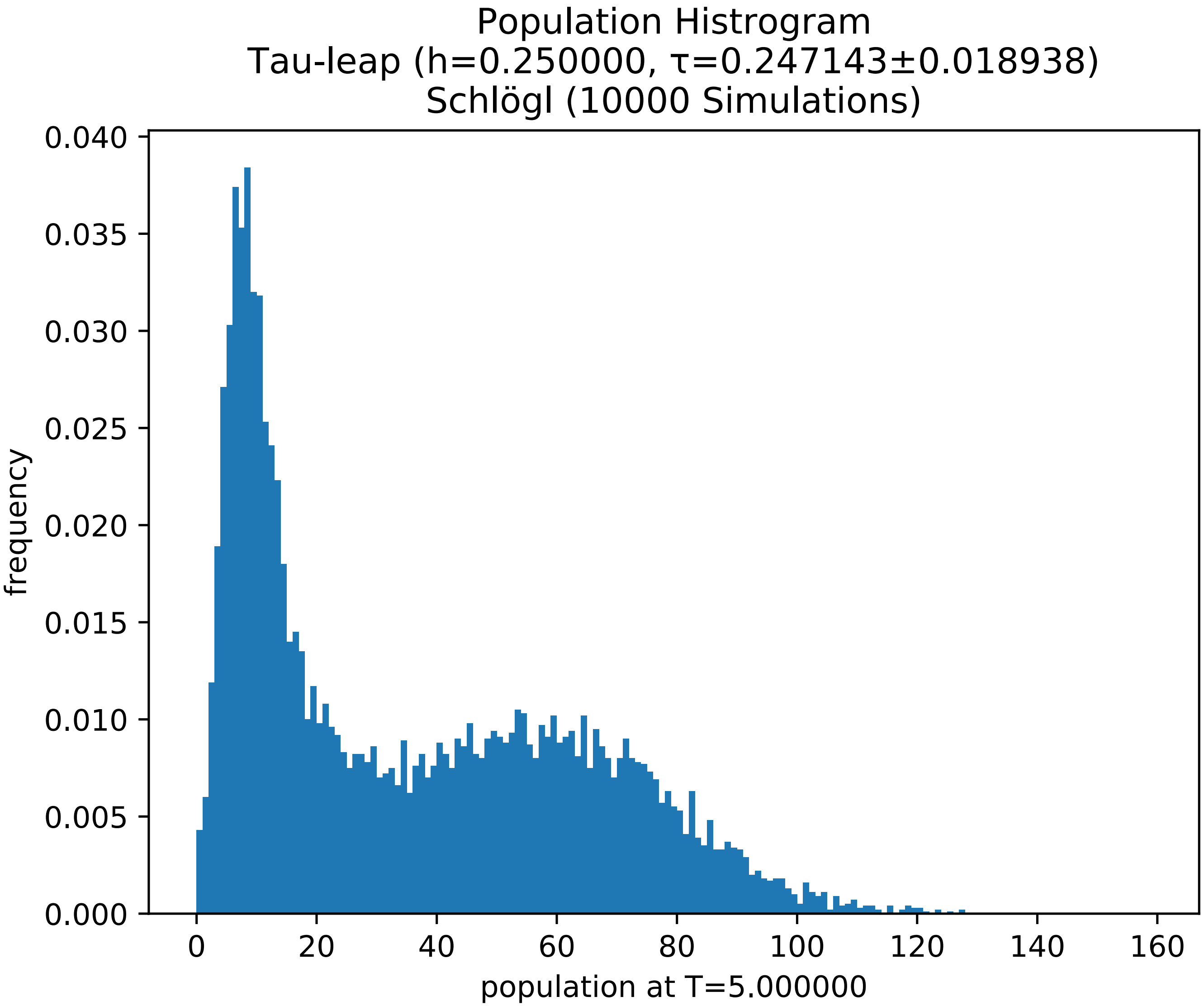
Freie Universität Berlin



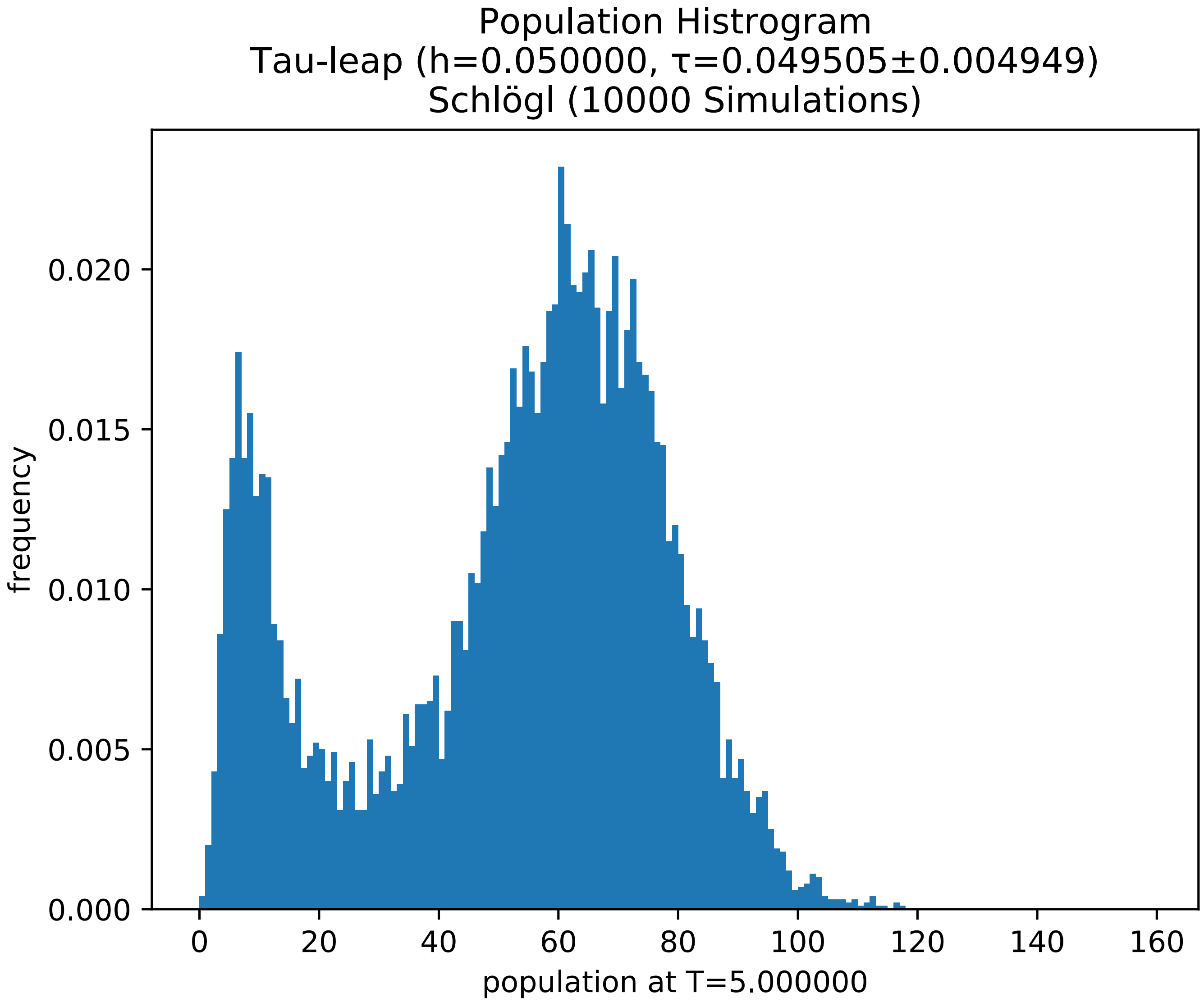
Schlögl Bistability



Schlögl Bistability



Schlögl Bistability



Conclusions

Birth-death model

- Tau-Leaping is a good approximation
- converges, but retains higher variance than SSA when stepsize is high

Banana model

- difficult, only similar to SSA solutions when stepsize approaches SSA-level
- → no gain from Tau-Leaping

Schlögl model

- although especially stepsize dependent, yields good results
- can benefit from Tau-Leaping

→ model dependent performance of Tau-Leaping

Discussion - so far

Have looked into:

- experimental behavior of Tau-Leaping for some elementary models
- → some models can be simulated a lot faster with Tau-Leaping, conserving dynamics, for other models dynamics break or are hard (i.e. small stepsize necessary)
- similar to the numerical integrators for ODEs, there is a trade-off between performance and accuracy

Discussion - go further

Further steps:

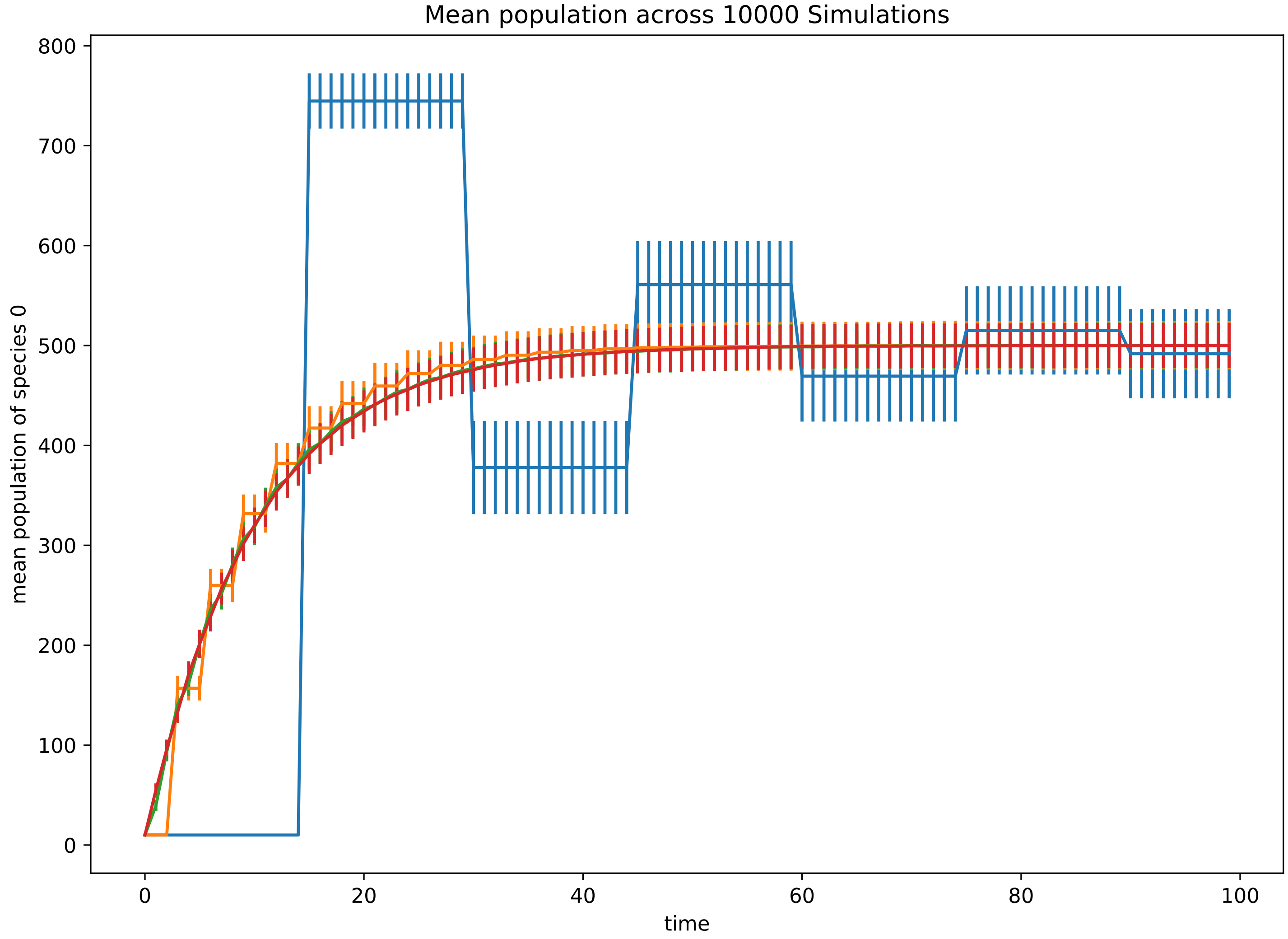
- evaluate Tau-Leaping for more complex models (more reactions, more species)
- look into numerical perturbation and maybe find generalizing principles from comparison to ODE integrators
- more rigorously test congruence of different simulations

References

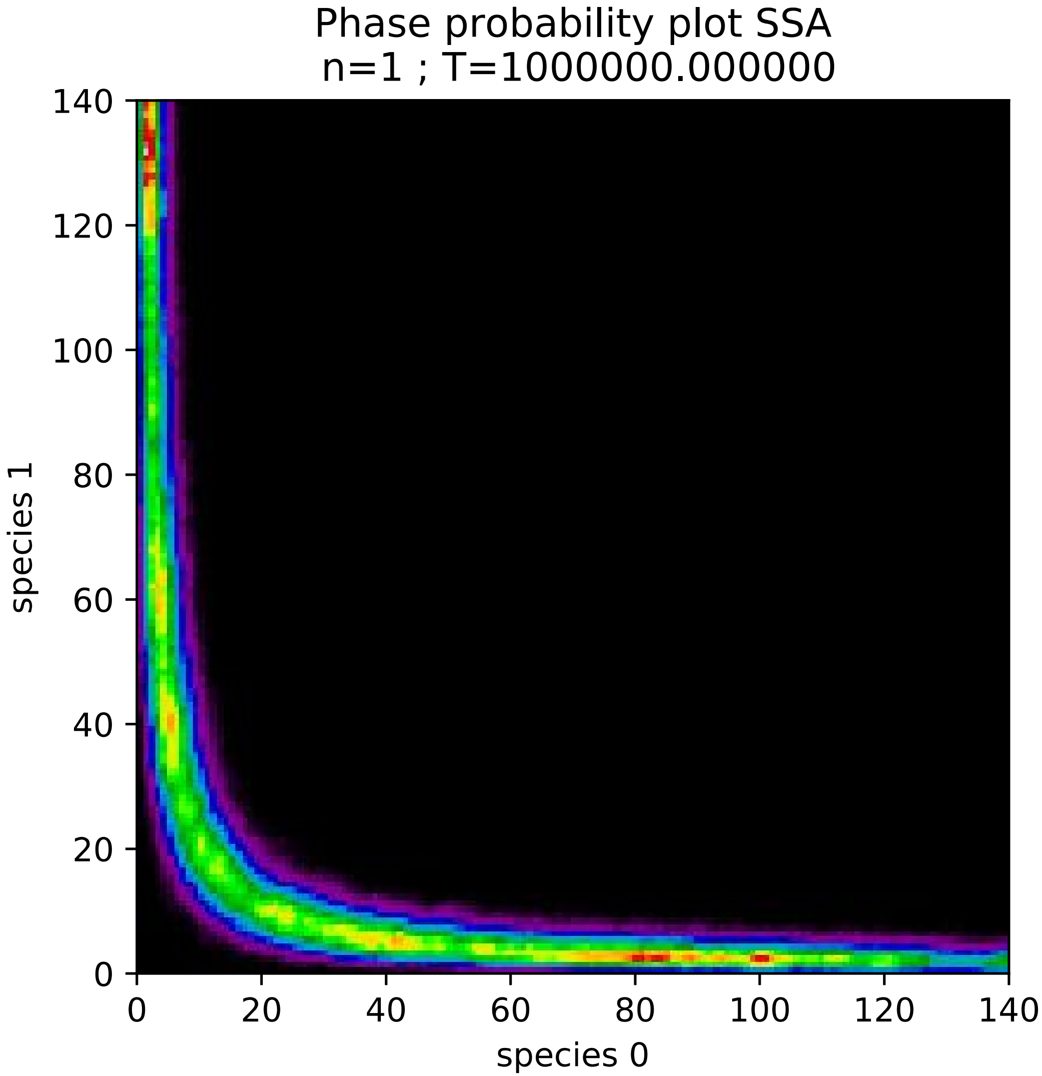
1. Approximate accelerated stochastic simulation of chemically reacting systems (Gillespie 2001)
2. Efficient step size selection for the tau-leaping simulation method (Cao et al. 2005)
3. Numerics for Bioinformaticians course material (12.07.17) http://systems-pharmacology.de/?page_id=724
4. Applied Numerics in Systemsbiology course material (12.07.17) http://systems-pharmacology.de/?page_id=971
5. Download more RAM https://downloadmoreram.com/

Additional Slides

Birth-death continued



Banana continued



Banana continued