Similarities and differences between stochastic and deterministic models of reaction networks

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1. Will discuss both deterministic and stochastic models of reaction systems – broad motivation is to understand relation between modeling choices.

2. From Kurtz’s Law of Large Numbers results, we know that they often give very similar behavior on compact time intervals.

3. **Broad question:** What about infinite time-frames?

4. **Result 1 (similar):** long term behavior of complex balanced systems is nice in both.

5. **Result 2 (different):** sometimes long-term behavior can be startlingly different (*Absolute stability vs. extinction*).

6. Matthew and Daniele will explore each question in a deeper manner.
Reaction Networks: \( \{S, C, R\} \)

Example

\[
A + B \rightarrow 2B \\
B \rightarrow A
\]

- \( S = \{A, B\} \).
- \( C = \{A + B, 2B, B, A\} \).
- \( R = \{A + B \rightarrow 2B, B \rightarrow A\} \).
Reaction Networks: \( \{S, C, R\} \)

Example:

Species: \( S = \{A, B, C, D, E\} \).

Complexes: \( C = \{A, 2B, A + C, D, B + E\} \).

Reactions:
\( R = \{A \rightarrow 2B, 2B \rightarrow A, A+C \rightarrow D, D \rightarrow A+C, D \rightarrow B+E, B+E \rightarrow A+C\} \).
Reaction Networks: \(\{S, C, R\}\)

Definition
A chemical reaction network, \(\{S, C, R\}\), consists of:

1. **Species**, \(S := \{S_1, \ldots, S_d\}\): constituent molecules undergoing a series of chemical reactions.

2. **Complexes**, \(C\): linear combinations of the species representing those used, and produced, in each reaction.

3. A set of **reactions**, \(R := \{y_k \rightarrow y'_k\}\), with **reaction vectors** \(y'_k - y_k \in \mathbb{Z}^d\).
Dynamics – deterministic with mass-action kinetics

Example:

\[ A + B \xrightarrow{\kappa_1} 2B \quad (R1) \]
\[ B \xrightarrow{\kappa_2} A \quad (R2) \]

Let \( x(t) \in \mathbb{R}^2_{\geq 0} \) give concentrations of molecules of \( A \) and \( B \):

\[
\dot{x} = r_1(x) \begin{bmatrix} -1 \\ 1 \end{bmatrix} + r_2(x) \begin{bmatrix} 1 \\ -1 \end{bmatrix}.
\]

Deterministic mass-action kinetics says:

\[
r_1(x) = \kappa_1 x_A x_B, \quad \text{and} \quad r_2(x) = \kappa_2 x_B.
\]

so

\[
\dot{x}_A = -\kappa_1 x_A x_B + \kappa_2 x_B \]
\[
\dot{x}_B = \kappa_1 x_A x_B - \kappa_2 x_B.
\]
Dynamics: deterministic

For general system, we have $S = \{S_1, \ldots, S_d\}$, with $k$th reaction

$$y_k \rightarrow y'_k$$

- The rate of $k$th reaction is $\kappa_k x^y_k$
- so

$$\dot{x} = \sum_k \kappa_k x^y_k (y'_k - y_k).$$
Dynamics: discrete – stochastic

Example:

\[
\emptyset \xleftrightarrow{\alpha} A \quad \text{(R1/R2)}
\]

\[
X(t) = X(0) + R_1(t) - R_2(t).
\]

For Markov models can take

\[
R_1(t) = Y_1(\alpha t)
\]

\[
R_2(t) = Y_2 \left( \beta \int_0^t X_A(s) ds \right)
\]

where \( Y_1, Y_2 \) are independent unit-rate Poisson processes.

\[
X(t) = X(0) + Y_1(\alpha t) - Y_2 \left( \beta \int_0^t X_A(s) ds \right).
\]
Dynamics: discrete – stochastic

Example:

\[ A + B \xrightarrow{\kappa_1} 2B \]  
\[ B \xrightarrow{\kappa_2} A \]  

\[ X(t) = X(0) + R_1(t) \begin{bmatrix} -1 \\ 1 \end{bmatrix} + R_2(t) \begin{bmatrix} 1 \\ -1 \end{bmatrix}. \]

For Markov models can take

\[ R_1(t) = Y_1 \left( \kappa_1 \int_0^t X_A(s)X_B(s)ds \right) \]
\[ R_2(t) = Y_2 \left( \kappa_2 \int_0^t X_B(s)ds \right) \]

where \( Y_1, Y_2 \) are independent unit-rate Poisson processes.

\[ R_1 \)  \quad T \xrightarrow{1} T + G, \quad R_2 \)  \quad G \xrightarrow{0.025} T, \quad R_3 \)  \quad T \xrightarrow{1000} T + S, \]
\[ R_4 \)  \quad T \xrightarrow{0.25} \emptyset, \quad R_5 \)  \quad S \xrightarrow{2} \emptyset, \quad R_6 \)  \quad G + S \xrightarrow{7.5 \times 10^{-6}} V, \]

\[ X_G(t) = X_G(0) + Y_1 \left( \int_0^t X_T(s) ds \right) - Y_2 \left( 0.025 \int_0^t X_G(s) ds \right) - Y_6 \left( 7.5 \times 10^{-6} \int_0^t X_G(s) X_S(s) ds \right) \]
\[ X_S(t) = X_S(0) + Y_3 \left( 1000 \int_0^t X_T(s) ds \right) - Y_5 \left( 2 \int_0^t X_S(s) ds \right) - Y_6 \left( 7.5 \times 10^{-6} \int_0^t X_G(s) X_S(s) ds \right) \]
\[ X_T(t) = X_T(0) + Y_2 \left( 0.025 \int_0^t X_G(s) ds \right) - Y_4 \left( 0.25 \int_0^t X_T(s) ds \right) \]
\[ X_V(t) = X_V(0) + Y_6 \left( 7.5 \times 10^{-6} \int_0^t X_G(s) X_S(s) ds \right). \]
Dynamics: discrete – stochastic

For general system, we have $S = \{S_1, \ldots, S_d\}$, with $k$th reaction

$$y_k \rightarrow y'_k$$

- The rate (or intensity or propensity) of $k$th reaction is $\lambda_k : \mathbb{Z}^d_{\geq 0} \rightarrow \mathbb{R}$.

- As before:

$$X(t) = X(0) + \sum_k R_k(t)(y'_k - y_k),$$

with

$$X(t) = X(0) + \sum_k Y_k \left( \int_0^t \lambda_k(X(s)) ds \right) (y'_k - y_k),$$

$Y_k$ are independent, unit-rate Poisson processes.
Mass-action kinetics

The standard intensity function chosen is **stochastic mass-action kinetics**:

\[
\lambda_k(x) = \kappa_k \prod_i \frac{x_i!}{(x_i - y_{ik})!}.
\]

Example: If \( S_1 \rightarrow \text{anything} \), then \( \lambda_k(x) = \kappa_k x_1 \).

Example: If \( S_1 + S_2 \rightarrow \text{anything} \), then \( \lambda_k(x) = \kappa_k x_1 x_2 \).

Example: If \( 2S_2 \rightarrow \text{anything} \), then \( \lambda_k(x) = \kappa_k x_2(x_2 - 1) \approx \kappa_2 x_2^2 \) if \( x_2 \gg 1 \).
Dynamics. Example

\[ A + B \xrightarrow{\alpha} 2B \]  \hspace{1cm} (R1)

\[ B \xrightarrow{\beta} A \]  \hspace{1cm} (R2)

**Stochastic equations**

\[
X(t) = X(0) + Y_1 \left( \alpha \int_0^t X_A(s)X_B(s)ds \right) \begin{bmatrix} -1 \\ 1 \end{bmatrix} + Y_2 \left( \beta \int_0^t X_B(s)ds \right) \begin{bmatrix} 1 \\ -1 \end{bmatrix}.
\]

**Deterministic equations**

\[
x(t) = x(0) + \alpha \int_0^t x_A(s)x_B(s)ds \begin{bmatrix} -1 \\ 1 \end{bmatrix} + \beta \int_0^t x_B(s)ds \begin{bmatrix} 1 \\ -1 \end{bmatrix},
\]
Other ways to understand model

Could just say that for $n \in \mathbb{Z}_{\geq 0}^d$,

$$
n \rightarrow \begin{cases} 
n + y'_1 - y_1, & \text{with rate } \lambda_1(n) \\
n + y'_2 - y_2, & \text{with rate } \lambda_2(n) \\
\vdots \\
n + y'_r - y_r, & \text{with rate } \lambda_r(n) 
\end{cases}
$$

where $y'_k - y_k \in \mathbb{Z}^d$.

I.e. a continuous time Markov chain with infinitesimal generator

$$\mathcal{A}f(x) = \sum_k \lambda_k(x)(f(x + y'_k - y_k) - f(x)).$$

and forward (chemical master) equation

$$p'_t(x) = \sum_k p_t(x - y'_k + y_k)\lambda_k(x - y'_k + y_k) - \sum_k p_t(x)\lambda_k(x)$$
First connection (Kurtz)

The ODE model is a limit of the stochastic model.

Assume

- $V$ is a scaling parameter: volume times Avogadro’s number, or 1000.

- $X_i = O(V)$, and $X^V(t) \overset{\text{def}}{=} V^{-1} \cdot X(t)$,

- $\lambda_k(X(t)) \approx V (\kappa_k X^V(t)^{y_k})$.

Example

Consider

$$A + B \xrightarrow{2/V} 2B \quad \text{(R1)}$$

$$B \xrightarrow{1} A \quad \text{(R2)}$$

with $X(0) = [3V, V]$

rate of R1 = $\frac{2}{V} X_A X_B = \frac{2}{V} \cdot (V \cdot X_A^V)(V \cdot X_B^V) = V \cdot 2X_A^V X_B^V$. 
Connection: Law of large numbers (Kurtz)

Then,

\[ X^V(t) \approx \frac{1}{V} X_0 + \sum_k \frac{1}{V} Y_k \left( V \int_0^t \kappa_k X^V(s)^{y_k} \, ds \right) (y'_k - y_k) \]

LLN for \( Y_k \) says

\[
\frac{1}{V} Y_k(Vu) \approx u \left( \limsup_{V \to \infty} \sup_{u \leq U} \left| V^{-1} Y_k(Vu) - u \right| = 0, \ \text{a.s.} \right)
\]

so a good approximation is solution to

\[ x(t) = x(0) + \sum_k \int_0^t \kappa_k x(s)^{y_k} \, ds \cdot (y'_k - y_k) , \]

where

\[ u^v = u_1^{v_1} \cdots u_d^{v_d} , \]

is standard mass-action kinetics. See Tom Kurtz’s works....
LLN: Example

- Stochastic models:

\[ A + B \xrightarrow{2/V} 2B \]  
\[ B \xrightarrow{1} A \]  

with \( X(0) = [3V, V] \) so that \([A^V, B^V] = X/V\) satisfies

\[ A^V(0) = 3, \quad B^V(0) = 1. \]

- ODE model of

\[ A + B \xrightarrow{2} 2B \]
\[ B \xrightarrow{1} A, \]

with \( x(0) = [3, 1] \).
LLN: Example, $A + B \xrightarrow{2/V} 2B \quad B \xrightarrow{1} A$
LLN: Example, $A + B^{2/V} \rightarrow 2B \quad B \rightarrow A$
LLN: Example, \( A + B^{2/V} \rightarrow 2B \) \( B \rightarrow A \)
The limit is:

\[ X^V \rightarrow x \]

over \([0, T]\) with \(T\) finite.

So what about infinite time-frames?
Story # 1: Complex balanced networks

Theorem (HJF - 1970s, Craciun - yesterday)
Let \( \{S, C, \mathcal{R}\} \) be a chemical reaction network with rate constants \( \kappa_k \).
Suppose:

1. the network is weakly reversible, and
2. has a deficiency of zero.

Then, ODE system is complex-balanced and,

(i) within each stoichiometric compatibility class (invariant manifold), there is a unique positive equilibria.

(ii) each equilibria is complex-balanced.

(iii) each equilibria is globally asymptotically stable relative to the interior of its compatibility class.

Question: what about same conditions on stochastic model?

What is the object we should look at?
Example

Consider

\[ \emptyset^{1/3} \rightarrow A \]

with

\[ P(X_A(0) = 10) = 1. \]
Example: population size - evolution of distribution
Long term dynamics

Deterministic: stable fixed point

Stochastic: convergence of distribution to equilibria
Theorem (A., Craciun, Kurtz, 2010)

Let $\{S, C, R\}$ be a chemical reaction network with rate constants $\kappa_k$. Suppose:

1. the network is weakly reversible, and
2. has a deficiency of zero.

Then, for any irreducible communicating equivalence class, $\Gamma$, the stochastic system has a product form stationary distribution

$$\pi(x) = \frac{1}{Z^V} \prod_{i=1}^{d} e^{-c_i} \frac{c_i^{x_i}}{x_i!}, \quad x \in \Gamma,$$

(1)

where $Z^V$ is a normalizing constant and $c$ is a complexed-balanced equilibrium of the corresponding ODE.

Same conditions give complex balanced, stability, for ODE.

Connectivity

Definition
The connected components of the reaction network are called the *linkage classes*.

Example

\[ A + B \xrightarrow{\alpha} 2B \]  
(Linkage Class 1)

\[ B \xrightarrow{\beta} A \]  
(Linkage Class 2)

Has two linkage classes.
Connectivity

Definition
A chemical reaction network, \( \{S, C, R\} \), is called \textit{weakly reversible} if each linkage class is strongly connected.

A network is called \textit{reversible} if \( y_k' \to y_k \in \mathcal{R} \) whenever \( y_k \to y'_k \in \mathcal{R} \).
Connectivity

The following is not weakly reversible:

Neither is the following:

\[ A + B \xrightarrow{\alpha} 2B \quad \text{(Linkage Class 1)} \]
\[ B \xrightarrow{\beta} A \quad \text{(Linkage Class 2)} \]
Network properties

Definition

\[ S = \text{span}\{y_k \rightarrow y'_k \in \mathbb{R}\} \{y'_k - y_k\} \]

is the *stoichiometric subspace* of the network.

Denote

\[ \text{dim}(S) = s. \]

**Implication:** Solutions bound to translations of \( S \).

**Example:** Reaction network

\[ A + B \rightleftharpoons 2B \]

\[ B \rightleftharpoons A \]
Deficiency.

\[
\text{deficiency of } \{S, C, R\} = \delta = n - \ell - s,
\]

where
1. \(n\) = # of complexes.
2. \(\ell\) = # of linkage classes.
3. \(s\) = dimension of span of reaction vectors.

So it is easy to check.

Example

\[
A + B \rightleftharpoons 2B \quad \text{(R1)}
\]

\[
B \rightleftharpoons A \quad \text{(R2)}
\]

\[n = 4, \ell = 2, s = 1 \implies \delta = 1.\]
Deficiency

Example

\[ n = 5 \]
\[ \ell = 2 \]
\[ s = 3 \]

\[ \implies \delta = 5 - 2 - 3 = 0. \]
Example: Enzyme kinetics

Consider the possible model of enzyme kinetics given by

\[ E + S \rightleftharpoons ES \rightleftharpoons E + P, \quad E \rightleftharpoons \emptyset \rightleftharpoons S \]

- Easy to see that deficiency is 0 and that \( \Gamma = \mathbb{Z}^4_{\geq 0} \).

- Thus, in distributional equilibrium, the species numbers are independent and have Poisson distributions.
Consider the slightly different enzyme kinetics given by

\[ E + S \rightleftharpoons ES \rightleftharpoons E + P \quad , \quad E \rightleftharpoons \emptyset \]

- We see \( S + ES + P = N \).
- In distributional equilibrium:
  - \( E \) has Poisson distribution,
  - \( S, \ ES, \ P \) have a multinomial distribution, and
  - \( E \) is independent from \( S, \ ES, \) and \( P \).
If

(i) \( X^V = V^{-1} X \)

satisfies “classical scaling”, and

(ii) unscaled model is complex balanced with equilibrium \( V^c \).

Then we still have our nice distribution and for \( x^V \in \mathbb{Z}^d / V \),

\[
\lim_{t \to \infty} P(X^V(t) = x^V) = \lim_{t \to \infty} P(X(t) = x^V V)
\]

\[= \frac{1}{Z^V} \prod_{i=1}^{d} e^{-c_i V (Vc_i)^{x_i V}} \frac{(x_i V)!}{(x_i V)!}. \]
π^V(x) = \frac{1}{Z^V} \prod_{i=1}^{d} e^{-c_i V} \frac{(Vc_i)^{x_i V}}{(x_i V)!}.

In this case, if \( x^V \to x \) with \( x^V \in \mathbb{Z}^d / V \), then

\[
\lim_{V \to \infty} -\frac{1}{V} \ln(\pi^V(x^V)) = \lim_{V \to \infty} \left[ \frac{1}{V} \ln(Z^V) - \frac{1}{V} \sum_{i=1}^{d} (-c_i V + x_i^V V \ln(Vc_i) - \ln((x_i^V V)!)) \right]
\]

= \lim_{V \to \infty} \sum_{i=1}^{d} (c_i - x_i^V \ln(Vc_i) + V^{-1} \ln((x_i^V V)!)).

where \( c \) is the complex-balanced equilibrium.

Stirling’s formula

\[
\ln(n!) = n \ln(n) - n + O(\ln(n)),
\]

yields

\[
\lim_{V \to \infty} -\frac{1}{V} \ln(\pi^V(x^V)) = \sum_{i=1}^{d} x_i(\ln(x_i) - \ln(c_i) - 1) + c_i.
\]

The deterministic model satisfies

\[ \dot{x} = 6 - 11x + 6x^2 - x^3 = -(x - 1)(x - 2)(x - 3), \]

and there are two asymptotically stable equilibria at \( c = 1, 3 \) and one unstable at \( c = 2 \).

Can find \( \pi^V(x) \) and show

\[
\lim_{V \to \infty} -\frac{1}{V} \ln(\pi^V(x)) = x \left( \ln \left( \frac{x(x^2 + 11)}{x^2 + 1} \right) - \ln(6) - 1 \right) + 2\sqrt{11} \arctan \left( \frac{x}{\sqrt{11}} \right) \\
- 2 \arctan(x) - 2\sqrt{11} \arctan \left( \frac{1}{\sqrt{11}} \right) + 1 + \frac{1}{2} \pi,
\]
One more connection here

Figure: Plots of the scaled non-equilibrium potential (NEP), $-\frac{1}{V} \ln(\pi^V(x^V))$, of the scaled birth-death process of are given for $V \in \{10, 10^2, 10^3\}$, as is the function $g(x)$.
We know: scaled stationary distribution of stochastic model limits to a Lyapunov function for deterministic model if:

1. Deterministic model is complex balanced.

Open question: what is the class of models for which this works?
Differences

Story #2: are there times the models behave very differently?
Story 2: Absolute Concentration Robustness


\[
\begin{align*}
A + B & \xrightarrow{\alpha} 2B \quad \text{(R1)} \\
B & \xrightarrow{\beta} A \quad \text{(R2)}
\end{align*}
\]

\[
\begin{align*}
\dot{x}_A(t) &= -\alpha x_A(t)x_B(t) + \beta x_B(t) \\
\dot{x}_B(t) &= \alpha x_A(t)x_B(t) - \beta x_B(t)
\end{align*}
\]

\[M \overset{\text{def}}{=} x_A(0) + x_B(0),\]

Solving for equilibria:

\[\bar{x}_A = \frac{\beta}{\alpha},\]

\[\bar{x}_B = M - \frac{\beta}{\alpha},\]

Network has *absolute concentration robustness* in species $A$. 
Fig. 2. The EnvZ-OmpR system. (A) A schematic diagram of an EnvZ-OmpR model in which ATP is the cofactor in phospho-OmpR dephosphorylation. P$_i$ denotes phosphate ion. (B) The mass-action model underlying (A). [T] denotes the ATP concentration, assumed fixed. Terminal nodes are colored pink, and nonterminal nodes are colored blue. (C) A schematic diagram of an EnvZ-OmpR model in which ADP is the cofactor in phospho-OmpR dephosphorylation. (D) The mass-action model underlying (C). [D] denotes the ADP concentration, assumed fixed.
Theorems: deterministic and stochastic


Consider a deterministic mass-action system that

- has a deficiency of one.
- admits a positive steady state and
- has two non-terminal complexes that differ only in species S,

then the system has absolute concentration robustness in S.

Theorem (A., Enciso, Johnston – stochastic)

Consider a reaction network satisfying the following:

- has a deficiency of one,
- the deterministic model admits a positive steady state,
- has two non-terminal complexes that differ only in species S,
- (new) is conservative,

then with probability one there there is a last time a nonterminal reaction fires.

Differing in one species

Examples:

1. \( A, \ A + B \) differ in species \( B \).

2. \( XT, \ XT + Y_p \) differ in species \( Y_p \).

3. \( T, \ T + G \) differ in species \( G \).
Terminal and non-terminal complexes

- The orange complexes are called **terminal**.
- The blue complexes are called **non-terminal**.
Theorems: deterministic and stochastic


Consider a deterministic mass-action system that

- has a deficiency of one.
- admits a positive steady state and
- has two non-terminal complexes that differ only in species S,

then the system has absolute concentration robustness in S.

Theorem (A., Enciso, Johnston – stochastic)

Consider a reaction network satisfying the following:

- has a deficiency of one,
- the deterministic model admits a positive steady state,
- has two non-terminal complexes that differ only in species S,
- (new) is conservative,

then with probability one there there is a last time a nonterminal reaction fires.

\[ \text{David F. Anderson, Germán Enciso, and Matthew Johnston, } \textit{Stochastic analysis of biochemical reaction networks with absolute concentration robustness}, \textit{J. Royal Society Interface}, \text{Vol. 11, 20130943, February 12, 2014}. \]
Example
Reaction network

\[ A + B \rightarrow 2B \]

\[ B \rightarrow A \]

has state space

![Graph showing the state space of the reaction network with points and arrows indicating transitions between states.](image-url)
\[
X_{\text{tot}} := X + XD + XT + X_p + X_p Y + XDY_p \\
Y_{\text{tot}} := Y + X_p Y + XDY_p + Y_p.
\]
Idea of proof

1. **Suppose not true:** then there is a positive recurrent state for which a nonterminal complex has positive intensity (rate).

2. This provides a series of stopping times, \( \tau_N \to \infty \).

3. Use stochastic equation:

\[
0 = X^*(\tau_N) - X^*(0) = \sum_k Y_k \left( \kappa_i \int_0^{\tau_N} (X^*(s))^{y_k} ds \right) (y'_k - y_k)
\]

\[
= \sum_k \kappa_k \left[ \frac{1}{\kappa_k \int_0^{\tau_N} (X^*(s))^{y_k} ds} Y_k \left( \kappa_k \int_0^{\tau_N} (X^*(s))^{y_k} ds \right) \times \frac{1}{t_N} \int_0^{\tau_N} (X^*(s))^{y_k} ds \right] (y'_k - y_k)
\]

4. In limit \( N \to \infty \), find something in kernel of \( YA_{\kappa} \) that can not be there.
Extinction can be rare event. What’s real behavior?

\[ \begin{align*}
A + B & \overset{\alpha}{\rightarrow} 2B \\
B & \overset{\beta}{\rightarrow} A \\
X_A(0) + X_B(0) &= M,
\end{align*} \]

Can show that quasi-stationary distribution for \( A \) converges to Poisson

\[ \pi^Q_M(x) \rightarrow e^{-\left(\frac{\beta}{\alpha}\right)} \frac{\left(\frac{\beta}{\alpha}\right)^x}{x!}, \quad \text{as } M \rightarrow \infty. \]
Quasi-stationary distribution: EnvZ-OmpR signaling system

Fig. 2. The EnvZ-OmpR system. (A) A schematic diagram of an EnvZ-OmpR model in which ATP is the cofactor in phospho-OmpR dephosphorylation. P_i denotes phosphate ion. (B) The mass-action model underlying (A). [T] denotes the ATP concentration, assumed fixed. Terminal nodes are colored pink, and nonterminal nodes are colored blue. (C) A schematic diagram of an EnvZ-OmpR model in which ADP is the cofactor in phospho-OmpR dephosphorylation. (D) The mass-action model underlying (C). [D] denotes the ADP concentration, assumed fixed.

1 Guy Shinar and Martin Feinberg, Structural Sources of Robustness in Biochemical Reaction Networks, Science, 2010
Quasi-stationary distribution

Molecules of $Y_p$

Quasi-stationary probabilities

$X_{\text{tot}} = 100$
$Y_{\text{tot}} = 3500$
$X_{\text{tot}} = 1000$
$Y_{\text{tot}} = 35000$
$X_{\text{tot}} = 10000$
$Y_{\text{tot}} = 350000$

Poisson
Behavior on compact time intervals

Let $N$ be a scaling parameter (total conserved value), and consider $N \gg 1$.

Let $q$ be the value of the ACR equilibrium value and let

$$J \sim \text{Poisson}(q).$$

(2)

Theorem (A., Cappelletti, Kurtz, 2015 – being written now)

Suppose $T > 0$ and that some technical assumptions hold on the reaction network and let $J$ be as in (2). Then, for any continuous function $\hat{g}: \mathbb{R}_{\geq 0}^{\chi_{ACR}} \rightarrow \mathbb{R}$ with at most polynomial growth rate we have

$$\int_0^{\cdot \wedge T} \left( \hat{g}(X_{ACR}^N(s)) - E[\hat{g}(J)] \right) ds \underset{N \rightarrow \infty}{\Rightarrow} 0.$$

or equivalently,

$$P \left( \sup_{t_1, t_2 \in [0, T], t_1 < t_2} \left| \int_{t_1}^{t_2} \left( \hat{g}(X_{ACR}^N(s)) - E[\hat{g}(J)] \right) ds \right| > \varepsilon \right) \underset{N \rightarrow \infty}{\longrightarrow} 0$$
Two more open problems.

1. ODE model: Stability of ACR equilibria?

2. Stochastic model: Why are Poisson’s showing up so much? Can we characterize this somehow?
That is the story. Thanks!

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