Math 289a Notes

Notetaker: Chris Chang
for 27 October 2008

Strong Approximations

(Komlós-Major-Tusnády, 1975)

A Poisson process $N$ (with rate 1) and a standard one-dimensional Brownian motion $W$ can be constructed on a common probability space so that

$$\sup_{t \in [0, \infty)} \left| N(t) - t - W(t) \right| \sim (\log t) \lor 2 = \xi < \infty \text{ a.s.}$$

where $E[\exp(\alpha \xi)] < \infty$ for some $\alpha > 0$. ($a \lor b$ means $\max(a, b)$.)

[Note that the renewal CLT for $N$ states that, if $\hat{N}^n(t) = N(nt) - nt \sqrt{n}$, $\forall t \geq 0$, then $\hat{N}^n$ converges in distribution to $W$.] See Ethier-Kurtz for more details.

Before moving on, here’s a handy “bilingual dictionary” for probabilists talking with chemists:

<table>
<thead>
<tr>
<th>Chemistry</th>
<th>Probability</th>
</tr>
</thead>
<tbody>
<tr>
<td>propensities</td>
<td>intensities</td>
</tr>
<tr>
<td>master equation</td>
<td>Kolmogorov forward equation</td>
</tr>
<tr>
<td>Langevin equation</td>
<td>diffusion approximations</td>
</tr>
<tr>
<td>van Kampen equation</td>
<td>(functional) central limit theorem</td>
</tr>
</tbody>
</table>

Biochemical Reaction Networks

General references


Chemical Reaction Network

Denoted by the 3-tuple $(S, C, R)$.

$S$ = finite set of species (e.g., $\{A_1, \ldots, A_n\}$ or $\{A, B, C, D, E\}$)

$C$ = finite set of complexes (a complex is the left- or right-hand side of a reaction). We represent elements of $C$ by vectors in $\mathbb{N}^n$ – each element of $C$ is an $n$-vector where the $i$th component of the vector designates the number of molecules of the $i$th species in the complex.

Examples: for the reaction $A + 2B \rightarrow C$, $A + 2B$ is represented by $egin{pmatrix} 1 \\ 2 \\ 0 \end{pmatrix}$, and $C$ is represented by $egin{pmatrix} 0 \\ 0 \\ 1 \end{pmatrix}$. For $\emptyset \rightarrow A$ (an “inflow” reaction), $\emptyset = \begin{pmatrix} 0 \\ 0 \\ 0 \end{pmatrix}$. ($A \rightarrow \emptyset$ would be an “outflow” reaction.)

Our model corresponds to a “continuous flow stirred tank reactor.” Imagine a mostly sealed tank with a stirrer in the middle, but with inflow and outflow tubes.

(Aside: If $\nu$ and $\nu'$ are complexes such that $\nu \rightarrow \nu'$ is a reaction, that reaction is “reversible” if $\nu' \rightarrow \nu$ is also a reaction.)

$R$ is a finite set of reactions of the form $\nu \rightarrow \nu'$ where $\nu, \nu'$ are in $C$.

Generically, a reaction has the form $\sum_{i=1}^n v_{ik} A_i \rightarrow \sum_{i=1}^n v'_{ik} A_i$. The $k$th reaction is $v_k \rightarrow v'_k$.

The stoichiometric matrix $S$ has a row for each chemical species, and a column for each reaction. The $k$th column is equal to $v'_k - v_k$, i.e. the change in species counts that the $k$th reaction induces.

Microscopic Stochastic Model for Dynamics of Reaction Network

For each species $i$,

$X_i(t) =$ number of molecules of species $i$ at time $t$.

$X = (X_1, \ldots, X_n)$ is assumed to be a Markov chain.

When the $k$th reaction is the only reaction that occurs at time $t$, $X(t) = X(t^-) + v'_k - v_k$, where $t^-$ represents a time infinitesimally before $t$.

Given $x = (x_1, \ldots, x_n)$ as the current state of the system, assign to the $k$th reaction an exponential “alarm clock” with rate $\lambda_k(x)$ (intensity). (Note that exponential distributions are memoryless.)

Let $N_1, \ldots, N_n$ be independent unit rate Poisson processes. Then for each $k$,
\[ R_k(t) = N_k \left( \int_0^t \lambda_k(X(s)) \, ds \right) \]

= number of times \( k \)th reaction has occurred by time \( t \).

Then
\[ X(t) = X(0) + \sum_{k=1}^{K} R_k(t)(\nu'_k - \nu_k) = X(0) + SR(t), \]

where \( R(t) := \begin{pmatrix} R_1(t) \\ \vdots \\ R_K(t) \end{pmatrix} \).

**Mass-action kinetics**

Example: Examples of binary reactions

\[ A_1 + A_2 \xrightarrow{k} A_3 \]
\[ \lambda(x) = \kappa x_1 x_2, \quad \kappa = \text{reaction rate constant} \]

\[ A_1 + A_1 \xrightarrow{k} A_2 \]
\[ \lambda(x) = \kappa x_1(x_1 - 1) \]

More generally for \( \sum_{i=1}^{n} \nu_{ik} A_i \xrightarrow{k} \sum_{i=1}^{n} \nu'_{ik} A_i \),
\[ A_k(x) = \kappa_k \prod_{i=1}^{n} \frac{x_i}{\nu_{ik}}. \]

We can define the concentration vector as \( \frac{X(t)}{V} \) (where \( V \) is volume)

For the reaction \( A + B \xrightarrow{k} C \), the o.d.e. approximation for concentration is (where \( c = (c_A, c_B, c_C) \) is the vector with all three species concentrations)
\[ \dot{c}_A = -\kappa A c_B \]
\[ \dot{c}_B = -\kappa A c_B \]
\[ \dot{c}_C = \kappa A c_B \]

**How does \( \kappa \) depend on volume: cf. Gillespie**

Consider the binary reaction \( A_1 + A_2 \rightarrow A_3 \) with mass action kinetics. How does the rate constant \( \kappa \) depend on volume?
Probability of producing a new molecule of $A_3$ in a small time interval of length $\delta t$: $\lambda(x) \delta t$, which is proportional to the probability that some molecule of $A_1$ collides with some molecule of $A_2$ in $\delta t$.

Take one molecule of $A_1$ and one of $A_2$. Geometrically, imagine $A_1$ as a sphere with radius $r_1$, and $A_2$ as a sphere with radius $r_2$, and let $r_{12} = r_1 + r_2$. A collision of the two occurs if the center of $A_1$ is within $r_{12}$ of the center of $A_2$. For the purposes of our calculation we can imagine the center of $A_2$ as having a fixed random position in the volume $V$ and $A_1$ as moving (relative to $A_2$) at an average speed of $v_{12}$. Also, at any instant of time, the “reaction sphere of $A_1$” is the sphere with center $A_1$ and radius $r_{12}$ (if the center of $A_2$ lies within this sphere, then $A_1$ will react with $A_2$ to produce $A_3$).

The new volume swept out by $A_1$ in $\delta t$ is proportional to $\pi r_{12}^2 v_{12} \delta t$, so the probability that the randomly distributed center of $A_2$ falls in this volume is proportional to $\pi r_{12}^2 v_{12} V \delta t$. So, to leading order, we have

$$\lambda(x) \delta(t) \propto \left( \frac{\pi r_{12}^2 v_{12} \delta t}{V} \right) \cdot \text{(number of ways of choosing a pair of molecules $(A_1, A_2)$)}$$

so

$$\lambda(x) \delta(t) = \tilde{\kappa} x_1 x_2 \frac{V}{V} \delta t$$

for some constant $\tilde{\kappa}$.

More generally, $\lambda_k(x) = \frac{\tilde{\kappa}}{\prod_{i=1}^n v_{ik}} \prod_{i=1}^n \binom{x_i}{v_{ik}}$, where $m_k$ is the number of molecules consumed in reaction $k$, i.e., $m_k = \sum_{i=1}^n v_{ik}$.