Foundations of Chemical Kinetics

Lecture 22: The chemical master equation

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The chemical master equation

- So far, we have looked at transitions between states of a single molecule using the master equation.
- If we want to go back to describing reactions at the level of elementary reactions, i.e. neglecting internal degrees of freedom, we can use the chemical master equation (CME), which is a master equation for the probabilities that the system has any given composition as a function of time.
Derivation of the chemical master equation

Preliminaries

Let $\mathbf{N}(t) = (N_1(t), N_2(t), \ldots, N_n(t))$ be the composition vector of the system, where $N_i$ is the number of molecules of type $i$ and $n$ is the number of distinct chemical species.

Let $\mathcal{N}$ be the space of all possible vectors $\mathbf{N}$.

Let $P(\mathcal{N}, t)$ be the probability distribution over the space $\mathcal{N}$, i.e. the vector containing the probabilities of all possible states, $P(\mathbf{N}, t)$, at time $t$.

Assume the system is well-mixed, i.e. that the probability of finding a particular molecule inside a subvolume $\Delta V$ is $\Delta V/V$.

Reactions are random events:

- First-order reactions occur when some essentially random condition is met within a molecule (e.g. IVR putting enough energy in a reactive mode).
- In a well-mixed system, the collisions necessary for a reaction to occur are random events.
Derivation of the chemical master equation

Preliminaries

Boltzmann’s Stosszahlansatz (assumption of molecular chaos): Collisions cause a rapid loss of memory, i.e. particle trajectories can be treated as essentially random.

Consequence: Chemical reactions can be treated as Markov (memoryless) processes, provided the Stosszahlansatz is satisfied. This in turn means that we can write a master equation for $P(N, t)$.

Limitation: A model based on this ansatz will not be valid for time scales shorter than the mean collision time (gas phase).
Derivation of the chemical master equation

- The transitions here are chemical reactions that change the composition of the system.
- The transition rates appearing in the master equation ought to depend on the chemical composition.
- Let $\mathcal{R}$ be the set of reactions occurring in a chemical system.
- In this theory, the transition rates are called reaction propensities, denoted $a_r(N)$, for $r \in \mathcal{R}$.
- The (chemical) master equation is

$$\frac{dP(N, t)}{dt} = \sum_{r \in \mathcal{R}} a_r(N - \nu_r)P(N - \nu_r, t) - \sum_{r \in \mathcal{R}} a_r(N)P(N, t)$$

where $\nu_r$ is the stoichiometric vector of reaction $r$, i.e. the vector that gives the change in the numbers of each species as a result of reaction $r$. 
The reaction propensities

\[ a_r(N) \] is the probability per unit time that reaction \( r \) occurs given that the composition of the system is \( N \).

First-order reactions: \( X_i \rightarrow \)

\[ \quad \text{Suppose that the probability per unit time that any given molecule of } X_i \text{ reacts is } \kappa_r. \]
\[ \quad \text{If } \Delta t \text{ is sufficiently small, then the probability that a molecule of } X_i \text{ reacts given that there are } N_i \text{ molecules of this type is } \kappa_r N_i \Delta t. \]
\[ \quad \text{Therefore } a_r = \kappa_r N_i. \]
Second-order reactions: $X_i + X_j \rightarrow$ with $j \neq i$

- We start by figuring out the probability that a particular pair of molecules of types $i$ and $j$ meet and react in time $\Delta t$.
- From collision theory, the reaction volume explored per unit time in the gas phase is $v_{ij} \sigma_{ij}$.
- This represents the fraction $(v_{ij} \sigma_{ij}/V) \Delta t$ of the total volume $V$ in time $\Delta t$.
- This is the probability of a collision between any particular pair of molecules in time $\Delta t$.
- If a fraction $\eta_r$ of the collisions lead to reaction, then the reaction probability per unit time is $(\eta_r v_{ij} \sigma_{ij}/V) \Delta t = \kappa_r \Delta t$. 

\[ \text{The reaction propensities (continued)} \]
The reaction propensities (continued)

Second-order reactions: $X_i + X_j \rightarrow$ (continued)

- Reaction probability per unit time for a particular pair of molecules of types $i$ and $j$: $\kappa_r \Delta t$
- There are $N_i N_j$ pairs of molecules, so if we take $\Delta t$ sufficiently small, the probability that one reaction of type $r$ occurs per unit time is $a_r = \kappa_r N_i N_j$. 
Second-order reactions: $X_i + X_i \rightarrow$

- Everything is as above, except
  - The collision rate is $\frac{1}{2} v_{ii} \sigma_{ii}$, leading to $\kappa_r = \left( \frac{1}{2} \eta_r v_{ii} \sigma_{ii} / V \right)$.
  - The number of different pairs of two molecules both of type $i$ is $N_i(N_i - 1)/2$.
- The propensity is therefore $a_r = \kappa_r N_i(N_i - 1)/2$. 
In general: The reaction propensity can always be written as the product of a \textit{stochastic rate constant} with units of inverse time, and of a \textit{combinatorial factor} which gives the number of different combinations of reactant molecules present prior to the reaction:

\[ a_r = \kappa_r h_r(N) \]
Example 1: $A + B \xrightleftharpoons[k_1]{k_{-1}} C$

- The composition vector is $(N_A, N_B, N_C)$.
- The stoichiometry vector for the forward reaction is $\nu_1 = (-1, -1, 1)$.
- The stoichiometry vector for the reverse reaction is
- The propensity of the forward reaction is $a_1 = k_1 N_A N_B$.
- The propensity of the reverse reaction is
- Suppose that we start out with four molecules of $A$, three of $B$ and none of $C$.
  Then the space of all possible compositions is
  $$\mathcal{N} = \{(4, 3, 0), (3, 2, 1), (2, 1, 2), (1, 0, 3)\}$$
- The probability space is $P(\mathcal{N}) = \{P(N_A, N_B, N_C)\}$. 
Example: $A + B \xrightleftharpoons[\kappa_{-1}]{\kappa_1} C$

(continued)

- The chemical master equation is

\[
\frac{dP(N_A, N_B, N_C)}{dt} =
\kappa_1(N_A + 1)(N_B + 1)P(N_A + 1, N_B + 1, N_C - 1) \\
+ \kappa_{-1}(N_C + 1)P(N_A - 1, N_B - 1, N_C + 1) \\
- (\kappa_1 N_A N_B + \kappa_{-1} N_C) P(N_A, N_B, N_C)
\]
Example 1: \( A + B \xrightleftharpoons{\kappa_1}{\kappa_{-1}} C \)

(continued)

- The CME is actually the four equations

\[
\begin{align*}
\frac{dP(4, 3, 0)}{dt} &= \kappa_{-1} P(3, 2, 1) - 12\kappa_1 P(4, 3, 0) \\
\frac{dP(3, 2, 1)}{dt} &= 12\kappa_1 P(4, 3, 0) + 2\kappa_{-1} P(2, 1, 2) \\
&\quad - (6\kappa_1 + \kappa_{-1}) P(3, 2, 1) \\
\frac{dP(2, 1, 2)}{dt} &= 6\kappa_1 P(3, 2, 1) + 3\kappa_{-1} P(1, 0, 3) \\
&\quad - (2\kappa_1 + 2\kappa_{-1}) P(2, 1, 2) \\
\frac{dP(1, 0, 3)}{dt} &= 2\kappa_1 P(2, 1, 2) - 3\kappa_{-1} P(1, 0, 3)
\end{align*}
\]
Properties of the CME

- At fixed concentrations, the number of molecules of each kind is proportional to $V$.
- Consider a chain of isomerizations
  
  \[ X_1 \rightleftharpoons X_2 \rightleftharpoons \ldots \rightleftharpoons X_n \]

  and suppose we start out with $N$ molecules of $X_1$.
- The number of different compositions is
  
  \[
  \frac{(N + n - 1)!}{N!(n - 1)!} \approx \left( \frac{eN}{n-1} \right)^{n-1},
  \]

  which grows as $N^{n-1} \propto V^\rho$, where $\rho$ is the number of reactions.

  Curse of dimensionality