1. A Markov chain model for the molecule dynamics

The molecules under consideration can be in four different states. These states correspond to the different geometric shapes. A given molecule will move from state to state. We are going to describe the dynamics, these changes from shape to shape, of this molecule by a random process. Consider the graph of figure 1.1.

Figure 1.1. Reaction Diagram
The vertices correspond to the different possible states (or shapes) of the molecule. They are called A, B, C, and D. The arrows in the graph represent a jump from a shape to another one.

The dynamics of the given molecule will be a random walk through this graph. A walk can be described by a sequence of letters giving how the molecule changed from shape to shape. For example, 

\[ ABBADABCC... \]

corresponds to a molecule which started in shape A, and eventually got to shape C.

This random walk is controlled by probabilities. For example, the probability \( p_{CB} \) that a molecule in shape C will jump to shape B in the next \( \Delta t \) seconds. This probability is given in terms of the reaction constants.

\[ p_{CB} = k_{CB} \cdot \Delta t. \]

We will use \( \Delta t = 10^{-5} \) seconds. We will collect all these transition probabilities in a 4 \( \times \) 4 matrix \( P_0 \). Let the set of states be denoted by

\[ S_0 = \{ A, B, C, D \}. \]

The matrix of transition probabilities is

\[
\begin{pmatrix}
p_{AA} & p_{AB} & p_{AC} & p_{AD} \\
p_{BA} & p_{BB} & p_{BC} & p_{BD} \\
p_{CA} & p_{CB} & p_{CC} & p_{CD} \\
p_{DA} & p_{DB} & p_{DC} & p_{DD}
\end{pmatrix}
\]

The transition probability \( p_{S_1,S_2} \) is the probability to jump from state \( S_1 \) to state \( S_2 \) in the next \( \Delta t \) seconds. Note that the elements in a row of the matrix add up to 1. The columns, \( p_{S_1,S_2} \) with \( S_2 \) fixed, describe the dynamics of jumping to state \( S_2 \).

The probabilities are given by

\[ p_{S_1,S_2} = k_{S_1,S_2} \cdot \Delta t, \]

when \( S_1 \neq S_2 \) and

\[ p_{S,S} = 1 - \sum_{S' \neq S} p_{S,S'}. \]

For example

\[ p_{AB} = k_{AB} \cdot \Delta t \]

and

\[ p_{AA} = 1 - k_{AB} \cdot \Delta t - k_{AC} \cdot \Delta t - k_{AD} \cdot \Delta t. \]

The random walk given by the graph and the transition matrix \( P_0 \) is called a Markov process. There is an extensive literature on such processes, see references [46], [47] of the main text. We will explore the
theory concerning the statistical properties of Markov processes to get estimates on the global rotation speed.

2. Equilibrium

Our material consists of enormous amounts of molecules, each of which is performing its own random walk through the graph. An equilibrium settles down: at any given moment the molecules will be distributed over the different shapes (or states) with well defined ratios. Let $w_S$ is the fraction of the molecules in shape $S \in S_0$ and collect these fractions in a vector $\mathbf{w} = (w_A, w_B, w_C, w_D)$. This equilibrium vector is given by the matrix equation

$$\mathbf{w} \mathbf{P}_0 = \mathbf{w}$$

This equilibrium does not depend on the chemical time scale $\Delta t$ we used.

3. Jumps

Unfortunately, the Markov process described by $\mathbf{P}_0$ is not appropriate for studying the rotation speed. It is only meant to study the chemical equilibrium given by $\mathbf{w}$. We are interested in dynamical information. Namely, the rotation speed of the molecules. We will introduce another Markov process $\mathbf{P}$ closely related to $\mathbf{P}_0$ and the states in $S_0$. At a given moment we will consider each molecule being busy with a transition. For example, it can be in state $AA$. This means that in the present time interval $\Delta t$ it began in shape $A$ and it will end in shape $A$. The molecule could also be in state $AB$. This means that it is actually turning from shape $A$ to $B$.

The proper state space $S$ we are going to use consists of these pairs, call them the jump-type:

$$S = \{AA, AB, AC+, AC-, AD, BB, BC, BD+, BD-, BA, CC, CD, CA+, CA-, CB, DD, DA, DB+, DB-, DC\}$$

The $+, -$ signs refer to a clockwise or counter clockwise jump.

There is a graph related to these jump types. There are 20 vertices in this graph. There is an arrow from state $SS'$ to state $S''S'''$ only if $S' = S''$. We will omit a figure of this graph. It will not add essential
information. The corresponding $20 \times 20$ matrix $P$ of transition probabilities is more important, see scheme 2 in the main text. Formally, it is given by

$$P_{SS',S''} = p_{S''} \text{ if } S' = S''.$$  

Our material consists of enormous amounts of molecules. They will settle down in an statistical equilibrium. At any given moment a fixed fractions of the molecules will be busy with a certain jump. Let us denote the fraction of molecules busy with jump $SS' \in S$ by $W_{SS'}$. Then

$$W_{SS'} = w_S \cdot p_{SS'}.$$  

The important ingredient which allows us to estimate the rotation speed is the \textit{jump observable}. This is a function

$$\phi : S \to \mathbb{Z}$$

which assigns to each jump type how many quarters it is jumping ahead. For example

$$\phi(AA) = 0,$$
$$\phi(AB) = 1,$$
$$\phi(AC(+)) = 2,$$
$$\phi(AC(-)) = -2,$$
$$\phi(AD) = -1.$$  

Similarly for the other jump types.

4. Rotation

Given a molecule, let us follow it for $t = n \cdot \Delta t$ seconds. It will start in a state $S_0 \in S$ and go from state to state. After $i \leq n$ intervals of length $\Delta t$ it got into state $S_i$. For this molecule, let

$$\phi_i = \phi(S_i).$$

Introduce the \textit{net jump counter}

$$\Phi_t = \sum_{i=0}^{n} \phi_i.$$  

Let us go back to the example of section 1 and keep track of the jumps and the net jump count.

$S_0 : A, B, B, A, D, A, B, C, C$

$S : AB, BB, BA, AD, DA, AB, BC, CC$

$\phi : +1, 0, -1, -1, +1, +1, +1, 0$
After these eight steps the net jump is $\Phi_t = +2$.

We observe our material, consisting of enormous amounts of molecules, from a moment $t = 0$ until $t > 0$. Each molecule will have its own net jump count $\Phi_t$. The enormous amount of final net jump counts $\Phi_t$ can be collected in a histogram. The theory of Markov processes tells that this $\Phi_t$ is distributed according to a normal distribution. The mean of the distribution is

$$\text{mean}(\Phi_t) = t \cdot V$$

and the standard deviation is

$$\sigma(\Phi_t) = \sqrt{Dt}.$$  

This means that the average rotation speed is $V$ quarts per second. In the next section we will give the precise formulas for $V$ and $D$.

The distribution of the net jumps $\Phi_t$ is given by the following formula

$$\mu([\Phi, \Phi + \Delta\Phi]) = \frac{1}{\sqrt{2\pi Dt}} \cdot e^{-\frac{(\Phi - tV)^2}{2Dt}} \cdot \Delta\Phi.$$  

where $\mu([\Phi, \Phi + \Delta\Phi])$ denotes the fraction of molecules with $\Phi_t \in [\Phi, \Phi + \Delta\Phi]$.

5. $V$ and $D$

The expression for the speed is natural. Namely, the expected jump per second,

$$V = \frac{1}{\Delta t} \sum_{SS' \in S} \phi(SS') \cdot W_{SS'}$$

Observe, that when $\phi(SS') \neq 0$ we have

$$W_{SS'} = w_S \cdot p_{SS'} = w_S \cdot k_{SS'} \cdot \Delta t.$$  

Indeed, the average speed $V$ is independent of the chemical time scale we used. Hence,

$$V = \sum_{SS' \in S} \phi(SS') \cdot w_S \cdot k_{SS'}$$

This can be calculated from the equilibrium $w$ of $P_0$ and the reaction constants.

The spread of the net jump around this average speed and the Péclet number

$$Pé = \frac{V}{D}$$

is given by a more involved formula, see references [36] and [39] in the main text. Denote the $n$–fold product of the matrix $P$ with itself by

$$P^n = P \times P \times \cdots \times P.$$
The expression for $D$ is as follows, see references [46], [47] and [50] in the main text.

$$D = \frac{1}{\Delta t} \sum_{SS' \in S} W_{SS'}(\phi(SS') - V \Delta t)^2 +$$

$$2 \sum_{k=1}^{\infty} \sum_{SS', S''S''' \in S} W_{SS'}(\phi(SS') - V \Delta t) P_{SS', S''S'''}^k (\phi(S''S''') - V \Delta t).$$

One can easily check that $D$ is independent of the chemical time scale $\Delta t$.

6. Unidirectionality

The Markov process described in section 3 is designed to calculate the rotation speed in the molecules. The question addressed there is how many jumps per second a molecule makes in average. If this average is nonzero there is a rotational speed. However, it might happen that the motion is very erratic on small time scales such that hardly ever the molecule makes a full turn, i.e. four quarter rotations in one specific direction.

In this section we will describe a Markov process which allows to calculate the number of full turns per second a molecule makes in average. The average is over a long period of time. If this average is non-zero, the molecule is said to be directional.

We will design a Markov process which allows to calculate the average full forward turns, $\Omega_+$. Similarly, we will design a Markov process which is able to count the full backward turns, $\Omega_-$. The constructions are symmetric. We will describe in detail the forward counting process.

The general idea is that for any observable of a chemical process one can design a Markov process which allows to calculate the observable. The equilibrium concentrations is the standard example. In section 3 we designed a process to calculate the rotation speed. In this section we design a process for unidirectionality. It is not possible to give a recipe. For each observable one needs to study the situation and some creativity to find an appropriate Markov process.

Markov processes can be successful in chemistry if the molecules do not have a memory of what they did before and if there are large amounts of molecules in the experiment.
The Markov process for counting forward full turns has twenty states. However, these states have a different definition compared to the situation in section 3. A molecule is in state 
\[ S_{s_1, s_2} \]
when it was at some point in the past in state \( s_1 \) and then only turned forward and now it is in state \( s_2 \). For example, 
\[ S_{A, C} \]
corresponds to a molecule which was in state \( A \) and then only turned forward to get to state \( C \) at this present moment. Molecules can also turn backward. To describe the molecules whose last jump was backward and now are in state \( s \) we use the states 
\[ S_s. \]
In total we have \( 4 \times 4 + 4 = 20 \) states. These states are grouped as follows. The states \( S_s \) of molecules which are turning backward are collected in \( G^- \). The states \( S_{A,X} \) for the molecules which started in state \( A \) with forward turning are collected in \( G_A \). The states \( S_{B,X} \) are collected in \( G_B \) and similarly, we define \( G_C \) and \( G_D \). These states grouped in their subgraphs with the possible transitions is illustrated in Figure 6.1

Observe, a given molecule will be at any moment in time in exactly one of the states described above. Our task is to determine the corresponding transition probabilities. These probabilities are collected in a 20x20 matrix
\[
M^+ = (m_{ij}^+).
\]
The indices \( i, j \) have values between 1 and 20. The numbering is as follows. \( S_A, S_B, S_C, S_D \) correspond to 1, 2, 3, 4. The states in \( G_A \), \( S_{A,A}, S_{A,B}, S_{A,C}, S_{A,D} \) correspond to 5, 6, 7, 8. The states in \( G_B \) are counted with 9, 10, 11, 12 etc. The matrix \( M^+ \) consists of 25 \( 4 \times 4 \) blocks. Each block corresponds to transitions between the \( G \)-matrices.

We need some preparation before we can describe the matrix \( M^+ \). Recall, the transition between the original states \( A, B, C, D \) is given by the matrix
\[
P_0 = \begin{pmatrix}
p_{AA} & p_{AB} & p_{AC} & p_{AD} \\
p_{BA} & p_{BB} & p_{BC} & p_{BD} \\
p_{CA} & p_{CB} & p_{CC} & p_{CD} \\
p_{DA} & p_{DB} & p_{DC} & p_{DD}
\end{pmatrix}
\]
where the transition probabilities are given by the reaction constants. For example,
\[
p_{AC} = k_{AC} \cdot \Delta t.
\]
We will decompose this matrix in two parts.

$$P_0 = F + B$$

where $F$ consist of the transition probabilities which correspond to forward jumps and $B$ is the matrix of probabilities which correspond to backward jumps. For example, $p_{CD}$ is a forward jump and $p_{CB}$ is a backward jump. Notice that the cross jumps has to be split

$$p_{AC} = p_{C+} + p_{AC-}$$

where $p_{AC+}$ is a forward jump and $p_{AC-}$ is a backward jump. We will consider the jumps $AA$, $BB$, $CC$, and $DD$ as forward jumps. Let

$$P_0 = F + B$$

with

$$F = \begin{pmatrix}
  p_{AA} & p_{AB} & p_{AC+} & 0 \\
  0 & p_{BB} & p_{BC} & p_{BD+} \\
  p_{CA+} & 0 & p_{CC} & p_{CD} \\
  p_{DA} & p_{DB+} & 0 & p_{DD}
\end{pmatrix}$$
and
\[
B = \begin{pmatrix}
0 & 0 & p_{AC}^- & p_{AD}^- \\
p_{BA} & 0 & 0 & p_{BD}^- \\
p_{CA}^- & p_{CB} & 0 & 0 \\
0 & p_{DB}^- & p_{DC} & 0 \\
\end{pmatrix}
\]

Observe, the matrix \(B\) describes the jumps within the graph \(G_-\) and \(F\) describes the dynamics in each of the graphs \(G_A, G_B, G_C, G_D\). This explains the diagonal part of \(M^+\). Namely,
\[
M^+ = \begin{pmatrix}
B & . & . & . \\
. & F & . & . \\
. & . & F & . \\
. & . & . & F \\
\end{pmatrix}
\]

We will fill the graph step by step. Observe, that as long as a molecule is turning forward its state will continue in one and the same \(G_S\). The first jump backward will give a transition to \(G_-\). There are no transitions between the different \(G_S\). Hence,
\[
M^+ = \begin{pmatrix}
B & . & . & . \\
. & F & 0 & 0 \\
. & 0 & F & 0 \\
. & 0 & 0 & F \\
\end{pmatrix}
\]

A molecule which is in a state in one of the \(G_S\) will give a transition to \(G_-\) once it jumps backward. Hence,
\[
M^+ = \begin{pmatrix}
B & . & . & . \\
B & F & 0 & 0 \\
B & 0 & F & 0 \\
B & 0 & 0 & F \\
B & 0 & 0 & F \\
\end{pmatrix}
\]

The last situation we have to discuss is when a molecule is in a state of \(G_-\), it has been jumping backward, makes its first jump forward. This jump can be either from \(A, B, C,\) or \(D\). If it jumps from \(B\) forward its means a transition into \(G_B\). Similarly for other initial forward jumps which give rise to transitions into the other \(G_S\).
The initial jump forward from $A \in G_-$ into $G_A$ is described by the following matrix.

\[
F_A = \begin{pmatrix}
    p_{AA} & p_{AB} & p_{AC} & 0 \\
    0 & 0 & 0 & 0 \\
    0 & 0 & 0 & 0 \\
    0 & 0 & 0 & 0
\end{pmatrix}
\]

The position of this matrix $F_A$ which represents transitions from $G_-$ to $G_A$, in $M^+$ is given by

\[
M^+ = \begin{pmatrix}
    B & F_A & \cdot & \cdot \\
    B & F & 0 & 0 \\
    B & 0 & F & 0 \\
    B & 0 & 0 & F \\
    B & 0 & 0 & F
\end{pmatrix}
\]

The initial jump forward from $B \in G_-$ into $G_B$ is described by the following matrix.

\[
F_B = \begin{pmatrix}
    0 & 0 & 0 & 0 \\
    0 & p_{BB} & p_{BC} & p_{BD} \\
    0 & 0 & 0 & 0 \\
    0 & 0 & 0 & 0
\end{pmatrix}
\]

The initial jump forward from $C \in G_-$ into $G_C$ is described by the following matrix.

\[
F_C = \begin{pmatrix}
    0 & 0 & 0 & 0 \\
    0 & 0 & 0 & 0 \\
    p_{CA^+} & 0 & p_{CC} & p_{CD} \\
    0 & p_{CA^+} & 0 & 0 \\
    0 & 0 & 0 & 0
\end{pmatrix}
\]

The initial jump forward from $D \in G_-$ into $G_D$ is described by the following matrix.

\[
F_D = \begin{pmatrix}
    0 & 0 & 0 & 0 \\
    0 & 0 & 0 & 0 \\
    0 & 0 & 0 & 0 \\
    p_{DA} & p_{DB^+} & 0 & p_{DD}
\end{pmatrix}
\]
The position of these matrix \( F_S \) which represents transitions from \( G_- \) to \( G_S \), in \( M^+ \) is given by

\[
M^+ = \begin{pmatrix}
B & F & F & F & F \\
B & F & 0 & 0 & 0 \\
B & 0 & F & 0 & 0 \\
B & 0 & 0 & F & 0 \\
B & 0 & 0 & 0 & F \\
\end{pmatrix}
\]

As before when we were calculating the rotation speed we determine the equilibrium concentrations. These concentrations form a horizontal vector with 20 entries.

\[
W = \begin{pmatrix}
W_- & W_A & W_B & W_C & W_D \\
\end{pmatrix}
\]

where each \( W_- \), \( W_A \), \( W_B \), \( W_C \), and \( W_D \) are vectors with four entries, the concentrations of the states in each \( G \)-matrix. For example,

\[
W_B = \begin{pmatrix}
W_B(A) & W_B(B) & W_B(C) & W_B(D) \\
\end{pmatrix}
\]

where \( W_B(C) \) is the concentration of molecules which started to turn forward when they were in state \( B \) and now there are in the state \( C \). Similarly,

\[
W_- = \begin{pmatrix}
W_-(A) & W_-(B) & W_-(C) & W_-(D) \\
\end{pmatrix}
\]

where \( W_-(B) \) is the concentration of molecules whose last jump was backward and now is in state \( B \).

The vector \( W \) of equilibrium concentrations is the unique solution of the eigenvalue problem

\[ W = WM^+ \]

and all concentrations have to be non-negative

\[ w_i \geq 0 \]

with \( W = (w_i) \), and all concentrations together have to sum to 1

\[ \sum_{i=1}^{20} w_i = 1. \]

As in the previous sections the concentrations are independent of the time interval. They only depend on the reaction constants.

The last step is to introduce the observable which counts full forward turns. This is a function \( \phi \) which assigns values to transitions. \( \phi \) is zero for all transitions except the transitions which assure a complete forward turn, to which it assigns 1.
We will locate the transitions which assure a full forward turn. In \( G_- \) there are no such transitions. In \( G_A \) the transitions
\[
G_A : DA, DB^+, CA^+ \\
\]
are exactly the transitions which assure a full turn forward. In \( G_B, G_C \) and \( G_D \) they are
\[
G_B : AB, AC^+, DB^+ \\
G_C : BC, BD^+, AC^+ \\
G_D : BD^+, CD, CA^+ \\
\]
These transitions are called **assuring**. Given a molecule we can record the value \( \phi_i \) which is the value \( \phi \) assigned to its \( i^{th} \) transition. Each time the molecule passes through an assuring transition it performed a full forward turn. Hence, the average of the number of full forward turns per second is
\[
\Omega_+ = \lim_{n \to \infty} \frac{1}{n \cdot \Delta t} \sum_{i=0}^{n-1} \phi_i \\
\]
The theory for Markov processes tells that the average forward speed \( \Omega_+ \) is the same for any typical molecule. It also says that this time average equals the “space average”
\[
\Omega_+ = \sum_t \phi(t) \text{weight}(t) \\
\]
where the sum is over transitions \( t \) and the weight of a transitions is the concentration of molecules which are performing the transition. The weight of the transition \( A \) to \( B \) in \( G_C \) is given by
\[
\text{weight}(AB) = W_C(A) \cdot k_{AB} \\
= W_C(A) \cdot k_{AB} \cdot \Delta t. \\
\]
Now we are ready to calculate \( \Omega_+ \). The observable only assigns values 0 and 1. Hence \( \Omega_+ \) is the total weight of the assuring transitions described above.
\[
\Omega_+ = W_A(D) \cdot k_{DA} + W_A(D) \cdot k_{DB^+} + W_A(C) \cdot k_{CA^+} + \\
W_B(A) \cdot k_{AB} + W_B(A) \cdot k_{AC^+} + W_B(D) \cdot k_{DB^+} + \\
W_C(B) \cdot k_{BC} + W_C(B) \cdot k_{BD^+} + W_C(A) \cdot k_{AC^+} + \\
W_D(B) \cdot k_{BD^+} + W_D(C) \cdot k_{CD} + W_D(C) \cdot k_{CA^+} \\
\]
The construction of the Markov process for the calculation of the average number of full backward turns per second is similar to the construction for the forward calculation. We will only include the main steps. The explanation is similar.
The Markov process for counting backward full turns has twenty states. A molecule is in state

\[ S_{s_1,s_2} \]

when it was at some point in the past in state \( s_1 \) and then only turned backward and now it is in state \( s_2 \). For example,

\[ S_{A,C} \]

corresponds to a molecule which was in state \( A \) and then only turned backward to get to state \( C \) at this present moment. Molecules can also turn forward. To describe the molecules whose last jump was forward and now are in state \( s \) we use the states

\[ S_s. \]

These states are grouped as follows. The states \( S_s \) of molecules which are turning forward are collected in \( G_+ \). The state \( S_{A,X} \) for the molecules which started in state \( A \) with backward turning are collected in \( G_A \). The states \( S_{B,X} \) are collected in \( G_B \) and similarly, we define \( G_C \) and \( G_D \).

Our task is to determine the corresponding transition probabilities. These probabilities are collected in a 20x20 matrix

\[ M^− = (m_{ij}^−). \]

We need some preparation before we can describe the matrix \( M^− \). We will decompose the matrix \( P_0 \) into two parts.

\[ P_0 = F + B \]

where \( B \) consist of the transition probabilities which correspond to backward jumps and \( F \) is the matrix of probabilities which correspond to forward jumps. For example, \( p_{CD} \) is a forward jump and \( p_{CB} \) is a backward jump. Notice that the cross jumps has to be split

\[ p_{AC} = p_{AC}^+ + p_{AC}^- \]

where \( p_{AC}^+ \) is a forward jump and \( p_{AC}^- \) is a backward jump. Notice, a transition \( p_{AA} \) was counted as a forward jump in the calculation of \( \Omega_+ \). Now we will count it as backward jump. The decomposition

\[ P_0 = F + B \]

will be in slightly different matrices. Namely, with

\[ F = \begin{pmatrix} 0 & p_{AB} & p_{AC}^+ & 0 \\ 0 & 0 & p_{BC} & p_{BD}^+ \\ p_{CA}^+ & 0 & 0 & p_{CD} \\ p_{DA} & p_{DB}^+ & 0 & 0 \end{pmatrix} \]
and

\[
B = \begin{pmatrix}
p_{AA} & 0 & p_{AC} & p_{AD} \\
p_{BA} & p_{BB} & 0 & p_{BD} \\
p_{CA} & p_{CB} & p_{CC} & 0 \\
0 & p_{DB} & p_{DC} & p_{DD}
\end{pmatrix}
\]

Observe, the matrix \( F \) describes the jumps within the graph \( G_+ \) and \( B \) describes the dynamics in each of the graphs \( G_A, G_B, G_C, G_D \). This explains the diagonal part of \( M^+ \). Namely,

\[
M^- = \begin{pmatrix}
F & . & . & . \\
. & B & . & . \\
. & . & B & . \\
. & . & . & B
\end{pmatrix}
\]

We will fill the graph step by step. Observe, that as long as a molecule is turning backward its state will continue in one and the same \( G_S \). The first jump forward will give a transition to \( G_+ \). There are no transitions between the different \( G_S \). Hence,

\[
M^- = \begin{pmatrix}
F & . & . & . \\
. & B & 0 & 0 & 0 \\
. & 0 & B & 0 & 0 \\
. & 0 & 0 & B & 0 \\
. & 0 & 0 & 0 & B
\end{pmatrix}
\]

A molecule which is in a state in one of the \( G_S \) will give a transition to \( G_+ \) once it jumps forward. Hence,

\[
M^+ = \begin{pmatrix}
F & . & . & . \\
F & B & 0 & 0 & 0 \\
F & 0 & B & 0 & 0 \\
F & 0 & 0 & B & 0 \\
F & 0 & 0 & 0 & B
\end{pmatrix}
\]

The last situation we have to discuss is when a molecule is in a state of \( G_+ \), it has been jumping forward, makes its first jump backward. This jump can be either from \( A, B, C, \) or \( D \). If it jumps from \( B \) backward it means a transition into \( G_B \). Similarly for other initial backward jumps which give rise to transitions into the other \( G_S \).
The initial jump backward from $A \in G_+$ into $G_A$ is described by the following matrix.

$$B_A = \begin{pmatrix}
 p_{AA} & 0 & p_{AC}^- & p_{AD} \\
 0 & 0 & 0 & 0 \\
 0 & 0 & 0 & 0 \\
 0 & 0 & 0 & 0 \\
\end{pmatrix}$$

The position of this matrix $B_A$ which represents transitions from $G_+$ to $G_A$, in $M^-$ is given by

$$M^- = \begin{pmatrix}
 B & B_A & \ldots & \ldots \\
 B & F & 0 & 0 & 0 \\
 B & 0 & F & 0 & 0 \\
 B & 0 & 0 & F & 0 \\
 B & 0 & 0 & 0 & F \\
\end{pmatrix}$$

The initial jump forward from $B \in G_+$ into $G_B$ is described by the following matrix.

$$B_B = \begin{pmatrix}
 0 & 0 & 0 & 0 \\
 p_{BA} & p_{BB} & 0 & p_{BD}^- \\
 0 & 0 & 0 & 0 \\
 0 & 0 & 0 & 0 \\
\end{pmatrix}$$

The initial jump forward from $C \in G_+$ into $G_C$ is described by the following matrix.

$$B_C = \begin{pmatrix}
 0 & 0 & 0 & 0 \\
 0 & 0 & 0 & 0 \\
 p_{CA}^- & p_{CB} & p_{CC} & 0 \\
 0 & 0 & 0 & 0 \\
\end{pmatrix}$$

The initial jump forward from $D \in G_+$ into $G_D$ is described by the following matrix.

$$B_D = \begin{pmatrix}
 0 & 0 & 0 & 0 \\
 0 & 0 & 0 & 0 \\
 0 & 0 & 0 & 0 \\
 0 & p_{DB}^- & p_{DC} & p_{DD} \\
\end{pmatrix}$$
The position of these matrix $B_S$ which represents transitions from $G_+$ to $G_S$, in $M^-$ is given by

$$M^- = \begin{pmatrix}
F & B_A & B_B & B_C & B_D \\
F & B & 0 & 0 & 0 \\
F & 0 & B & 0 & 0 \\
F & 0 & 0 & B & 0 \\
F & 0 & 0 & 0 & B \\
\end{pmatrix}$$

As before we determine the equilibrium concentrations. The concentrations form a horizontal vector with 20 entries.

$$W = \begin{pmatrix}
W_+ & W_A & W_B & W_C & W_D \\
\end{pmatrix}$$

where each $W_+$, $W_A$, $W_B$, $W_C$, and $W_D$ are vectors with four entries, the concentrations of the states in each $G$-matrix. For example,

$$W_B = \begin{pmatrix}
W_B(A) & W_B(B) & W_B(C) & W_B(D) \\
\end{pmatrix}$$

where $W_B(C)$ is the concentration of molecules which started to turn backward when they were in state $B$ and now there are in the state $C$. Similarly,

$$W_+ = \begin{pmatrix}
W_+(A) & W_+(B) & W_+(C) & W_+(D) \\
\end{pmatrix}$$

where $W_+(B)$ is the concentration of molecules whose last jump was forward and now are in state $B$.

The vector $W$ of equilibrium concentrations is the unique solution of the eigenvalue problem

$$W = WM^+$$

and all concentrations have to be non-negative

$$w_i \geq 0,$$

where $W = (w_i)$, and all concentrations together have to sum to 1

$$\sum_{i=1}^{20} w_i = 1.$$

As in the previous sections the concentrations are independent of the time interval. They only depend on the reaction constants.

The last step is to introduce the observable which counts full backward turns. This is a function $\phi$ which assigns values to transitions. $\phi$ is zero for all transitions except the transitions which assure a complete backward turn, to which it assigns 1.

We will locate the transitions which assure a full backward turn. In $G_+$ there are no such transitions. In $G_A$ the transitions

$$G_A: BA, BD^-, CA^-$$
are exactly the transitions which assure a full turn forward. In $G_B$, $G_C$ and $G_D$ they are

$$G_B : CB, DB^-, CA^-$$

$$G_C : DC, DB^-, AC^-$$

$$G_D : BD^-, AD, AC^-$$

These transitions are called *assuring*. Given a molecule we can record the value $\phi_i$ which is the value $\phi$ assigned to its $i^{th}$ transition. Each time the molecule passes through an assuring transition it performed a full backward turn. Hence, the average of the number of full backward turns per second is

$$\Omega_- = \lim_{n \to \infty} \frac{1}{n \cdot \Delta t} \sum_{i=0}^{n-1} \phi_i$$

The theory for Markov processes tells that the average backward speed $\Omega_-$ is always the same for a typical molecule. It also says that this time average equals the “space average”

$$\Omega_- = \sum_t \phi(t) \text{weight}(t)$$

where the sum is over transitions $t$ and the weight of a transitions is the concentration of molecules which are performing the transition. The weight of the transition $A$ to $B$ in $G_C$ is given by

$$\text{weight}(AB) = W_C(A) \cdot p_{AB}$$

$$= W_C(A) \cdot k_{AB} \cdot \Delta t.$$ 

Now we are ready to calculate $\Omega_-$. The observable only assigns values 0 and 1. Hence $\Omega_-$ is the total weight of the assuring transitions described above.

$$\Omega_- = W_A(B) \cdot k_{BA} + W_A(B) \cdot k_{BD^-} + W_A(C) \cdot k_{CA^-} +$$

$$W_B(C) \cdot k_{CB} + W_B(D) \cdot k_{DB^-} + W_B(C) \cdot k_{CA^-} +$$

$$W_C(D) \cdot k_{DC} + W_C(D) \cdot k_{DB^-} + W_C(A) \cdot k_{AC^-} +$$

$$W_D(B) \cdot k_{BD^-} + W_D(A) \cdot k_{AD} + W_D(A) \cdot k_{AC^-}$$

Finally, the unidirectionality is measured by

$$r.e. = 100\% \cdot \frac{\Omega_+ - \Omega_-}{\Omega_+ + \Omega_-}.$$