

Laboratory exercise 2: Chemical reactions

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1 Introduction

In this report we model and analyze different chemical reactions and investigate how different setups and different models might affect the outcome of our simulations – i.e. the occurrence of equilibrium states, oscillating behaviour and general dynamics within the systems in question.

Since chemical reactions are complex, we here present iterative enhancements of simple models in order to successively better approximate the intended behaviour of our chemical reactions in question.

2 Theory and methodology

2.1 A model using two state reactions

In a so called *two state reaction*, reactions can happen, as the name suggests, between two different states, and is most easily represented by the chemical equation



between the two states A and B . Resultingly, the concentration change in say A can then be described naively by

$$\frac{\partial[A]}{\partial t} = k_- [B] - k_+ [A] \quad (2.2)$$

whereas the change in $[B]$ is simply the negative of this.

How this reaction actually takes place is determined by an energy barrier ΔG^\ddagger , where $\Delta G = \sum_i \mu_i dN_i$ is the change in Gibbs' free energy under constant temperature and pressure, that must be overcome for the reacting molecule, or *reactant*, to go into the inbetween state of transition. Our above introduced rate constants k_+ and k_- are thusly given by

$$k_+ = \frac{k_B}{h} e^{-\beta \Delta G^\ddagger} \quad (2.3)$$

for the forward rate, and correspondingly for k_- . Here k_B is the Boltzmann constant, while h is the unreduced Planck constant.

At equilibrium, the change in concentration between the two states is equal, so that

$$\frac{[B]}{[A]} = \frac{k_+}{k_-} \equiv K_{eq}. \quad (2.4)$$

This result demonstrates a feature of how the activation barrier affects the level of equilibrium – it simply does not, as the quota between the rates will remain constant. It does however seem reasonable that it would affect the time needed for an equilibrium state to be established, although the model does not provide any telling information about this.

2.2 Catalyzed reaction

Enzymes can act as catalysts for reactions by binding to the different molecules, lowering their effective potential barrier.

A simplified model for this sort of reaction, between our earlier states A and B can be described by the reaction formula



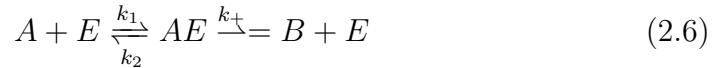
so that the enzyme itself is unchanged after the transition.

In this case, the change in the concentration of the different substrates can collectively be described analogously to the two-state case by

$$\begin{aligned} \frac{\partial[A]}{\partial t} &= -k_+[A][E] \\ \frac{\partial[B]}{\partial t} &= -\frac{\partial[A]}{\partial t} \\ \frac{\partial[E]}{\partial t} &= 0 \end{aligned}$$

where the product of the concentrations is due to the effective reactions being able to take place. Notably, as $[A]$ would tend towards infinity, so would the the rate of change.

In a more evolved model on the other hand, the reaction could instead be written as



to account for the inbetween state where the enzyme E binds to A , forming a substrate complex. This reaction would in turn be more aptly described

by the equations

$$\begin{aligned}\frac{\partial[A]}{\partial t} &= -k_1[A][E] + k_2[AE] \\ \frac{\partial[E]}{\partial t} &= -k_1[A][E] + k_2[AE] + k_+[AE] \\ \frac{\partial[AE]}{\partial t} &= -k_2[AE] + k_1[A][E] - k_+[AE] \\ \frac{\partial[B]}{\partial t} &= k_+[AE]\end{aligned}$$

in exactly the same manner as before. Reasonably, this would limit the rate at which $[A]$ changes, though it however still contains anomalies with respect to exactly this extreme.

In the so called Michaelis-Menten equation however, also the enzymes' working speed comes into play, as it before has been implicitly assumed to be infinite. In this case, the concentration of the substrate complex is assumed to be constant, as well as the enzyme itself, so that the following conditions hold:

$$\begin{aligned}\frac{\partial[AE]}{\partial t} &= -k_1[A][E] + k_2[AE] + k_+[AE] = 0 \\ [E^{tot}] &= [E] + [AE]\end{aligned}$$

Here E^{tot} is, as the name suggests, the total amount of enzyme available in any form. Applying this to our earlier set of equations we attain

$$(k_2 + k_+)[AE] = k_1[A](E^{tot} - [AE])$$

and thus ultimately

$$\frac{\partial[B]}{\partial t} = k_+ \frac{[A][E^{tot}]}{k_2 + k_1[A] + k_+}.$$

Defining

$$\begin{aligned}v_{max} &\equiv k_+[E^{tot}] \\ k_m &\equiv \frac{k_2 + k_+}{k_1}\end{aligned}$$

we achieve the final expression

$$v = v_{max} \frac{[A]}{k_m + [A]}.$$

2.3 Diffusion

Substrates mainly travel through diffusion between cells, so it is therefore necessary to be able to model also this phenomenon. In a one-dimensional case, this is a very simple procedure. Just assume that the cells are lain out in a vector-like structure, so that a typical cell with concentration c_i have the two neighbors with the dito c_{i-1} and c_{i+1} . The diffusion, i.e. the rate of transport between the cells, is then easiliy described by the equation

$$\frac{dc_i}{dt} = D(c_{i-1} - 2c_i + c_{i+1}) \quad (2.7)$$

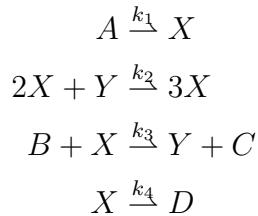
which can be proven quite trivially through assuming that all particles move randomly every time step with a probability p , and do not have significant bias towards either direction. Let the number of particles in a cell i be defined by the value N_i . The number of particles moving into this cell i from both neighbors must then equal $pN_{i-1} + pN_{i+1}$, wheras the flow out of the cell must be $2pN_i$. This gives the resulting equation

$$\frac{dN_i}{dt} = p(N_{i-1} - 2N_i + N_{i+1})$$

where if we divide by the volume (assuming it common across the different cells), the concentration is gained. This looks very much like the discretized case of the diffusion equation apart from the fact that we here cannot relate our constant D to physical entities, such as distance and time.

2.4 The brusselator

Introducing the brusselator, chemical reactions can be modelled according to the reaction equations



where A , and B are held constant. For the substrates of interest, X and Y , the time derivatives are given as

$$\begin{aligned} \frac{\partial[X]}{\partial t} &= k_1[A] + k_2[X]^2[Y] - k_3[B][X] - k_4[X] \\ \frac{\partial[Y]}{\partial t} &= -k_2[X]^2[Y] + k_3[B][X] \end{aligned}$$

where we can note for mere curiosity that the absence of either of A and B would imply that the concentration of both X and Y would go towards 0. Whereas the lack of the “outflow” k_4 would mean that both the concentration of X and Y would tend towards infinity instead. [1]

3 Results and conclusions

Calculating the forward rate constant using numerical values of $\mu_A^0 = 8, \mu_B^0 = 3$ and $\Delta G^\ddagger = 75$, with all units measured in kJ/mol, as well as approximate room temperature, renders the forward rate as $k_+ = 0.89$, whereas the backward rate correspondingly assumes the a value of $k_- = 6.01 \cdot 10^{-3}$.

Simulation results are visible in fig. 1 and fig. 2, where the dynamics of our system is apparent. Here the flux in the forward direction is many times larger than the backward flux, why the equilibrium state, i.e. the state where the concentrations converge, biases $[B]$ so heavily. When the initial concentrations are altered, the translation is clearly visible, as is expected of our simple model.

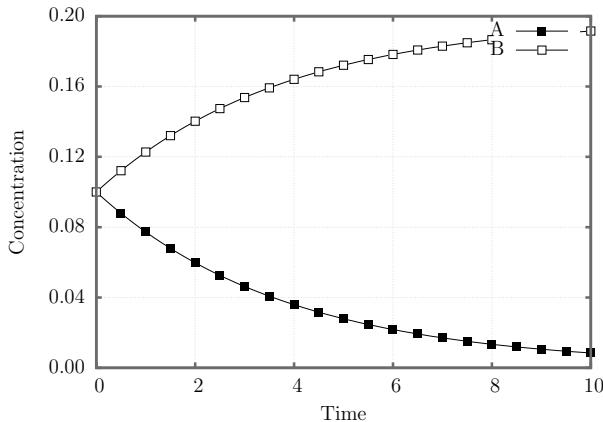


Figure 1: Simulation of a two-state system with equal initial concentration.

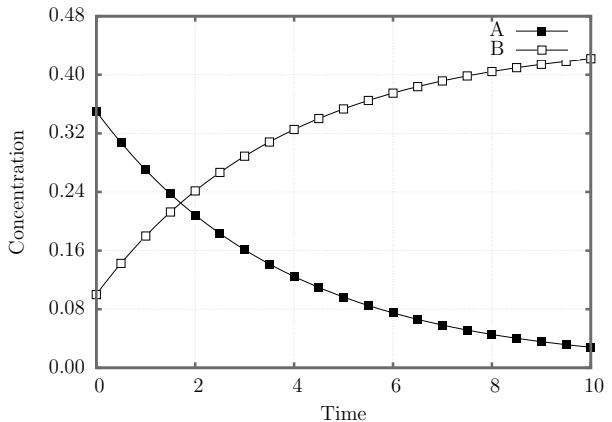


Figure 2: Under asymmetric initial concentrations, a clear translation within the system is noticeable. Otherwise the dynamics stay unaffected.

As fig. 3 suggests, the convergence appears even quicker when the barrier is lowered. Comparison between fig. 2 and fig. 3 also emphasises that the

systems reaches its plateau at the same level, i.e. at the same fraction between $[A]$ and $[B]$, in both cases, independently of the barrier amplitude.

Our model also suggests that we, if we were to have a barrier height of $\Delta G_E^\ddagger = 65 \text{ kJ/mol}$, our forward rate especially, would instead be given $k_+ = 15.7$, whereas k_- increases proportionally, which explains the rapid convergence in fig. 3.

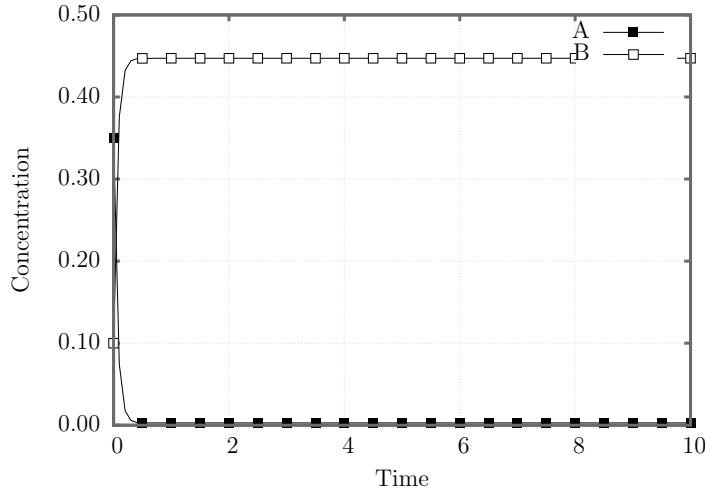


Figure 3: When the barrier is decreased in amplitude, the foremost consequence is that the rate from state $A \rightarrow B$ is increased multiply, whereas the rate $B \rightarrow A$ only increases slightly.

Introducing our catalysed reaction scheme, the introduction of the enzyme E is apparent in both fig. 4 where $[E]$ is low, and fig. 5 where $[E]$ is high, as also the dynamics emphasise.

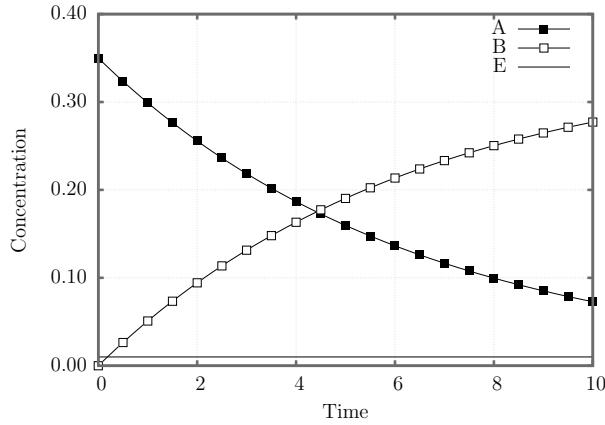


Figure 4: Catalysed system. Enzyme concentration low.

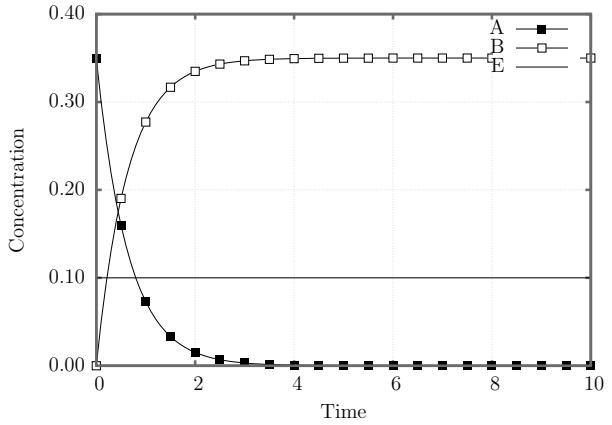


Figure 5: Catalysed system with high, constant concentration of enzyme. Note the increased convergence compared to the system with low concentration of enzyme.

When instead applying the Michaelis-Menten equation in our model, we can easily attain the same behaviour as without the introduced in-between step. We do however see that when the concentration of substance $[A]$ is increased so that the enzymes are in clear minority, we instead get the behaviour visible in fig. 6, i.e. a linear increase in the concentration of B , until the point where the concentration of A no longer is sufficient to uphold this behaviour. As apparent, we do not get our earlier assumed infinite rate, as a fraction of the enzymes now are bound to the complex substance AE , which bottlenecks this behaviour by limiting the amount of E available for more complexes to be produced. The linearity ought thereby be inherent to the rate k_+ , which also is the case.

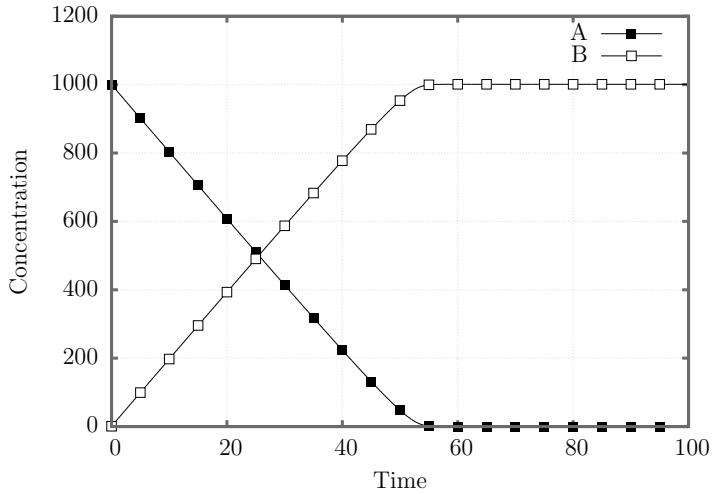


Figure 6: Concentration of $[A]$ in heavy supply, whereas the total amount of enzymes is constant. We achieve a linear behaviour until the concentration of A is insufficient.

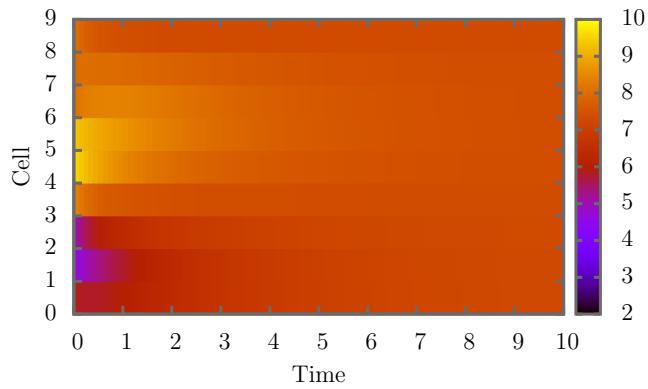


Figure 7: Simple diffusion network. Gradient corresponds to concentration, as in all following images.

Figure 7 displays the dynamics of a 10-cell system undergoing diffusion after all cells have been initialized with random initial concentrations. As in Nelson [2], the effects of diffusion are clearly visible, as all cells trend towards a common, steady-state concentration.

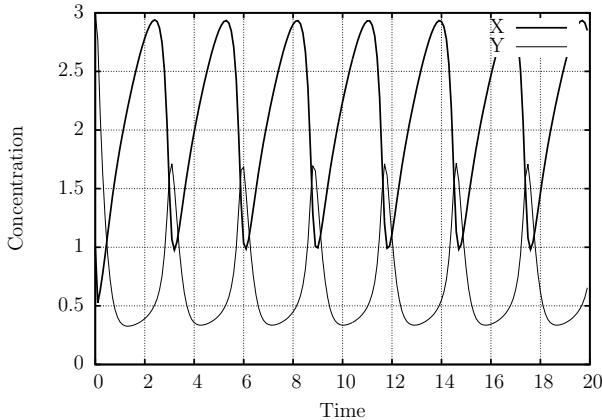


Figure 8: Concentration change for a single cell in the brusselator model. Rate value set $\mathcal{K} = \{2, 4, 6, 3\}$ for the different parameters respectively.

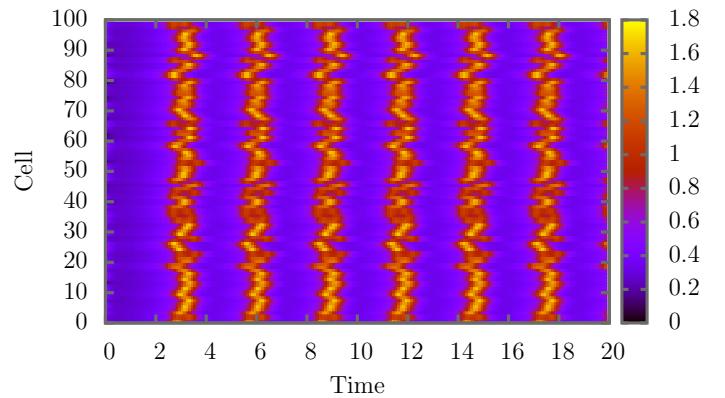


Figure 9: Development of system in the brusselator model. Note how all cells exhibit the same oscillating behaviour, only slightly differing in time.

Analysis of the brusselator model shows that a stable oscillating behaviour appears when $k_1[A]/k_3[B] \approx 1/3$ and $k_2/k_4 \approx 4/3$. The certainty in this claim is however dubious, since the software for simulating the model seems to dislike settings of large enough magnitudes. Divergence from these settings do however tend to dampen the system, driving it towards steady concentrations for X and Y respectively.

The same dynamics apply for a system holding many cells, as they all in the absence of diffusion will adhere to affect each other. Both these cases are shown in fig. 8 and fig. 9 correspondingly.

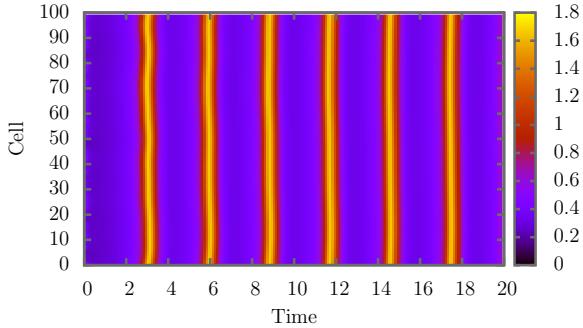


Figure 10: Brusselator system with the inclusion of diffusion. In comparison to fig. 9 the smoothness is apparent.

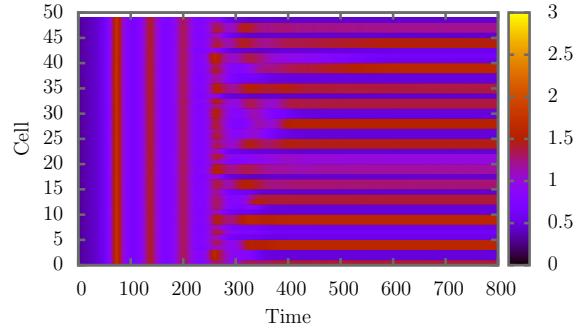


Figure 11: With only the second diffusion parameter set, the system oscillates heavily before all cells reach steady states.

When diffusion instead is introduced, the oscillations smoothen out as in fig. 10, showing that the system is more heavily driven by the dynamics caused by the reaction rates for smaller diffusion rates.

A steady state is once again realised when diffusion only is allowed to happen for the substrate Y , after some initial oscillating. This ought to be due to the equation system introduced in the brusselator model assuming a self-maintaining equilibrium state at a certain concentration for X and Y , such that all derivatives with respect to time are effectively zero.

When the diffusion rates for both X and Y instead are equal or biased towards the $D_X \gg D_Y$, and of magnitude where the system does not break, the model tends to assume and maintain an ongoing oscillating behaviour. In particular, when examining the concentrations over all cells at a single time step this sinusoidal tendency is apparent. In other words, it emphasises how the diffusive tendencies push the concentration from one end of the spectrum to the other, in a periodical manner.

In conclusion, it is clear that chemical reactions can extensively be explained by different models, where the amount of details taken into account heavily will determine the final behaviour, and in effect render results more or less accurate to this correspondingly. We can however in our cases adjust our model accordingly to achieve the intended behaviour. As a consequence we can furthermore investigate even wider implications of our model, as in the brusselator case where the complex nature of pattern forming appears.

The dynamics, and in particular the equilibriums and *states*, of our chem-

ical reactions can indeed to a high extent be explained and modeled by statistical probabilities and energetic compositions. When a large amount of different substances are of essence in the analysis, our numerical methods are certainly preferable, as the analytical case would contain numerous coupled differential equations.

References

- [1] Bozorg, Behruz, *Computer Assignment 2: Chemical reaction networks and diffusion*, Lund University, 2015.
- [2] Nelson, Philip, *Biological Physics: Energy, Information, Life*, W.H. Freeman and Company, New York, 2008.