

Theoretische Biophysik

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10. Februar 2020

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Literatur

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„Stochastic & Bio“, P. Bresloff (Empfohlen von Santen)

„Nonlinear Dynamics & Chaos“, Steven H. Strogatz, Perseus

„Stochastic Processes in Physics and Chemistry“, N. G. van Kampen,
North Holland

„Stochastic Methods“, Crispni Gardiner, Springer

Moodle-Passwort

TheoBio1920 (if this won't work, then "Bio" must be written small: "bio")

1 A short introduction to systems biology

1.1 Complex systems in biology

Fundamental problems:

- 1) We don't have a construction plan!
How can we understand a computer by pure observation?
- 2) The answer of a biological system is often non-linear
Example: The dosis of a drug has to be optimized - it might be lethal if it is too high
- 3) Biological Systems strongly interact with the environment
Immune system: Cell-cell interaction may induce killing of cells

Resume: Compared to engineered systems we have to work with less knowledge, less control and a high degree of non-linearity

What are the goals of systems biology?

- Explain, how biological systems work!
- Make reliable predictions of biological systems to different external conditions in a controlled fashion

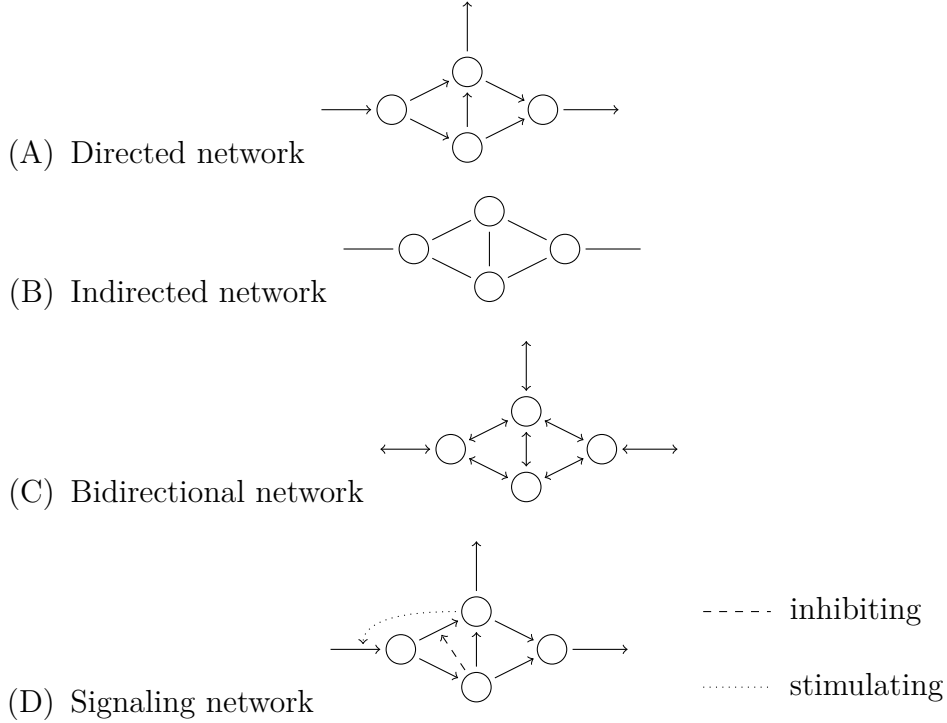
1.2 Static network models

In biological systems static networks often describe the steady state of a system. There are two different kinds of approaches to network analysis: First, one may ask how a given network actually works, and second, one can try to construct the underlying network structure by analysing the known part of the network.

1.2.1 Interaction graphs

Graphs consist of nodes (or vertices) and edges. Nodes represent the interacting components (molecules, species, subpopulations) and edges their interactions (chemical reactions, competition in evolution).

1.2.2 Examples of networks

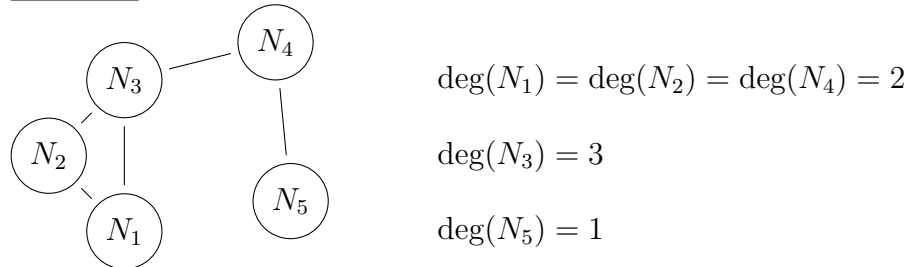


1.2.3 The properties of graphs

We represent a biological network with a Graph \mathcal{G} which consists of nodes N_i and edges $e(N_i, N_j)$ connection nodes.

Degree of a node - $\deg(N_i) = \#$ of associated edges

Example:



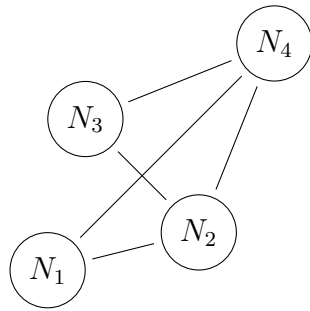
In case of directive graphs it's useful to distinguish between in-degree $\deg_{in}(N_i)$ and out-degree $\deg_{out}(N_i)$ which refer to the number of in- and outgoing edges.

The structure of a graph can be represented in an adjacency matrix A

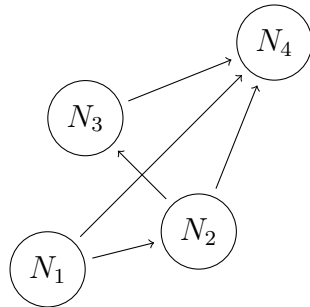
$$A = (a_{ij}) = \begin{cases} 1 & \text{if } e(N_i, N_j) \text{ is an edge in } \mathcal{G} \\ 0 & \text{else} \end{cases}$$

Remark: Undirected edges between nodes i and j are accounted twice, $a_{ij} = a_{ji} = 1$

Example:



$$A = \begin{pmatrix} 0 & 1 & 0 & 1 \\ 1 & 0 & 1 & 1 \\ 0 & 1 & 0 & 1 \\ 1 & 1 & 1 & 0 \end{pmatrix}$$



$$A = \begin{pmatrix} 0 & 1 & 0 & 1 \\ 0 & 0 & 1 & 1 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 \end{pmatrix}$$

Using the adjacency matrix, some problems in graph theory can be solved with linear algebraic methods

E.g.: Which nodes are counted by 2-step paths? This can be obtained from $B = A^2$. In case of the directed graph from above we get:

$$A^2 = \begin{pmatrix} 0 & 1 & 0 & 1 \\ 0 & 0 & 1 & 1 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 \end{pmatrix} \begin{pmatrix} 0 & 1 & 0 & 1 \\ 0 & 0 & 1 & 1 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 \end{pmatrix} = \begin{pmatrix} 0 & 0 & 2 & 1 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix}$$

This means there are two 2-step-paths connecting 1&3 and one connecting 1&4 and 2&3. All other pairs of nodes are not connected via two-step-path.

1.2.4 Cluster-coefficient

c_N characterizes the connectivity of a node. It's given by the number of edges between neighbors of a node divided by the maximum number of edges among them. An undirected (directed) Graph with k nodes may have $\frac{k(k-1)}{2}$ $((k-1)k)$ edges, since each node can be connected with $(k-1)$ neighbors.

Undirected: $c_N = \frac{e}{k(k-1)/2} = \frac{2e}{k(k-1)}$ where $e = \#$ edges between neighbors

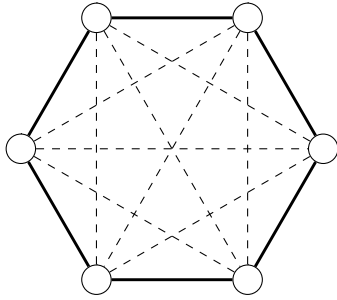
Directed: $c_N = \frac{e}{k(k-1)}$

c_N obviously takes values between 0 and 1, where 1 corresponds to a fully connected graph or clique.

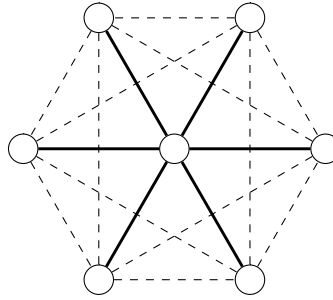
The graphs clustering coefficient is simply given by the mean of all nodes

$$c_G = \frac{1}{m} \sum_{N=1}^m c_N \text{ where } m = \# \text{ nodes of } \mathcal{G}$$

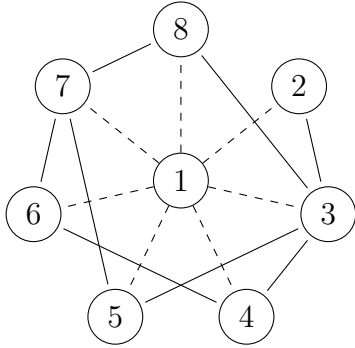
Remark: In real biological networks C_G is typically low. There exists only a relatively small number of hubs, i.e. nodes that are highly connected to dense clusters.



----- possible connection
 — connection



----- possible connection
 — connection



- undirected graph
- 7 neighbours of 1
- 8 edges connecting neighbours
- $c_1 = \frac{8}{7 \cdot \frac{6}{2}} = \frac{8}{21}$
- $c_5 = 2 \cdot \left(3 \cdot \frac{2}{2}\right)^{-1} = \frac{2}{3}$

Another important characteristic of a graph \mathcal{G} with m nodes is its degree distributio

$$P(k) = \frac{m_k}{m}, \text{ where } m_k = \# \text{ nodes with degree } k$$

$P(k)$ is obviously normalized.

Random graphs: $P(k)$ = Binomial distribution

Biological graphs: $P(k) \propto k^{-\gamma}$ (scale-free network)

Scale-free networks are dominated by a few hubs and many sparsely connected nodes

- The shortest paths, i.e. the shortest distance between randomly selected nodes is significantly lower than for random graphs, where it is $\sim \log(m)$ ($m = \#$ nodes)
- “Small-world” networks¹ are scale-free networks with high clustering coefficients. Typically average path-lengths are 2 – 5 steps.

1.2.5 Construction of small world networks

- The edges of new node are connected to an existing node with a probability $\sim \deg(N) \rightarrow \gamma = 3$
- Variations of the mechanism lead to other values of γ

¹Barabasi Rev. Mod. Phys

1.2.6 Dependencies among network components

- Causality analysis: True cause must be necessary and sufficient to execute an effect (Galileo).
Causes in networks are often studied with statistical methods, from which one obtains typically cause-effect diagrams which are directed graphs. In biology, networks often contain cycles, which complicate the analysis.
- Mutual information: The mutual dependence of two variables is often much easier to access. Typical question: How likely is it that gene X is expressed if gene Y is expressed as well?

1.2.7 Bayesian construction (cond. probabilities)

We first recall some elementary results of probability theory

Random variables A random variable X is a quantity which may take different values with certain probabilities.

Entropy $H(x)$ The entropy measures the uncertainty associated with the variable x . The uncertainty may depend on the knowledge of another random variable (e.g. two genes, that are likely to be expressed together)

Joint entropy $H_I(X, Y)$ = uncertainty in finding X and Y .

Conditional Entropy $H(X|Y)$ = uncertainty for X given Y .

$$\leadsto H_I(X, Y) = H(X) + H(Y|X) = H(Y) + H(X|Y)$$

mutual information: $I(X, Y) = [H(X) + H(Y)] - H_I(X, Y)$

Shannon entropy $H_S(X)$ A concrete realization of an information entropy is given by the Shannon entropy

$$H_S = - \sum_i P(x_i) \log_2(P(x_i)) = -k_S \sum_i P(x_i) \ln(P(x_i)) \quad k_S = \ln(2)$$

The Shannon entropy measures entropy in bits. If we consider a random variable X with possible values X_i where $i = 1, 2, \dots, \Omega$, $p_i = P(x_i)$ and

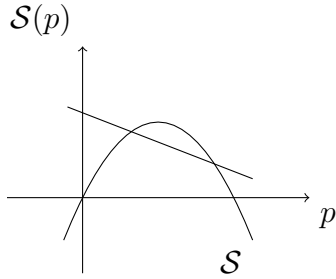
$$\sum_{i=1}^{\Omega} p_i = 1.$$

Properties:

(1) Entropy is maximum for equal probabilities

$$H_I\left(\frac{1}{\Omega}, \dots, \frac{1}{\Omega}\right) > H_I(p_1, \dots, p_{\Omega}) \quad \text{unless } p_i = \frac{1}{\Omega} \forall i$$

We note that $\mathcal{S}(p) = -p \ln(p)$ is concave in $]0, 1[$, since $\mathcal{S}''(p) = -\frac{1}{p} < 0$



$$\begin{aligned} x &= \lambda a + (1 - \lambda)b \quad \lambda \in]0, 1[\\ \rightarrow f(x) &= \mathcal{S}(\lambda a + (1 - \lambda)b) > \lambda \mathcal{S}(a) + (1 - \lambda)\mathcal{S}(b) \end{aligned}$$

For a concave function, we get:

$$\frac{1}{\Omega} \sum_k \mathcal{S}(p_k) \leq \mathcal{S}\left(\frac{1}{\Omega} \sum_k p_k\right)$$

This property can be shown by induction. For $\Omega = 2$ we use $\lambda = \frac{1}{2}$,
 $a = p$ and $b = p_2 \quad \leadsto \quad \mathcal{S}\left(\frac{p_1+p_2}{2}\right) \geq \frac{1}{2} (\mathcal{S}(p_1) + \mathcal{S}(p_2))$

For general Ω we use $\lambda = \frac{\Omega-1}{\Omega}$, $a = \sum_{k=1}^{\Omega-1} \frac{p_k}{\Omega-1}$ and $b = p_\Omega$

$$\begin{aligned} \mathcal{S}\left(\frac{\sum_{k=1}^{\Omega} p_k}{\Omega}\right) &= \mathcal{S}\left(\frac{\Omega-1}{\Omega} \frac{\sum_{i=1}^{\Omega-1} p_k}{\Omega-1} + \frac{1}{\Omega} p_\Omega\right) \\ &\geq \frac{\Omega-1}{\Omega} \mathcal{S}\left(\frac{\sum_{k=1}^{\Omega-1} p_k}{\Omega-1}\right) + \frac{1}{\Omega} \mathcal{S}(p_\Omega) \\ &\geq \frac{\Omega-1}{\Omega} \frac{1}{\Omega-1} \sum_{k=1}^{\Omega-1} \mathcal{S}(p_k) + \frac{1}{\Omega} \mathcal{S}(p_\Omega) = \frac{1}{\Omega} \sum_{k=1}^{\Omega} \mathcal{S}(p_k) \end{aligned}$$

The identity leads to:

$$\begin{aligned} H_S(p_1, \dots, p_\Omega) &= - \sum_{k=1}^{\Omega} p_k \log_2(p_k) = \sum \mathcal{S}(p_k) \\ &\leq \Omega \mathcal{S}\left(\frac{1}{\Omega} \sum_k p_k\right) = \Omega \mathcal{S}\left(\frac{1}{\Omega}\right) = - \sum_{k=1}^{\Omega} \frac{1}{\Omega} \log_2\left(\frac{1}{\Omega}\right) \\ &= H_S\left(\frac{1}{\Omega}, \dots, \frac{1}{\Omega}\right) \end{aligned}$$

(2) Entropy has the property that

$$H_I(p_1, \dots, p_{\Omega-1}, 0) = H_I(p_1, \dots, p_{\Omega-1})$$

i.e. it does not change if we add states with probability 0.

This property is given, since $p \ln(p) \underset{p \rightarrow 0}{=} 0$.

(3) Entropy changes for conditional probabilities

We know that $P(A_k, B_l)$, i.e. the probability to find A_k **and** B_l , can be expressed as $P(B_l)P(A_k|B_l) = P(A_k)P(B_l|A_k) = P(A_k, B_l)$ where $P(A_k|B_l)$ denotes the probability to find A_k given that we have B_l . Obviously $P(A_k|B_l) = \frac{P(A_k, B_l)}{P(B_l)}$.

Conditional probabilities are normalized, i.e. we have

$$\sum_k P(A_k|B_l) = 1$$

We now consider conditional probabilities for our ignorance function. If we have $H_I(A) = H_I(p_1, \dots, p_\Omega)$; $H_I(B) = H_I(q_1, \dots, q_\mu)$ for the two sets of states.

Then the ignorance function for the combined state space is given by

$$\begin{aligned} H_I(AB) &= H(r_{11}, r_{12}, \dots, r_{\Omega\mu}) \\ &= H(c_{11}q_1, c_{12}q_2, \dots, c_{\Omega\mu}q_\mu) \end{aligned}$$

where $r_{ij} = P(A_i, B_j)$; $q_i = P(B_i)$; $c_{ij} = P(A_i|B_j)$

If we now select a state q_l for our ignorance function, we get:

$$H_I(A|B_l) = H_i(c_{1l}, \dots, c_{\Omega l})$$

What is the amount of information we typically gain by selecting q_l ?

$$\langle H_I(A|B_l) \rangle = \sum_l q_l \mathcal{S}_I(A|B_l)$$

i.e. the average of the joint ignorance function.

For a proper ignorance function we would expect that:

$$\langle H_I(A|B_l) \rangle = H(A, B) - H_I(B)$$

$$\begin{aligned} H_S(A, B) &= -k_s \sum_{kl} c_{kl} q_l \ln(c_{kl} q_l) \quad P_{kl} = P(A_k, B_l) = c_{kl} q_l \\ &= -k_S \left(\sum_{kl} q_l [\ln(c_{kl}) + \ln(q_l)] \right) \\ &= \sum_l q_l \left(\underbrace{-k_S \sum_k c_{kl} \ln(c_{kl})}_{H_S(A|B_l)} \right) - \underbrace{k_S \sum_l \left(q_l \ln(q_l) \sum_k c_{kl} \right)}_{H_S(B)} \\ &= \langle H_S(A|B_l) \rangle_B + H_S(B) \end{aligned}$$

If A and B are uncorrelated, the knowledge of B_l does not change the ignorance function. We get $H_S(A|B_l) = H(A)$

$$\rightsquigarrow H_I(A, B) = H_I(A) + H_I(B), \text{ i.e. the } \underline{\text{entropy is extensive}}$$

Bayes' Rule can be obtained simply from the product rule:
We have $P(A, B) = P(A|B)P(B)$ and $P(B, A) = P(B|A)P(A)$.
Now using $P(A, B) = P(B, A)$ we get:

$$P(A|B) = \frac{P(B|A)P(A)}{P(B)} \quad \text{Bayes' theorem}$$

If we replace A with hypothesis and B with data, we get:

$$P(\text{hypothesis}|\text{data}) \propto P(\text{data}|\text{hypothesis})P(\text{hypothesis})$$

The use of the formula is the following:

We relate the quantity of interest - the probability that the hypothesis is true given the data - to the probability that we measured the data given the hypothesis was true.

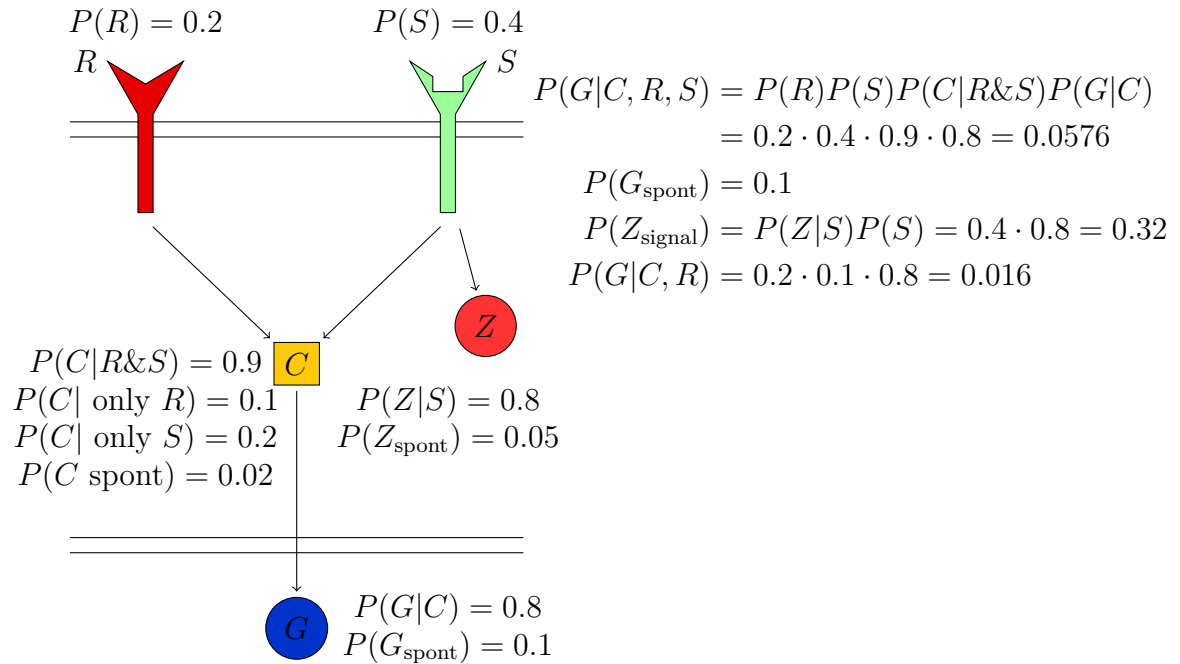
$P(\text{hypothesis})$ is called the prior probability. It represents the state of knowledge about the hypothesis before we analysed the data.

$P(\text{data}|\text{hypothesis})$ is called the likelihood function which modifies the prior.

$P(\text{hypothesis}|\text{data})$ is called posterior, which represents the state of knowledge after about the truth of the hypothesis given the data.

→ recipes in parameter estimation!

1.2.8 Signaling Networks



Signaling networks consist of receptors that bind independently to **Ligands**

- the trigger same signal cascade of individually or collectively activated
- genomic response.

Typically signaling is not deterministic, examples:

- spontaneous trigger of the cascade with small probability
- no signaling even if both/all receptors are active

Using statistical data we can for example establish the expression of a gene if the regular signaling cascade is activated.

Bayesian inference is mostly applied if the probability tables are not known a priori.

- A Bayesian network is constructed as a "directed acyclic graph"(DAG), i.e. the Graph has only directed edges and there is no probability to return to any of the nodes

- parents of a node X_i : nodes j that have an outgoing link to x_i ; $\text{Par}_j(X_i)$
- States of parents: "On"(1); "Off"(0) or other values x_j
- configurations of a network with n nodes

$$P(X_1 = x_1, X_2 = x_2, \dots, X_n = x_n) = \prod_{i=1}^n P(X_i = x_i | \{\text{Par}_j(X_i) = X_j\})$$

The r.h.s of the probability reflects that the probability of x_i depends on the state of the parental sites (and not from any other). This decomposition is only possible if there are no loops in the graph.

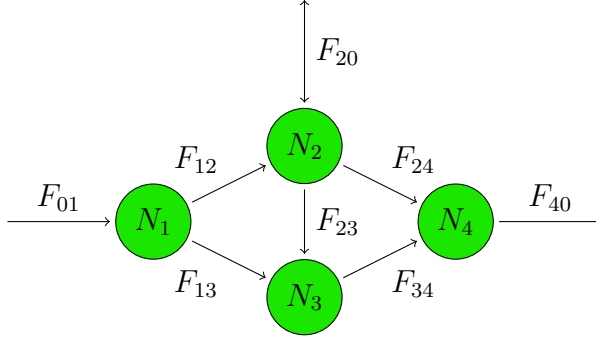
- In Bayesian inference the conditional probabilities are typically unknown. Instead we have usually a rough idea about the connectivity of a graph and a large data set of states.
- General strategy:
 - compose a graph with all known or hypothesized connections
 - define the direction of causality between nodes
 - assign the ranges of probabilities
 - run an optimization scheme → the outcome of the measurements serve as a reference for statistical tests.

1.2.9 Static metabolic networks

Metabolic networks are well suited for analysis since the networks represent the actual flow of material. Generically metabolic systems describe how one organic material is converted from one chemical to another (e.g. conversion of glucose to glucose-6-phosphate in the first reaction of glycolysis).

Compounds of interest in metabolic networks are represented as nodes, enzymatic reactions and transitions as edges.

1.3 Stoichiometric networks



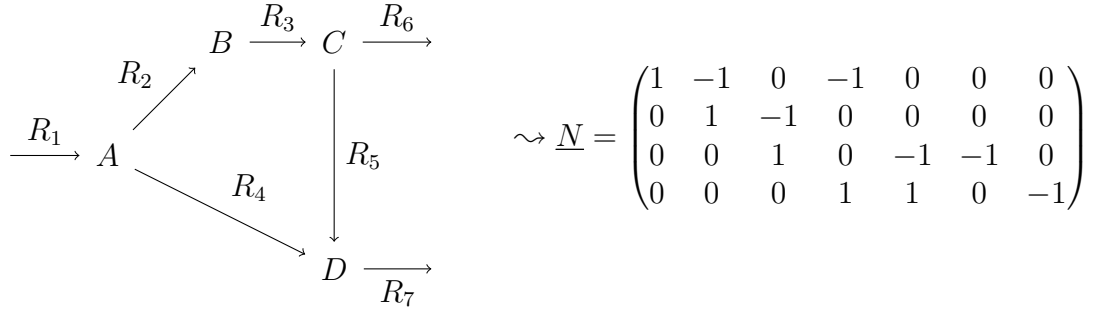
We consider a stationary state, i.e. incoming and outgoing fluxes balance each other at a given node.

The constraint of conservation of mass leads to relations between fluxes, e.g. $F_{13} + F_{23} = F_{34}$ (*). The set of relations is called stoichiometry.

Reminder For bidirectional fluxes we consider two edges, e.g. F_{20} and F_{02} . It is easy to see that equations as (*) are valid in the stationary state since the time evolution of N_3 is given by:

$$\frac{dN_3(t)}{dt} = F_{13}(t) + F_{23}(t) - F_{34}(t)$$

The analysis of stoichiometric networks is relatively simple since it results in a linear system, where the vector \underline{S} represents the metabolites and \underline{N} (stoichiometric matrix) the connectivity of the network.



± 1 represent incoming (outgoing) fluxes. Here, we consider that one molecule creates one product. If two or more molecules would be needed, one would have to assign the fluxes accordingly.

The time evolution of the network is given by:

$$\underbrace{\underline{S}}_{\text{metabolites}} = \underbrace{\underline{N}}_{\text{stoichiometric matrix}} \cdot \underbrace{\underline{R}}_{\text{Fluxes between pools (nodes)}}$$

The stationary state is given by a set of linear equations of the kind:

$$0 = N_{i1}R_1 + N_{i2}R_2 + \dots + N_{iM}R_M$$

1.3.1 Reconstruction of metabolic networks

- the reconstruction of (metabolic) networks in case of unknown edges is very labor intensive
- Metabolites can be obtained with mass-spectroscopy
- Pathways can be obtained from the presence of genes, homologies with other organisms etc.
- The combined knowledge is used in order to fill the missing links

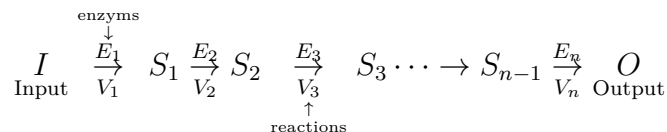
1.3.2 Metabolic control analysis (MCA)

Traditional view: Every pathway has one limiting step which controls the output of the pathway

MCA: Shared control replaces rate-limiting steps, i.e. every step in the pathway contributes to the control of the steady state flux.

Formal analysis via control-coefficients and so called "elasticities"

1.3.3 Generic metabolic pathway



Steady state:

- All concentrations are constant, i.e. $\dot{I} = \dot{S}_i = \dot{O} = 0$

- All reaction rates must be the same $V_1 = V_2 = \dots V_n$ where J denotes the overall flux (conservation of mass)

Small perturbations: We are interested in small perturbations of the steady state and ask which reaction rates v_i and metabolic concentrations have the strongest impact.

We characterize this by the following quantities:

$$c_{V_i}^J = \frac{v_i}{J} \frac{\partial J}{\partial v_i} = \frac{\partial \ln(J)}{\partial \ln(v_i)} \quad (\text{flux control coefficient})$$

The flux control coefficient measures the relative change of the flow via v_i .

1.3.4 Metabolite Control Coefficient

$$c_{v_i}^{S_k} = \frac{v_i}{S_k} \frac{\partial S_k}{\partial v_i} = \frac{\partial \ln(S_k)}{\partial \ln(v_i)}$$

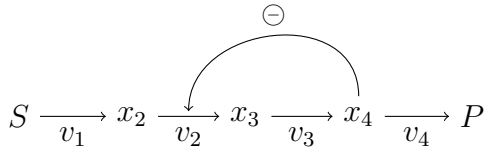
The influence of an enzyme on a flux or on a metabolite concentration can be very different. The impact of S_k on v_i is measured by the **elasticity coefficient**

$$\epsilon_{S_k}^{v_i} = \frac{S_k}{v_i} \frac{\partial v_i}{\partial S_k} = \frac{\partial \ln(v_i)}{\partial \ln(S_k)}$$

One can show that $\sum_{i=1}^{n+1} c_{v_i}^J = 1$ and $\sum_{i=1}^{n+1} c_{v_i}^{S_k} = 0$

This relation is useful in order to determine whether all reactions of the pathway have been detected.

1.3.5 Example



We consider a linear pathway with feedback. The following elasticities are known a priori.

$$\epsilon_{x_2}^{v_1} = -0.9; \quad \epsilon_{x_2}^{v_2} = 0.5; \quad \epsilon_{x_3}^{v_2} = -0.2; \quad \epsilon_{x_3}^{v_3} = 0.7; \quad \epsilon_{x_4}^{v_2} = -1; \quad \epsilon_{x_4}^{v_4} = 0.9$$

The other elasticities are 0.

Now we can use the identity $\sum_{i=1}^w c_{v_i}^J \epsilon_{s_k}^{v_i} = 0$ in order to determine all flux coefficients; e.g:

$$c_{v_1}^J \epsilon_{x_2}^{v_1} + c_{v_2}^J \epsilon_{x_2}^{v_2} = -0.9c_{v_1}^J + 0.5c_{v_2}^J = 0 \quad c_{v_4}^J = 0.38$$

Solving the set of equations, we get:

$$c_{v_1}^J = 0.19, \quad c_{v_2}^J = 0.34, \quad c_{v_3}^J = 0.10$$

The information can be used in order to identify the bottle necks of the pathway and manipulate, e.g. the enzyme concentration or binding affinity to reduce the inhibition effects.

2 Non-linear Systems in Biology

2.1 Examples and linear systems

2.1.1 Discrete linear systems - Recursive deterministic Models

Recursive models Discrete time, the state at time t is determined by a linear function of the state variable at time $t - 1$.

E.g.: Bacterial population: $P_{t+1} = 2P_t$

$$\leadsto P_{t+n} = 2^n P_t$$

A slightly more complicated example is given by the production and degradation of red blood cells. Red blood cells are produced by the bone marrow and eventually degraded.

In the model we consider the evolution of the number of cells on a day by day basis:

$$R_n = (1 - f)R_{n-1} + M_{n-1} \quad M_n = gfR_{n-1}$$

M_n = # of new blood cells

g = production rate per degraded blood cell

R_n = # of circulation blood cells

f = fraction of degraded cells

Steady state?

→ eliminate M_{n-1}

$$R_n = (1 - f)R_{n-1} + M_{n-1} = (1 - f)R_{n-1} + gfR_{n-2}$$

Steady state if: $R_n = R_{n-1} = R_{n-2} = R$

$$\Rightarrow R = (1 - f)R + gfR \leadsto \text{Steady state for } f = 0 \text{ \& } R = 0$$

We get a non-trivial stationary state if

$$Rf = fgR \leadsto g = 1$$

This implies that the system is at a steady state for any value of R if g equals 1

Remark: The equation can conveniently be written in a matrix form

$$\begin{pmatrix} R \\ M \end{pmatrix}_{n+k} = \begin{pmatrix} 1-f & 1 \\ gf & 0 \end{pmatrix}^k \begin{pmatrix} R \\ M \end{pmatrix}_n$$

2.1.2 Continuous linear systems

It is often appropriate to describe the time evolution of a dynamic system in continuous time, even if discrete events take place, e.g. the description of a bacterial biofilm in terms of mass and density rather than in terms of the number of bacteria.

We first consider the case of linear systems, e.g.

$$\begin{aligned} \dot{x} &= y & \dot{x} &= \frac{d}{dt}x \\ \dot{y} &= -x \end{aligned}$$

The system is linear, since the rhs of the system of differential equations is linear in x and y .

Systems of linear differential equations of first order can be described by

$$\frac{d\underline{x}}{dt} = \underline{\dot{x}} = \underline{\underline{A}}\underline{x}$$

$\underline{x}(t)$ is a vector of functions $x_i(t)$ and $\underline{\underline{A}}$ is a matrix with coefficients a_{ij} . A generalization of a linear system is the affine system

$$\underline{\dot{x}} = \underline{\underline{A}}\underline{x} + \underline{u}$$

where the vector \underline{u} represents the "perturbations" of the system. The coefficients of \underline{A} can be constants or functions $a_{ij}(t)$. The time evolution of $x_i(t)$ is given by:

$$\dot{x}_i(t) = \frac{dx_i(t)}{dt} = \sum_{j=1}^n a_{ij}x_j(t) + u_i(t) \quad i = 1, \dots, n$$

In case of $u(t) = 0$, we have a homogeneous system, which has a fixpoint if $\underline{Ax} = 0$

If $\text{rank}(\underline{A}) = n$, it follows that $\det(\underline{A}) \neq 0$. Then the solution of the linear system is unique and given by $\underline{x} = 0 \quad \forall t$.

If $\det(\underline{A}) = 0$, the linear equations are dependent and the solutions exist on a hyperplane.

2.1.3 Solutions of a linear system

The matrix exponential

The Taylor-Series of an exponential function is given by:

$$e^x = \sum_{n=0}^{\infty} \frac{x^n}{n!}$$

Analogously, we can define the **matrix exponential**

$$H = \sum_{k=0}^{\infty} \frac{P^k}{k!} =: e^P$$

Here, we are particularly interested in the matrix $\underline{P} = \underline{At}$; i.e.:

$$e^{\underline{At}} = \sum_{k=0}^{\infty} \frac{(\underline{At})^k}{k!} \text{ and } e^{-\underline{At}} = \sum_{k=0}^{\infty} (-1)^k \frac{(\underline{At})^k}{k!}$$

We can easily verify that (\underline{A} const.)

$$\frac{d}{dt} e^{\underline{At}} = \sum_{k=1}^{\infty} \frac{\underline{A}^k t^{k-1}}{(k-1)!} = \underline{A} \sum_{k=0}^{\infty} \frac{(\underline{At})^k}{k!} = \underline{A} e^{\underline{At}}$$

(Similarly: $\frac{d}{dt} e^{-\underline{At}} = -\underline{A} e^{-\underline{At}}$)

Solution of the linear system $\dot{x} = \underline{Ax}$

Theorem: Let \underline{A} be a constant matrix; i.e. a_{ij} are not time-dependent.

$$\text{Then we get: } \underline{x}(t) = \underline{x}_0 e^{\underline{A}t}$$

The proof follows from Taylorexansion of the rhs.

The inhomogeneous system $\dot{\underline{x}} = \underline{A}\underline{x} + \underline{u}$

Theorem: The solutions $\underline{x}(t)$ of the inhomogeneous system $\underline{x}(t) = \underline{A}\underline{x} + \underline{u}$ given the initial conditions \underline{x}_0 are given by:

$$\underline{x}(t) = \underline{x}_n(t) + \underline{x}_p(t)$$

where $\underline{x}_n = e^{\underline{A}(t-t_0)}\underline{x}_0$; $\underline{x}_p = \int_{t_0}^t e^{\underline{A}(t-\tau)}\underline{u}(\tau)d\tau$ and $\underline{x}_0 = \underline{x}(t_0)$

Proof: From $\dot{\underline{x}} = \underline{A}\underline{x} + \underline{u}$ we get $\dot{\underline{x}} - \underline{A}\underline{x} = \underline{u}$

$$\leadsto e^{-\underline{A}t}\dot{\underline{x}} - e^{-\underline{A}t}\underline{A}\underline{x} = e^{-\underline{A}t}\underline{u}$$

The left hand side of the equation can be understood as the derivative of the product $e^{-\underline{A}t}$

$$\leadsto \frac{d}{dt} (e^{-\underline{A}t}\underline{x}) = e^{-\underline{A}t}\underline{u}$$

$$\int \frac{d}{dt} (e^{-\underline{A}t}\underline{x}) dt = e^{-\underline{A}t}\underline{x}(t) = \int e^{-\underline{A}t}\underline{u}(t)dt$$

Or, integrating from t_0 to t :

$$e^{-\underline{A}t}\underline{x}(t) - e^{-\underline{A}t_0}\underline{x}(t_0) = \int_{t_0}^t e^{-\underline{A}\tau}\underline{u}(\tau)d\tau$$

$$\leadsto \underline{x}(t) = e^{\underline{A}(t-t_0)}\underline{x}(t_0) + \int_{t_0}^t e^{\underline{A}(t-\tau)}\underline{u}(\tau)d\tau$$

Remarks:

- 1) This is the formal solution of the linear system with constant coefficient. For big linear systems, this solution is difficult to obtain explicetly, since it involves an infinite number of matrix multiplications
- 2) The homogeneous solution $\underline{x}_n(t)$ depends on the set of initial conditions

$$\underline{x}_0 = \underline{x}(t_0); \quad \underline{x}_p \text{ depends only on the pertubation of } \underline{u}(t)$$

- 3) The answer of the system depends on $\underline{\underline{H}} = e^{\underline{\underline{A}}t}$. If $\underline{\underline{H}}(t)$ is given, we can calculate the time evolution for arbitrary perturbations of $\underline{u}(t)$ and

Example: Linear system in 1D

$$\begin{aligned}\dot{x} &= ax + u \\ u(t) &= \begin{cases} 0 & t \leq 0 \\ u & t > 0 \end{cases}; \quad a \in \mathbb{R} \\ \leadsto x(t) &= x_0 e^{at} + \int_0^t u e^{a(t-\tau)} d\tau\end{aligned}$$

Simple examples of non-linear systems

- (i) The pendulum: The dynamics of the pendulum is described by the ordinary differential equation (ODE)

$$\ddot{x} + \frac{g}{l} \sin(x) = 0$$

We can rewrite the equation of 1st order ODEs:

$$\begin{aligned}\dot{x}_1 &= x_2 \\ \dot{x}_2 &= -\frac{g}{l} \sin(x_1)\end{aligned} \quad \begin{array}{l} \text{Obviously the rhs of the 2nd equation} \\ \text{is non-linear and therefore} \\ \text{the whole system.} \end{array}$$

- (ii) The forced harmonic oscillator:

$$m\ddot{x} + b\dot{x} + kx = F \cos(t)$$

Again the ODE can be rewritten as a system of ODEs of first order:

$$\begin{aligned}\dot{x}_1 &= x_2 \\ \dot{x}_2 &= \frac{1}{m} (-kx_1 - bx_2) + \frac{F}{m} \cos(x_3) \\ \dot{x}_3 &= 1, \quad \text{where } x_3 = t\end{aligned}$$

The solution of a non-linear system is much more difficult than solving linear systems because linear systems often can be broken into parts.

In case of non-linear systems one often applies a geometric approach by using directly the properties of the system. This way, one might be able to construct the trajectories in phase space. **One-dimensional flow**

As an introductory example we consider the simple non-linear system $\dot{x} = \sin(x)$

This system can be solved analytically by separation of variables:

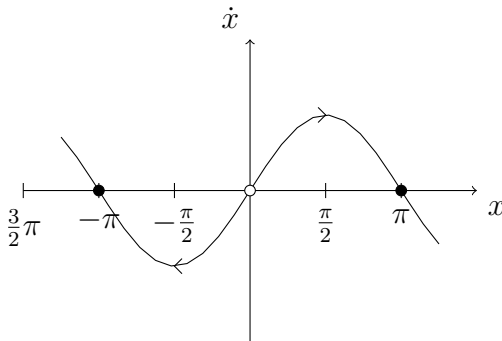
$$dt = \frac{1}{\sin(x)} dx \underset{t_0=0}{\rightsquigarrow} t = \int_{x_0}^x \frac{1}{\sin(x')} dx'$$

$$\text{using } \int \frac{1}{\sin(x)} dx = \ln \left| \frac{\sin(x)}{1 + \cos(x)} \right| + c = \ln \left| \tan \left(\frac{x}{2} \right) \right| + c$$

$$\rightsquigarrow t = \ln \left| \frac{1 + \cos(x_0)}{\sin(x_0)} \frac{\sin(x)}{1 + \cos(x)} \right|$$

The result is obviously difficult to interpret. By contrast, a graphical analysis of the system is simple.

We consider $\dot{x} = \sin(x)$ as a vector field on a line.

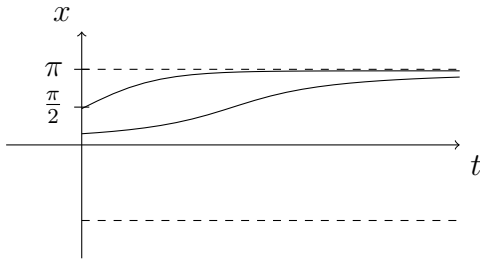


The flow is to the right, if $\dot{x} > 0$ and to the left if $\dot{x} < 0$. At points where $\dot{x} = 0$ there is no flow.

$\rightsquigarrow \dot{x} = 0$ corresponds to a fixed point.

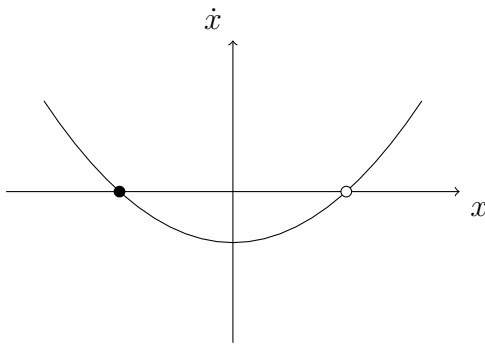
- stable fixed point - flow is oriented toward the FP
- unstable fixed points - flow points away from the fixed point

Particle starting at $x = \frac{\pi}{4}$. The particle is moving to the right and will ultimately reach the FP at $x = \pi$.



Fixed points and stability

We now generalize our system and consider $\dot{x} = f(x)$ Again, we get



For the qualitative analysis of the trajectory. We consider $x(t)$ as a "phase fluid", flowing with velocity $\dot{x}(t) = f(x(t))$

To find the solution $x(t)$, we place a particle at the phase point x_0 at $t = 0$ and observe how it moves along the x -axis. This function is called trajectory. A picture showing all qualitatively different trajectories is called phase portrait. FP represent stationary solutions, since we reach a FP x^* , where $f(x^*) = 0$, $x(t) = x^*$ holds for all times. **Example:** Find the FP of $f(x) = x^2 - 1$ and classify their stability:

$$x^* = -1 \text{ (stable), } x^* = 1 \text{ (instable)}$$

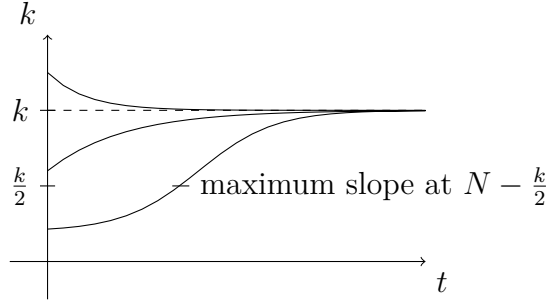
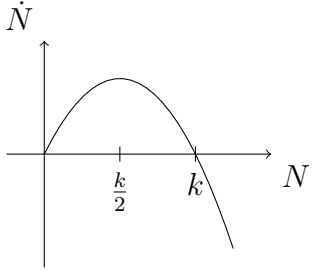
Population growths:

Simplest model: $\dot{N} = rN \leadsto N(t) = N_0 e^{rt}$

→ unrestricted growth

More realistic: Finite resources have to be considered:

$$\dot{N} = rN \left(1 - \frac{N}{k}\right)$$



Linear stability analysis

Let x^* be a fixed point and let $\eta(t) = x(t) - x^*$ be a small perturbation away from x^* . We are now interested whether the perturbation grows or decays:

$$\dot{\eta} = \frac{d}{dt}(x - x^*) = \dot{x} \quad \Rightarrow \quad \dot{\eta} = \dot{x} = f(x) = f(x^* + \eta)$$

We now expand $f(x)$ at x^* :

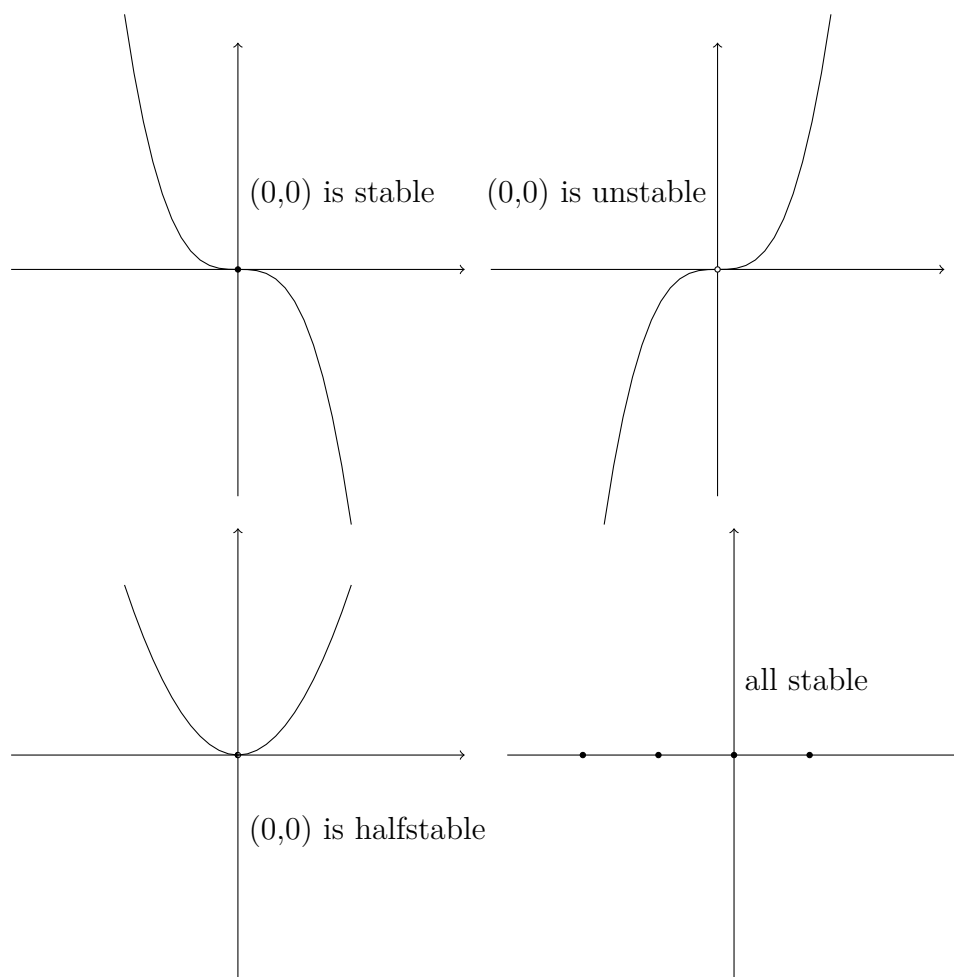
$$\begin{aligned} f(x^* + \eta) &= f(x^*) + \eta \frac{df}{dx}(x^*) + \mathcal{O}(\eta^2) \\ &\leadsto \dot{x} = \dot{\eta} = \eta \frac{df}{dx}(x^*) + \mathcal{O}(\eta^2) \end{aligned}$$

Now, if $\frac{df}{dx}(x^*) \neq 0$ we can neglect the η^2 terms and get

$$\dot{\eta} \approx \eta \frac{df}{dx}(x^*)$$

This equation is linear in $\eta(t)$ and called **linearization** about x^* . The perturbation $\eta(t)$ grows exponentially if $\frac{df}{dx}(x^*) > 0$ and decays if $\frac{df}{dx}(x^*) < 0$. This information has already been obtained by the graphical analysis. The new feature is that we obtain a time scale $\frac{1}{\left|\frac{df}{dx}(x^*)\right|}$ which governs the exponential growth or decay. Remark: In cases where $\frac{df}{dx}(x^*) = 0$ nothing can be said

in general and we have to determine the stability on a case-by-case basis.
Examples:



So far we did not consider the existence and uniqueness of the solutions. The importance of that issue is illustrated by the following example:

Example: Consider $\dot{x} = \sqrt[3]{x}$ and use the initial condition $x_0 = 0$. The obvious solution is $x(t) = 0$. But there is also another solution. Separating variables we get

$$\int x^{-\frac{1}{3}} = \int dt \rightsquigarrow \frac{3}{2}x^{\frac{2}{3}} + c = t$$

The initial condition leads to $c = 0 \rightsquigarrow x(t) = \left(\frac{2}{3}t\right)^{\frac{3}{2}}$ is also a solution!
 In case of a non-unique solution our analysis obviously fails!
 So, we have to ask, which conditions are necessary to obtain a unique solution.

Existence and uniqueness theorem: Consider the initial value problem

$$\dot{x} = f(x); \quad x(0) = x_0$$

Suppose that $f(x)$ and $\frac{df}{dx}(x)$ are continuous on an open interval R of the x -axis and suppose that x_0 is a point in R . Then the initial value problem has a solution $x(t)$ on some time interval $] -\tau, \tau[$ about $t = 0$, and the solution is unique.

Remark: Please note that the theorem does **not** imply that the solution exists for all times.

Example: $\dot{x} = 1 + x^2$; $x(0) = x_0$. The uniqueness theorem applies for all values x_0 since $f(x)$ and $\frac{df}{dx}(x)$ are continuous. But for $x_0 = 0$ we get:

$$\int \frac{1}{1+x^2} dx = \int dt \rightsquigarrow t = \arctan(x) + c$$

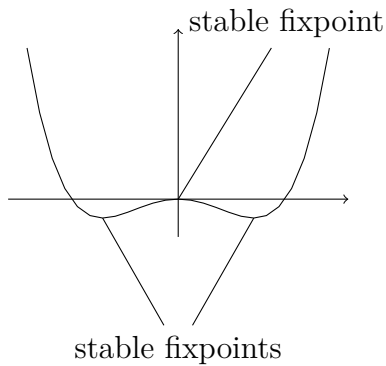
$\rightsquigarrow c = 0$ & $x(t) = \tan(t)$. Obviously x diverges for $t \rightarrow \frac{\pi}{2}$, i.e. in finite time!

Remark: FP dominate the dynamics of 1st order systems in one dimension. More specifically trajectories either approach a fixed point or diverge to $\pm\infty$. These are actually the only things that may happen to a vector field on a real line. In particular, trajectories cannot reverse direction (oscillate) since they had to cross a fixpoint. **Potentials** provide another possibility to characterize a dynamic system graphically. We introduce a potential via $f(x) = -\frac{dV}{dx}$, using this picture one should consider the particle damped, its inertia completely negligible. As in physics, the particle always moves downhill.

$$\begin{aligned} \frac{dV}{dt} &= \frac{dV}{dx} \frac{dx}{dt} & \& \quad \frac{dx}{dt} = f(x) = -\frac{dV}{dx} \\ \rightsquigarrow \frac{dV}{dt} &= -\left(\frac{dV}{dx}\right)^2 & \rightsquigarrow V & \text{always decreases along trajectories} \end{aligned}$$

At an equilibrium point we have $\frac{dV}{dt} = 0$. Local minima correspond to stable fixpoints, local maxima to unstable fixpoints.

Example: $\dot{x} = \underbrace{x - x^3}_{f(x)} \rightsquigarrow V(x) = -\frac{1}{2}x^2 + \frac{1}{4}x^4 + c$

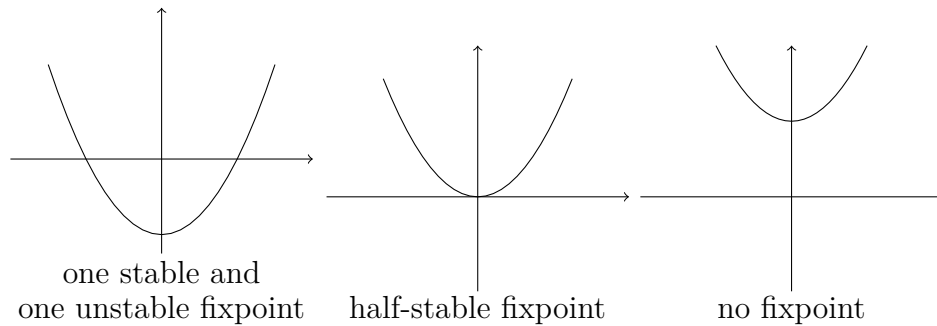


Bifurcations: 1D flows are simple: Either they converge to a fixed point or head on to $\pm\infty$. The most interesting aspect of 1D flows is their parameter dependence.

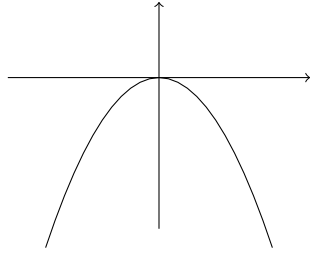
Qualitative changes of the dynamics upon variation of the parameters are called **bifurcations**, and the corresponding parameter **values** are called **bifurcation points**.

Saddle-Node-Bifurcation

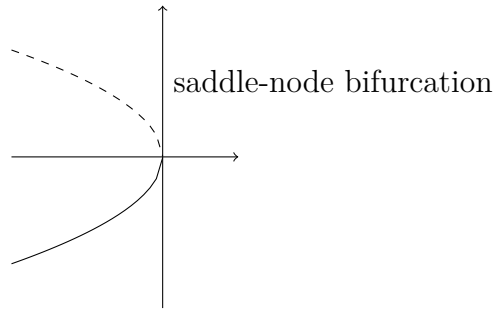
- Basic mechanism by which fixpoints are created or destroyed
- Introductory example $\dot{x} = r + x^2$



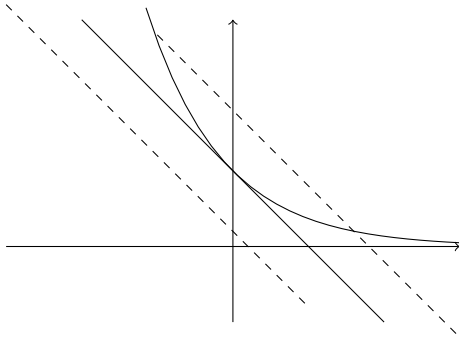
The fixpoints are located on the curve $r = -x^2$



Typically the axes are inverted since r is the independent variable
Bifurcation diagram:



Example: We consider the 1st order system $\dot{x} = r - x - e^{-x} = f(x)$
For this choice of $f(x)$ the fixpoints are difficult to obtain analytically. But we notice the following: fixpoints are located where the two curves e^{-x} and $r - x$ intersect upon variation of r we get:



Normal forms: The form $\dot{x} = r \pm x^2$ is prototypical for saddle-node bifurcations. This can be understood from the following argument:

We consider $\dot{x} = f(x, r)$ near the bifurcation point at $x = x^*$ and $r = r_c$.

$$\leadsto \dot{x} = f(x, r) = f(x^*, r_c) + (x - x^*) \left. \frac{\partial f}{\partial x} \right|_{(x^*, r_c)} + (r - r_c) \left. \frac{\partial f}{\partial r} \right|_{(x^*, r_c)} + \frac{1}{2} (x - x^*)^2 \left. \frac{\partial^2 f}{\partial x^2} \right|_{(x^*, r_c)} + \dots$$

We neglect terms of the order $(r - r_c)^2$ and $(x - x^*)^3$. We also realize that $f(x^*, r_c) = 0$ because x^* is a fixed point.

We also have $\left. \frac{\partial f}{\partial x} \right|_{(x^*, r_c)} = 0$ by the tangency condition. Therefore, we are left with:

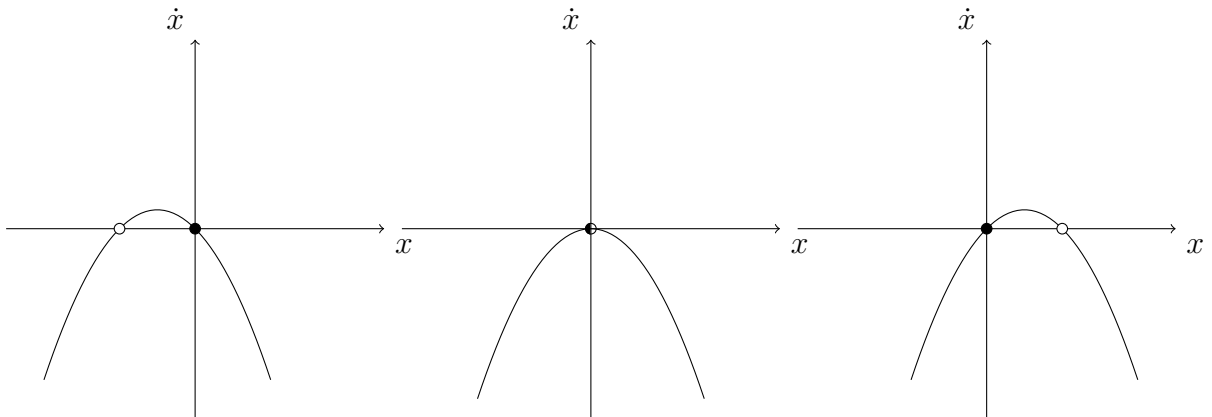
$$\dot{x} = a(r - r_c) + b(x - x_c)^2 + \dots \quad \text{"normal form" of the bifurcation}$$

where $a = \left. \frac{\partial f}{\partial r} \right|_{(x^*, r_c)}$ and $b = \left. \frac{\partial^2 f}{\partial x^2} \right|_{(x^*, r_c)}$

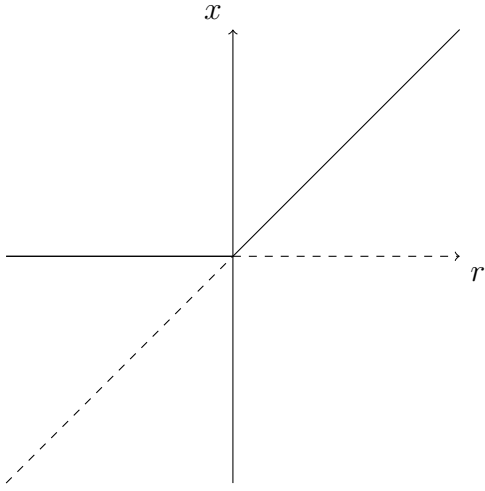
Transcritical bifurcation

Normal form of a transcritical bifurcation

$$\dot{x} = rx - x^2 \quad r \text{ can be a positive or negative (or zero)}$$



In case of the transcritical bifurcation we always have a fixpoint at $x^* = 0$ independent of r . There is an exchange of stability between the fixed points at $r = 0$. The bifurcation diagram is given as follows:



Example: Show that the first-order system

$$\dot{x} = x(1 - x^2) - a(1 - e^{-bx})$$

undergoes a transcritical bifurcation at $x^* = 0$ for certain parameter values a, b .

Solution: We first notice that $\dot{x} = 0$ at $x = 0$ independent of a, b .

For small values of x , we get:

$$1 - e^{-bx} = 1 - \left[1 - bx + \frac{1}{2}b^2x^2 + \mathcal{O}(x^3) \right] = bx - \frac{1}{2}b^2x^2 + \mathcal{O}(x^3)$$

This leads to:

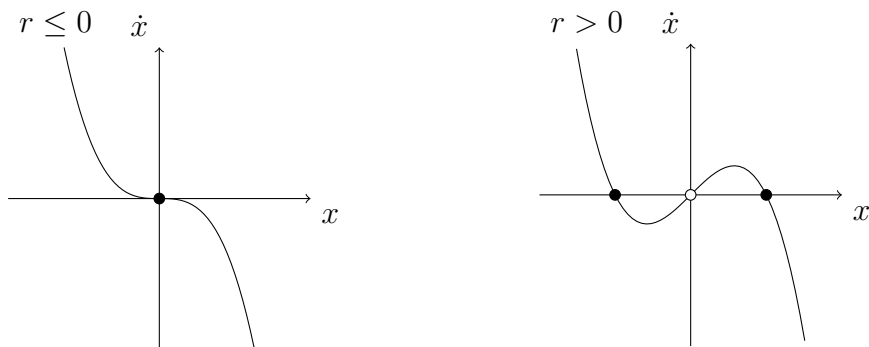
$$\begin{aligned} \dot{x} &= x - a \left(bx - \frac{1}{2}b^2x^2 \right) + \mathcal{O}(x^3) \\ &= (1 - ab)x + \left(\frac{1}{2}b^2 \right) x^2 + \mathcal{O}(x^3) \\ \Rightarrow \text{The non-zero fixed point is given at } (1 - ab) + \frac{1}{2}ab^2x &= 0 \\ \Rightarrow x^* &= \frac{2(ab - 1)}{ab^2} \end{aligned}$$

Note that this result is only valid if x^* is small.

Supercritical Pitchfork bifurcation

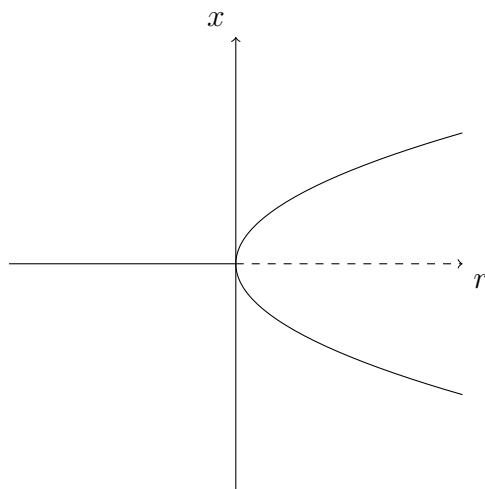
Normal form: $\dot{x} = rx - x^3$

Note that this equation is invariant under the exchange of the variable $x \rightarrow -x$. We get the following vector fields for different values of r

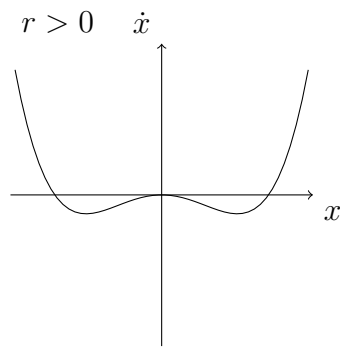
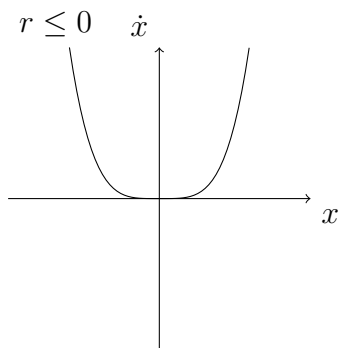


At $r = 0$ we observe a transition from a single stable Fixpoint at $x^* = \pm\sqrt{r}$. The fixpoint at $x^* = 0$ gets unstable.

Bifurcation diagram:



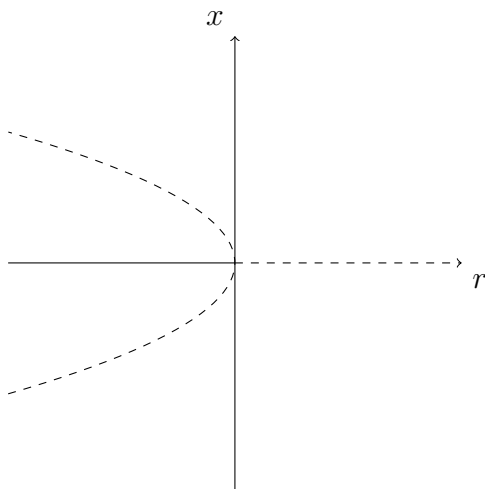
Example: We consider the potential $V(x)$ for the system $\dot{x} = rx - x^3$. The potential is given by $f(x) = -\frac{dV}{dx} \leadsto V(x) = -\frac{1}{2}rx^2 + \frac{1}{4}x^4$



Subcritical pitchfork bifurcation

Normal form: $\dot{x} = rx + x^3 \leftarrow$ the cubic term is destabilizing.

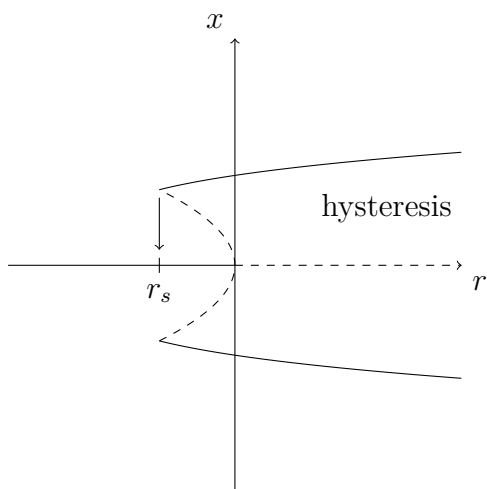
Bifurcation diagram



The nonzero fixed points are located at $x^* = \pm\sqrt{r}$. They are unstable.

The pitchfork-bifurcation is inverted.

Remark: In real physical systems one often has a stabilizing higher order term, such that a canonical form of a system with a subcritical pitchfork bifurcation is given by: $\dot{x} = rx + x^3 - x^5$. The system has still the $x \rightarrow -x$ symmetry.



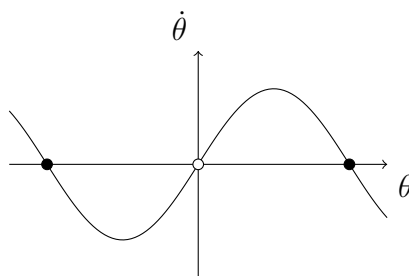
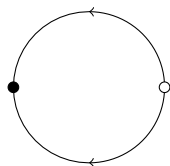
Remark:

- 1) In the range $r_s < r < 0$ two qualitatively different stable fixed points exist. The fixed points at the origin is locally stable, since for large values of x_0 the system may converge to the large amplitude fixed point.
- 2) We may observe jumps and hysteresis upon variation of r .
- 3) the bifurcation at r_s is a saddle-node bifurcation.

2.1.4 Flows on the circle

We now consider vector fields as the following: $\dot{\theta} = f(\theta)$ where θ is a point on a circle and $\dot{\theta}$ is the velocity vector at that point. This choice of the variable allows us to get periodic solutions in a 1D-system.

Example: Vector field corresponding to $\dot{\theta} = \sin(\theta)$



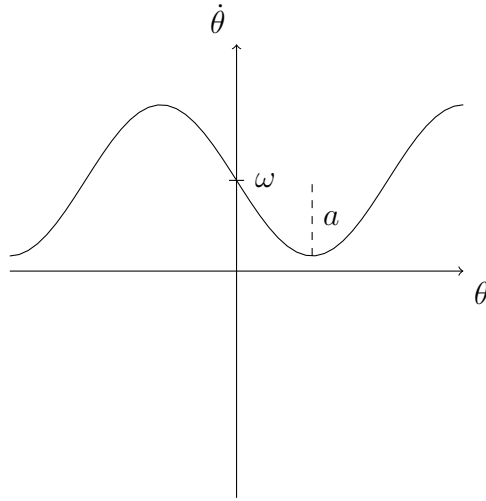
A vector field on a circle is a rule that assigns a unique velocity vector to a point on the circle. Therefore $f(\theta)$ has to be a periodic function. There is for example no unique velocity for $\dot{\theta} = \theta$ since $\theta = 0$ and $\theta = 2\pi$ correspond to the same point on a circle but to different velocities.

Uniform oscillator: A point on a circle is often called phase or angle. And

the simplest oscillator is given by $\dot{\theta} = \omega \leadsto \theta(t) = \omega t + \theta_0$. After the period of $T = \frac{2\pi}{\omega}$ the oscillator returns to the same point.

Nonuniform oscillator: $\dot{\theta} = \omega - a \sin(\theta)$, $a, \omega > 0$

In this realization of the oscillator its velocity is not constant anymore.

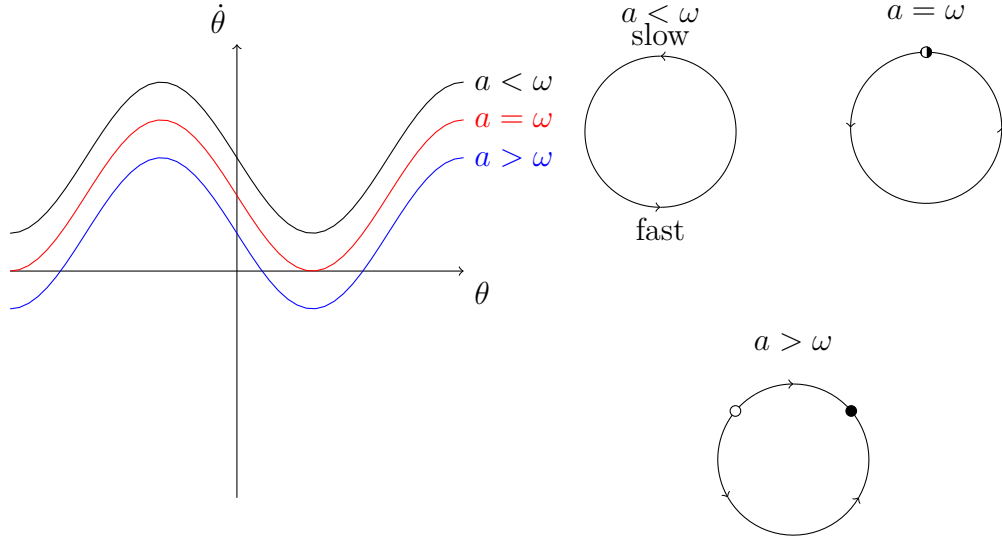


We now discuss the parameter space of the system:

$a = 0$ We return to the uniform oscillator

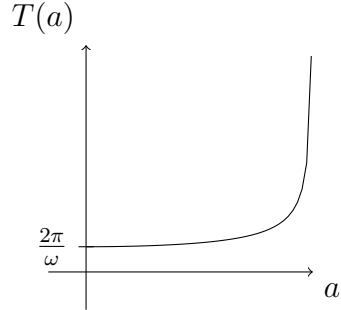
$a \neq 0$ $\theta = -\frac{\pi}{2}$ corresponds to the fastest flow, $\theta = \frac{\pi}{2}$ the slowest flow

Bottleneck: If $\omega > 0$ but $\omega - a \ll 1$ the system slows down considerably. The phase point $\theta(t)$ takes a long time to pass the bottleneck. For $a \geq \omega$ the oscillator stops.



For this simple system one can calculate the oscillation period as well

$$T = \int dt = \int_0^{2\pi} \frac{dt}{d\theta} d\theta = \int_0^{2\pi} \frac{d\theta}{\omega - a \sin(\theta)} = \frac{2\pi}{\sqrt{\omega^2 - a^2}}$$



Obviously, we get $T = \frac{2\pi}{\omega}$ for $a = 0$.
The order of the divergence can be
obtained from

$$\sqrt{\omega^2 - a^2} = \sqrt{\omega + a} \sqrt{\omega - a} \underset{\omega \approx a}{\approx} \sqrt{2\omega} \sqrt{\omega - a}$$

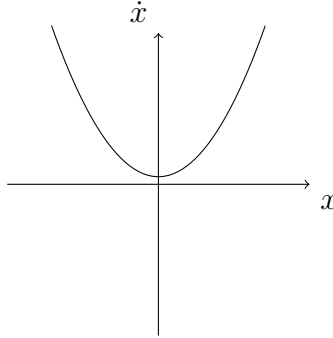
$$T \approx \frac{\pi\sqrt{2}}{\sqrt{\omega}} \frac{1}{\sqrt{\omega - a}} \approx (a_c - a)^{-\frac{1}{2}}$$

This behaviour is generic, since it is driven by the local minimum of $\dot{\theta}$ at $a = a_c$. Therefore the bottleneck can be described by:

$$\dot{x} = r + x^2 \quad (0 < r \ll 1)$$

$$T_{\text{bottleneck}} \approx \int_{-\infty}^{\infty} \frac{dx}{r+x^2} = \frac{\pi}{\sqrt{r}}$$

i.e. the square root scaling law



2.2 Higher dimensional dynamic systems

2.2.1 Linear Systems

1D flows are qualitatively simple - either the system moves in one direction or it stops. This is different in higher dimensions, where one may observe a more complex behaviour.

We first discuss the most simple system in 2D; i.e. a linear system

$$\begin{aligned}\dot{x} &= ax + by \\ \dot{y} &= cx + dy\end{aligned}$$

This system can be rewritten as:

$$\underline{\dot{x}} = \underline{\underline{A}}\underline{x} \quad \text{where} \quad \underline{\underline{A}} = \begin{pmatrix} a & b \\ c & d \end{pmatrix} \quad \text{and} \quad \underline{x} = \begin{pmatrix} x \\ y \end{pmatrix}$$

Linearity implies that $\underline{x} = c_1 \underline{x}_1 + c_2 \underline{x}_2$ is a solution of the system if \underline{x}_1 and \underline{x}_2 are solutions of the system (c_1, c_2 are arbitrary parameters)

Example: Oscillator

$$m\ddot{x} + kx = 0 \quad \begin{cases} \dot{x} = v \\ \dot{v} = -\frac{k}{m}x \end{cases}$$

Again, we obtain a vectorfield which we want to analyse in the following:

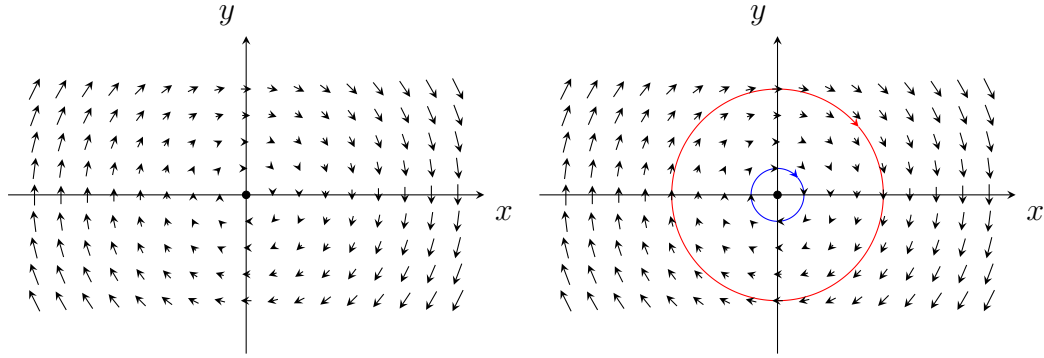
At the x -axis (i.e. $v = 0$) we get:

$$\dot{x} = 0 \quad \dot{v} = -\omega^2 x \quad \left(\omega^2 = \frac{k}{m} \right)$$

Similarly, we get:

$$\begin{aligned} \dot{x} &= v & \text{at the } v\text{-axis} \\ \dot{v} &= 0 \end{aligned}$$

Using similar arguments we get:



Classification of linear systems:

We are now going to classify all possible phase portraits in 2D-linear systems

Straight line trajectories:

$$\underline{x}(t) = e^{\lambda t} \underline{v}$$

\underline{v} constant vector, λ : growth rate

We take this form as an ansatz for our linear equation:

$$\underline{x}(t) = \lambda e^{\lambda t} \underline{v} = \underline{A} \underline{x}(t) = \underline{A} e^{\lambda t} \underline{v}$$

$$\leadsto \lambda \underline{v} = \underline{A} \underline{v}$$

This eigenvalue problem can be easily solved. The eigenvalues are given by:

$$\lambda_{1,2} = \frac{\tau \pm \sqrt{\tau^2 - 4\Delta}}{2} \quad (\tau = \text{tr}(A) = a + d, \Delta = \det(A) = ad - bc)$$

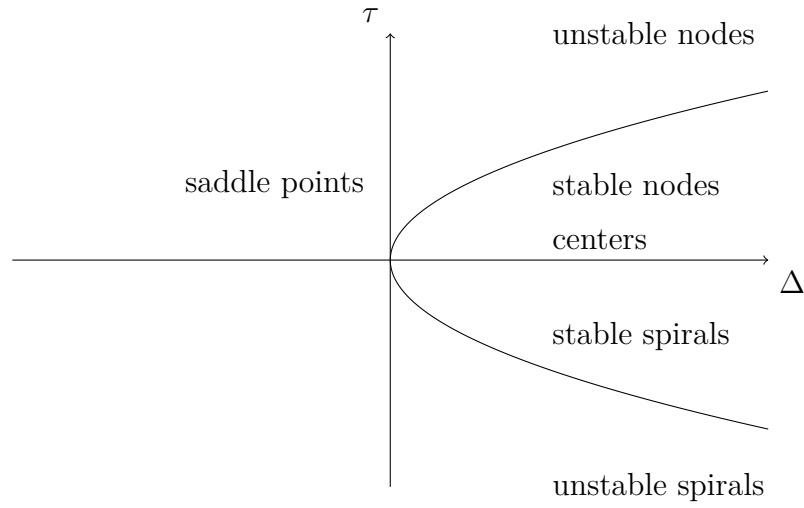
The general solution of the system is given by

$$\underline{x}(t) = c_1 e^{\lambda_1 t} \underline{v}_1 + c_2 e^{\lambda_2 t} \underline{v}_2$$

where $\underline{v}_1, \underline{v}_2$ are the eigenvectors of the system.

The eigenvalues determine obviously the properties of the system.

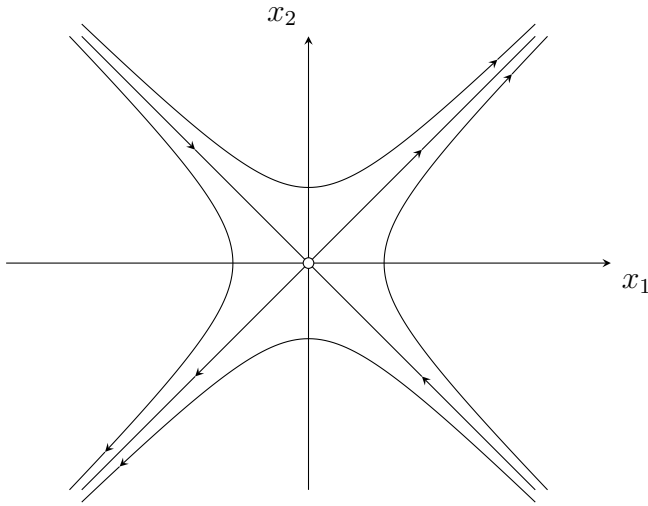
We obtain the following classification of fixed points:



The classification can be obtained by using the following equations

$$\lambda_{1,2} = \frac{1}{2} \left(\tau \pm \sqrt{\tau^2 - 4\Delta} \right), \quad \Delta = \lambda_1 \lambda_2, \tau = \lambda_1 + \lambda_2$$

$\Delta < 0$: The eigenvalues are real and have opposite sign \rightarrow saddle point



If $\Delta > 0$ the eigenvalues are either real with the same sign (nodes) ($\tau^2 - 4\Delta > 0$) or complex conjugate (spirals and centers, $\tau^2 - 4\Delta < 0$)

$\tau < 0$: Both eigenvalues have negative real parts \rightarrow stable spirals

$\tau > 0$: unstable nodes and spirals

$\tau = 0$: stable

$\Delta = 0$: At least one of the eigenvalues is zero \rightarrow origin is not an isolated fixed point

Phase plane: From now on we consider non-linear two-dimensional systems

Phase-Portrait: Vectorfield:

$$\underline{x}_1 = f_1(x_1, x_2)$$

$$\underline{x}_2 = f_2(x_1, x_2)$$

$$\text{or } \dot{\underline{x}} = \underline{f}(\underline{x})$$

where $\underline{x} = (x_1, x_2)$ and $\underline{f}(\underline{x}) = (f_1(\underline{x}), f_2(\underline{x}))$

A solution $\underline{x}(t)$ of (*) corresponds to a trajectory in the 2D phaseplane

Typically (*) cannot be solved for non-linear systems. One way to approach the equation (*) is numerical, e.g. the Runge-Kutta method

$$\underline{x}_{n+1} = \underline{x}_n + \frac{1}{6} (\underline{k}_1 + 2\underline{k}_2 + 2\underline{k}_3 + \underline{k}_4) + \mathcal{O}((\Delta t)^5)$$

where

$$\begin{aligned}\underline{k}_1 &= f(\underline{x}_n) \Delta t & \underline{k}_2 &= f\left(\underline{x}_n + \frac{1}{2}\underline{k}_1\right) \Delta t \\ \underline{k}_3 &= f\left(\underline{x}_n + \frac{1}{2}\underline{k}_2\right) \Delta t & \underline{k}_4 &= f(\underline{x}_n + \underline{k}_3) \Delta t\end{aligned}$$

Example: We consider the system

$$\dot{x} = x + e^{-y} \quad \dot{y} = -y$$

Fixed point: $\dot{x} = 0, \dot{y} = 0 \Rightarrow y = 0; x = -1$ corresponds to a fixed point

The solution of $\dot{y} = -y$ is given by $y(t) = y_0 e^{-t}$

$\underset{t \rightarrow \infty}{\rightsquigarrow} y(t) = 0 \underset{t > 1}{\rightsquigarrow} \dot{x} = x + 1$ This equation has exponentially growing solution, which indicates, that the fixed point is unstable.

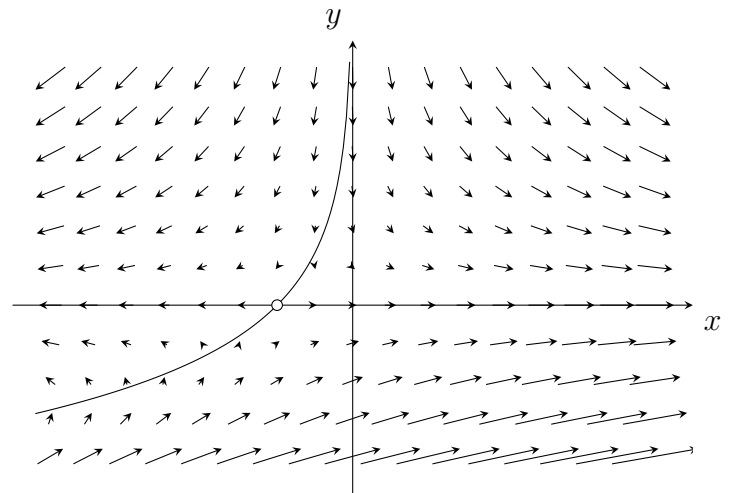
The phaseportrait can be constructed by using the following consideration:

- 1) We consider $y_0 = 0 \rightsquigarrow \dot{y} = 0$ for all times
- 2) To sketch the phase space it is useful to plot the mill lines, i.e. the curves where either $\dot{x} = 0$ or $\dot{y} = 0$.

$\dot{y} = 0 \rightsquigarrow$ horizontal flow

$\dot{x} = 0 \rightsquigarrow$ vertical flow.

We have $x + e^{-y} = 0 \rightsquigarrow y = \ln\left(-\frac{1}{x}\right)$



Existence, uniqueness and topological consequences

Theorem: Consider the initial value problem $\dot{x} = f(x); x(0) = x_0$. Suppose that f is continuous and that all its partial derivatives $\frac{\partial f_i}{\partial x_j}$, $i, j = 1, 2, \dots, n$ are continuous for x in some open connected set $D \in \mathbb{R}^n$. Then for $x_0 \in D$, the initial value problem has a solution $x(t)$ on some time interval $] - \tau, \tau[$ about $t = 0$, and the solution is unique.

Remark:

- 1) The theorem implies that the trajectories don't intersect.
- 2) The Poincaré-Bendixson theorem states, that if a trajectory is confined to a closed bounded region, then the trajectory must eventually approach a closed orbit.

Fixed points and linearization

Linearization: Approximation of the phase portrait near a fixed point by a corresponding linear system.

Consider:

$$\begin{aligned} \dot{x} &= f(x, y) & f(x^*, y^*) &= 0 = g(x^*, y^*) \\ \dot{y} &= g(x, y) & u &= x - x^*; v = y - y^* \end{aligned}$$

$\dot{u} = \dot{x} = f(x^* + u, y^* + v) = f(x^*, y^*) + u\partial_x f + v\partial_y f + \mathcal{O}(u^2, v^2, uv)$ analogous for \dot{v} .

Therefore the linearized system is given by

$$\begin{pmatrix} \dot{u} \\ \dot{v} \end{pmatrix} = A \begin{pmatrix} u \\ v \end{pmatrix} \quad \text{where} \quad A = \begin{pmatrix} \partial_x f & \partial_y f \\ \partial_x g & \partial_y g \end{pmatrix}$$

Remark: The Jacobian is evaluated at x^*, y^* .

2.3 Random Walks on a lattice

We consider a random walker on a 1-D lattice. The walker moves to the right (left) with probability p ($q = 1 - p$). The probability distribution $P(x)$ evolves according to the recursion relation

$$P_N(x) = pP_{N-1}(x-1) + qP_{N-1}(x+1)$$

The solution can be obtained from the following consideration:

The probability to move r steps to the right is given by

$$\Pi(r) = \underbrace{\binom{N}{r}}_{\substack{\uparrow \\ \# \text{ possible trajectories}}} \cdot \underbrace{p^r q^{N-r}}_{\substack{\uparrow \\ \text{probability of a given trajectory}}}$$

If we now use Stirling's approximation, i.e. $N! \sim \sqrt{2\pi N} \left(\frac{N}{e}\right)^N$, we get:

$$\begin{aligned} \Pi(r) &\sim \frac{1}{\sqrt{2\pi N}} \left(\frac{r}{N}\right)^{-r-\frac{1}{2}} \left(\frac{N-r}{N}\right)^{-N+r-\frac{1}{2}} p^r q^{N-r} \\ &= \frac{1}{\sqrt{2\pi N}} \exp\left(-\left(r + \frac{1}{2}\right) \ln\left(\frac{r}{N}\right) - \left(N - r + \frac{1}{2}\right) \ln\left(\frac{N-r}{N}\right) + r \ln(p) + (N-r) \ln(q)\right) \end{aligned}$$

Now, assuming that $1 \ll y \ll Np$, where $y = r - Np$, we get

$$\Pi(r) \approx \frac{1}{\sqrt{2\pi Npq}} \exp\left(-2 \frac{(r - Np)^2}{Npq}\right)$$

Considering that the displacement x is given by $x = 2r - N$ we have

$$P(x) \approx \frac{1}{\sqrt{2\pi Npq}} \exp\left(-\frac{(x - N(p - q))^2}{2Npq}\right)$$

This is a gaussian with mean $\mu = N(p - q)$ & $\sigma = \sqrt{Npq}$

Discrete time random walks are often not appropriate in describing nature since time is a continuous variable.

In the continuous time version of the random walk, the time evolution is given by:

$$\frac{\partial P_n}{\partial t} = \underset{\text{gain}}{P_{n+1}} - \underset{\text{loss}}{2P_n} + \underset{\text{gain}}{P_{n-1}} \quad (*)$$

where we have considered symmetric hopping rates (not probabilities!) $s = 1$ to the left and to the right. Eq. (*) is called Master-equation.

In order to determine the solution of the problem, we consider a slightly more general master-equation:

$$\frac{\partial P_n}{\partial t} = \gamma (P_{n-1} + P_{n+1}) - 2P_n$$

Initial condition: $P_n(t = 0) = \delta_{n,0}$. We now introduce the discrete Fourier-transform:

$$P(k, t) = \sum_{n=-\infty}^{\infty} P_n(t) e^{ikn}$$

and multiply each master-equation for a given n by e^{ikn} .

The sum of all Master-equations is given by:

$$\begin{aligned} \frac{\partial P(k, t)}{\partial t} &= \sum_{n=-\infty}^{\infty} e^{ikn} \frac{\partial P_n}{\partial t} = \sum_{n=-\infty}^{\infty} e^{ikn} (\gamma(P_{n-1} + P_{n+1}) - 2P_n) \\ &= \left(\gamma(e^{ik} + e^{-ik}) - 2 \right) P(k, t) \quad (**) \end{aligned}$$

Initial condition: $P(k, 0) = \sum_n \underbrace{P_n(0)}_{\delta_{n,0}} e^{ikn} = 1$ Eq. (**) can be solved easily:

$$\int_1^{P(k,t)} \frac{dP'}{P'} = \int_0^t [2\gamma \cos(k) - 2] dt \rightsquigarrow \ln(P(k, t)) = 2(\gamma \cos(k) - 1)t$$

or:

$$P(k, t) = \exp(2(\gamma \cos(k) - 1)t) = \sum_{n=-\infty}^{\infty} P_n(t) e^{ikn}$$

Generating function of the modified Bessel-function

$$e^{z \cos(k)} = \sum_{n=-\infty}^{\infty} I_n(z)$$

Comparieing to the solution of $P(k, t)$ we get:

$$P(k, t) = e^{-2t} e^{2\gamma t \cos(k)} \Rightarrow P_n(t) = I_n(2\gamma t) e^{-2t}$$

We now consider the transition to continuous space. We first notice that

$$\begin{aligned} f'(x) &= \lim_{\Delta x \rightarrow 0} \frac{f(x + \Delta x) - f(x)}{\Delta x} \quad \text{and} \\ f''(x) &= \lim_{\Delta x \rightarrow 0} \frac{f'(x + \Delta x) - f'(x)}{\Delta x} \\ &= \lim_{\Delta x \rightarrow 0} \frac{f(x + 2\Delta x) - f(x + \Delta x) - f(x + \Delta x) + f(x)}{(\Delta x)^2} \end{aligned}$$

If we now identify $f(x + 2\Delta x)$ by P_{n+1} and consider $\Delta x = 1$ we get by comparison:

$$\frac{\partial P(x, t)}{\partial t} = \frac{\partial^2 P(x, t)}{\partial x^2}$$

This partial differential equation (PDE) is called **diffusion equation**. It is more generally given by:

$$\frac{\partial P(x, t)}{\partial t} = D \frac{\partial^2 P(x, t)}{\partial x^2}$$

This equation is solved by Fouriertransform, where

$$\begin{aligned} P(k, t) &= \int_{-\infty}^{\infty} P(x, t) e^{ikx} dx; P(x, t) = \frac{1}{2\pi} \int_{-\infty}^{\infty} P(k, t) e^{-ikx} dk \\ &\leadsto \frac{\partial P(k, t)}{\partial t} = -Dk^2 P(k, t) \Rightarrow P(k, t) = P(k, 0) e^{-k^2 Dt} \end{aligned}$$

using $P(x, t = 0) = \delta(x) \leadsto P(k, 0) = 1$ $P(k, t) = e^{-k^2 Dt}$

Inverting the Fouriertransform we obtain:

$$P(x, t) = \frac{1}{2\pi} \int e^{-Dk^2 t} e^{-ikx} dk = \frac{1}{\sqrt{4\pi Dt}} e^{-\frac{x^2}{4Dt}}$$

Central limit theorem (CLT)

We notice that the different kinds of random walk **converge** to a gaussian, independent of the details of the single step distribution. This result is related to the CLT.

We consider a 1-D random walk in discrete time with a displacement X_N drawn from continuous distribution $p(x)$. The displacement $y_N = \sum_{n=1}^N x_n$ in the large n -limit is accordingly to the CLT given by:

$$P_N(y) = \frac{1}{\sqrt{2\pi N\sigma^2}} e^{-\frac{(y - N\langle x \rangle)^2}{2N\sigma^2}}$$

where $\sigma^2 = \langle x^2 \rangle - \langle x \rangle^2$.

The necessary conditions for the CLT are the following

(i) $\langle x \rangle$ & $\langle x^2 \rangle$ are finite

(ii) The first two moments of the **initial** spatial distribution are finite

(iii) The steps are independent

We immediately see that:

$$\langle y_n \rangle = N \langle x \rangle \text{ and } \text{var}(y_N) = N \sigma^2$$

The CLT can be motivated from the following consideration: $P_N(Y)$ can be obtained from the recursion relation:

$$P_N(Y) = \int_{-\infty}^{\infty} P_{N-1}(y') p(y - y') dy'$$

(Chapman-Kolmogorov-equation)

The Chapman-Kolmogorov equation is a convolution which leads to the recurrence $P_N(k) = P_{N-1}(k)p(k)$ in Fourier-space. The recurrence is solved by $P_N(k) = P_0(k)[p(k)]^N$. For $P_0(x) = \delta_{x,0}$ we get $P_0(k) = 1$ & $P_N(k) = [p(k)]^N$. The distribution in real space is then given by

$$P_N(y) = \frac{1}{2\pi} \int_{-\infty}^{\infty} [p(k)]^N e^{-iky} dk$$

We now find that

$$\begin{aligned} p(k) &= \int_{-\infty}^{\infty} p(x) e^{ikx} dx = \int_{-\infty}^{\infty} p(x) \left[1 + ikx - \frac{1}{2}k^2x^2 + \mathcal{O}(x^3) \right] dx \\ &= 1 + ik\langle x \rangle - \frac{1}{2}k^2\langle x^2 \rangle + \dots \end{aligned}$$

The first two moments exist by assumption. Therefore, we get:

$$\begin{aligned} P_N(y) &\approx \frac{1}{2\pi} \int_{-\infty}^{\infty} \left[1 + ik\langle x \rangle - \frac{1}{2}k^2\langle x^2 \rangle \right]^N e^{-iky} dk \\ &= \frac{1}{2\pi} \int_{-\infty}^{\infty} \exp \left[N \ln \left(1 + ik\langle x \rangle - \frac{1}{2}k^2\langle x^2 \rangle \right) \right] e^{-iky} dk \\ &\underset{\mathcal{O}(\langle x \rangle^2, \langle x^2 \rangle)}{\approx} \frac{1}{2\pi} \int_{-\infty}^{\infty} \exp \left[N \left(ik\langle x \rangle - \frac{k^2}{2} (\langle x^2 \rangle - \langle x \rangle^2) \right) \right] e^{-iky} dk \end{aligned}$$

From which follows the assumption by completing the square.

Natural boundaries

So far we discussed only processes which have been defined on infinite lattices. For many applications however, the boundaries play an important role. Here, we discuss the boundaries for a stochastic process, which is described by the following Master-equation.

$$\dot{p}_n = r(n+1)p_{n+1} + g(n-1)p_{n-1} - \{r(n) + g(n)\} p_n$$

where $g(n), p(n)$ are simple analytic functions of the position. Next to the bulk equation, the dynamics has to be specified at the boundaries, e.g.

$$\dot{p}_0 = r(1)p_1 - g(0)p_0; \quad \dot{p}_N = g(N-1)p_{N-1} - r(N)p_N$$

The boundaries are called natural if the bulk equation is valid down to $n = 1$ and $r(0)$ and similar for N . The latter condition makes shure that if one considers $p_N(0)$ for $n < 0$ $p_n(t)$ remains zero at all times for negative values of n .

Example: The linear one-step process with natural boundary conditions:

$$\dot{p}_n = a(r + (n+1))p_{n+1} + b(g + (n-1))p_{n-1} - \{a(r+n) + b(g+n)\} p_n$$

with the condition $p_n(0) = \delta_{nm}$ & $a \neq 0; b \neq 0, a \neq b$

Multiplikation by z^n and summation over n gives:

$$\begin{aligned} \frac{\partial F(z, t)}{\partial t} &= \sum_{n=0}^{\infty} \dot{p}_n(t) z^n = a \sum (z^{n-1} - z^n) (r+n)p_n + b (z^{n+1} - z^n) (g+n)p_n \\ &= ar \left(\frac{1}{z} - 1 \right) F + a(1-z) \frac{\partial F}{\partial z} + bg(z-1)F + b(z^2 - z) \frac{\partial F}{\partial z} \\ &= (1-z)(a-bz) \frac{\partial F}{\partial z} + (1-z) \left(\frac{ar}{z} - bg \right) F \end{aligned}$$

Solution of the equations by the method of characteristics. The characteristic curves in the (z, t) -plane are given by:

$$-dt = \frac{dz}{(1-z)(a-bz)} \quad (*)$$

The characteristics are curves along which the information about the solution propagates. Integration of the equation above leads to:

$$\frac{1-z}{a-bz} e^{(b-a)t} = C \quad \text{which is an integration constant}$$

The variation of the F along the characteristic curve is given by:

$$\begin{aligned} -\frac{dz}{a-bz} &= \frac{d \log(F)}{\frac{ar}{z} - bg} \rightsquigarrow F(z, t) = \text{const } z^{-r} (a - bg)^{r-g} \\ &= z^{-r} (a - bz)^{r-g} \Omega \left(\frac{1-z}{a-bz} e^{(b-a)t} \right) \end{aligned}$$

Initial condition: $p_n(0) = \delta_{nm} \Rightarrow F(z, 0) = z^m$

$$\begin{aligned} \Rightarrow z^m &= z^{-r} (a - bz)^{r-g} \Omega \left(\frac{1-z}{a-bz} \right) \\ \Rightarrow \Omega \left(\frac{1-z}{a-bz} \right) &= z^{m+r} (a - bz)^{g-r} \end{aligned}$$

By defining $\frac{1-z}{a-bz} = \eta$ we get:

$$\Omega(\eta) = \left(\frac{a\eta - 1}{b\eta - 1} \right)^{m+r} \left(\frac{b-a}{b\eta - 1} \right)^{a+r}$$

and therefore (replacing η again by $\frac{1-z}{a-bz} e^{b-a}t = \frac{1-z}{a-bz} \epsilon$)

$$F(z, t) = z^m \left[\frac{a\epsilon - b + a(1-\epsilon)z^{-1}}{a-b} \right]^{m+r} \left[\frac{a-b\epsilon - b(1-\epsilon)z}{a-b} \right]^{-m-g}$$

Now introducing the boundary:

Lower boundary $n = 0$ such that negative values or r_n & g_n are avoided.

$\rightsquigarrow m \geq 0 \rightsquigarrow F(z)$ has positive powers of z

$\rightsquigarrow r = 0$ which implies natural boundaries

case (i) : Range $[0, \infty[\rightsquigarrow g_n = b(n+g) \geq 0 \forall n \geq 0$

\Rightarrow either $b > 0$ & $g \geq 0$ or $g_n = \beta \geq 0$

$$\Rightarrow F(z, t) = (a-b)^g [a(1-\epsilon) + (a\epsilon - b)z]^m [a-b\epsilon - b(1-\epsilon)z]^{-m-g} \quad (i)$$

$$\text{or } F(z, t) = [1 - \epsilon + \epsilon z]^m \exp \left[-\frac{\beta}{a} (1-\epsilon)(1-z) \right] \quad (ii)$$

Analogous, we get some conditions for a, b, g, r for finite intervals.

Artificial boundaries

- Infinite possibilities
- "pure boundaries" Boundary equations where only the endsite has to be specified
- **Reflecting boundary conditions:** Probability is conserved
- **Absorbing boundary conditions:** Probability is not conserved

Example

$$\begin{aligned}\dot{p}_n &= p_{n-1} + p_{n+1} - 2p_n \quad (n \geq 1) \\ \dot{p}_0 &= p_1 - 2p_0\end{aligned}$$

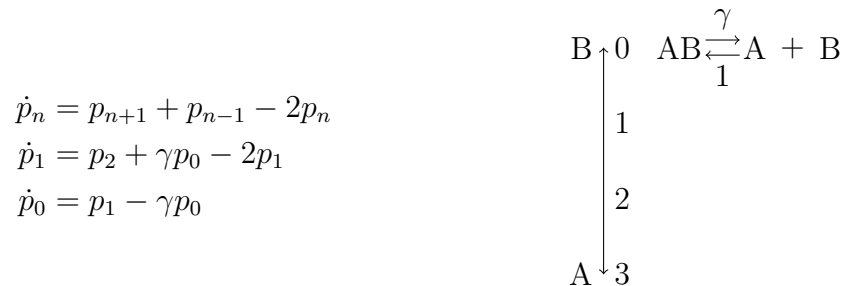
Here, the probability is not conserved since $\frac{d}{dt} \left(\sum_{n=0}^{\infty} p_n \right) = \sum_{n=0}^{\infty} \dot{p}_n = -p_0$
 Probability conservation by introducing an extra site

$$p_* = 1 - \sum_{n=0}^{\infty} p_n \rightsquigarrow \dot{p}_* = p_0$$

Average survival time:

$$\int_0^{\infty} t \dot{p}_* dt = - \sum_{n=0}^{\infty} \int_0^{\infty} t \dot{p}_n dt = \sum_{n=0}^{\infty} \int_0^{\infty} p_n dt$$

Example: Diffusion controlled chemical reaction



Reflection principle

Random walker with absorbing boundary at $n = 0$

$$\begin{aligned}\leadsto \dot{p}_n &= p_{n+1} + p_{n-1} - 2p_n \quad (n > 1) \\ \dot{p}_1 &= p_2 - p_1\end{aligned}$$

Ansatz: Solution of a Master-equation with initial condition

$$p_n(0) = \delta_{n,m} - \delta_{n,-m} \text{ and restriction to } p_n(t) \text{ for } n > 0$$

First-passage properties of RW

- Important for many biological processes including the firing of neurons or signaling processes.

Here we briefly summarise first-passage properties of random walks. We first ask the question: Does a random walk, that starts at the origin of an infinite lattice at $t = 0$ eventually return to its starting point?

The answer is the following (d spatial dimension):

$d \leq 2$: The random walk returns with probability 1 (recurrent random walk)

$d > 2$: There is a finite probability that the random walker never returns (transient random walk)

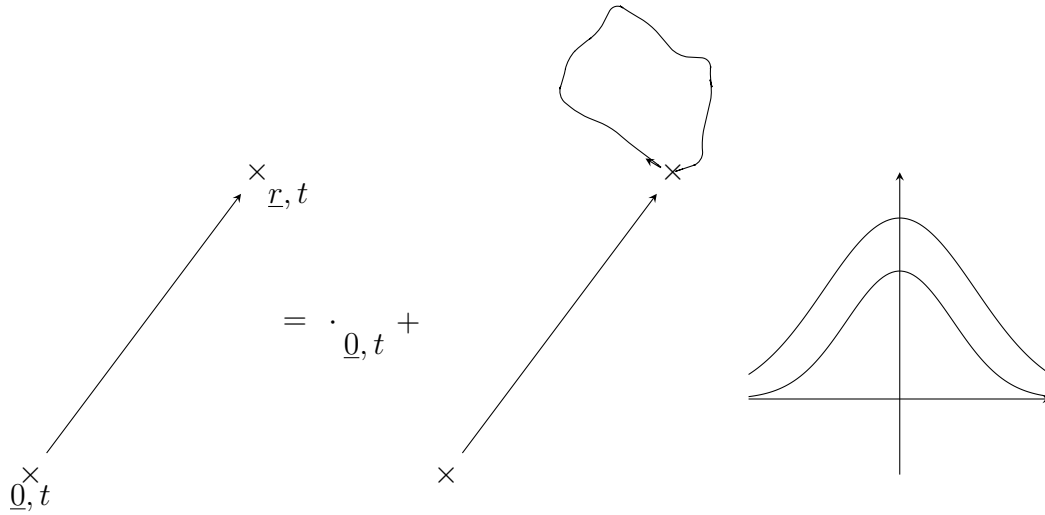
This can be understood from a simple scaling argument. The region that is explored by the random walk grows as $l \sim \sqrt{Dt}$. The number of visited sites is obviously $\sim t$. Therefore the density of visited sites in the explored region behaves as $\rho \sim \frac{t}{l^d} \sim t^{1-\frac{d}{2}}$

The density is obviously decreasing for $d > 2$.

We now give a more detailed discussion of the first passage probability $F(\underline{r}, t)$ which is related to the recurrence or transience of random walks.

We first note that:

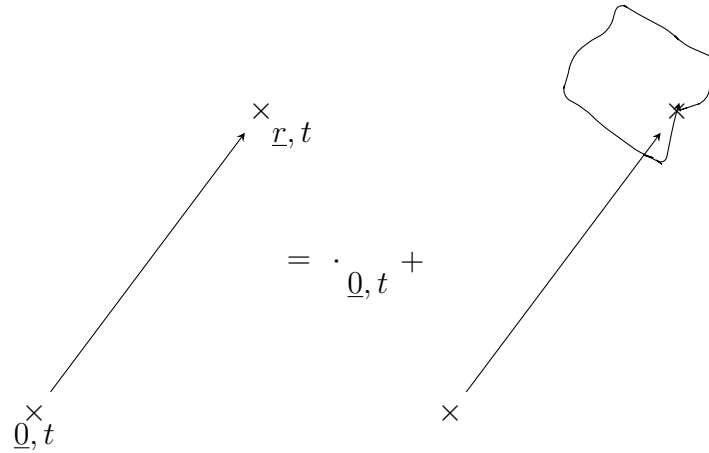
$$P(\underline{r}, t) = \int_0^t F(\underline{r}, t') \underline{P}(\underline{0}, t - t') dt' + \delta_{I,0} \delta(t)$$



- $\delta_{r,0}$ denotes the kronecker δ , $\delta(t)$ the Dirac-Delta Function
- $P(r, t)$ the probability that a given site at r is occupied at time t
- $F(r, t)$ the probability that the random walk **first** reaches r at time t .

The validity of the equation can be occupied from the following decomposition:

$F(r, t')$ denotes the probability that the random walk reaches r first at time t' . Then the probability $P(r, t)$ is given by the probability that a first visit at time t' is followed by a loop during $t - t'$. In terms of a diagrammatic expression this decomposition can be visualized by



lik in a Chapman-Kolmogorov equation the expression above involves a convolution. Since the lower boundary is given by 0 rather than $-\infty$ we Laplace- instead of Fourier-transform.

The Laplace transforms are given by:

$$P(\underline{r}, s) = \int_0^\infty P(\underline{r}, t) e^{-st} dt \quad \& \quad F(\underline{r}, s) = \int_0^\infty F(\underline{r}, t) e^{-st} dt$$

Applying the Laplace-Transform the equation above, we get:

$$\begin{aligned} P(\underline{r}, s) &= F(\underline{r}, s)P(\underline{0}, s) + \delta_{\underline{r},0} \\ &\leadsto F(\underline{r}, s) = \frac{P(\underline{r}, s) - \delta_{\underline{r},0}}{P(\underline{0}, s)} \end{aligned}$$

From now on we consider $\underline{r} = 0$. The eventual return probability is given by:

$$R = \int_0^\infty F(\underline{0}, t) dt; \quad \text{i.e. the probability that the walk returns at any time}$$

We now specify our considerations for a lattice random walk in continuous time. Then we have for the occupation of the origin:

$$P(t) = [I_0(2t)e^{-2t}]^d \simeq \frac{1}{(4\pi t)^{\frac{d}{2}}} \quad t \rightarrow \infty$$

In order to compute R we first recall that:

$$f(s) = \int_0^\infty t^{-r} e^{-st} dt \quad \text{for } f(t) = t^{-r}$$

By substituting $x = st$ we get:

$$f(s) = s^{\mu-1} \int_0^\infty x^{-\mu} e^{-x} dx = \underbrace{\Gamma(1-\mu)}_{\text{gamma-function}} s^{\mu-1}$$

using the definition of the Γ -Function:

$$\Gamma(z) = \int_0^\infty x^{z-1} e^{-x} dx$$

We use this relation at low dimensions, where the entire probability distribution $P(x, t)$ is dominated by the algebraic tail in the large t limit, which in turn governs the small s asymptotics of $P(s)$. By now using $\Gamma\left(\frac{1}{2}\right) = \sqrt{\pi}$ and the result above, we get $P(s) \simeq \frac{1}{\sqrt{4s}}$ and therefore: $F(0, s) \equiv F(s) \simeq 1 - \sqrt{4s}$. By definition, we have $R = F(0) = 1$ which implies that the 1D random walk is recurrent!

In order to get the asymptotic behaviour of $F(t)$, we apply the following trick:

$$\frac{dF(s)}{ds} = - \int_0^\infty F(t) e^{-st} dt = \frac{1}{\sqrt{s}}$$

By using the fact, that the Laplace transform of $t^{-\mu}$ is given by $\Gamma(1-\mu)s^{\mu-1}$ we obtain that:

$$tF(t) \simeq (\pi t)^{-\frac{1}{2}} \quad \text{or} \quad F(t) \simeq \frac{1}{\sqrt{\pi}} t^{\frac{3}{2}}$$

The case $d = 2$ is more subtle since the time integral diverges only logarithmically for $t \rightarrow \infty$. In this case, we get:

$$F(s) \simeq 1 + \frac{4\pi}{\ln(s)} \quad (\text{for } s \rightarrow 0)$$

Again the random walk is recurrent since $\lim_{s \rightarrow 0} F(s) = R = 1$.

The asymptotic behaviour is obtained from

$$\int_0^\infty tF(t) e^{-st} dt \simeq \frac{4\pi}{s (\ln(s))^2} \quad \text{when } s \rightarrow \infty \rightsquigarrow_{t \rightarrow \infty} F(t) \simeq \frac{4\pi}{t [\ln(t)]^2}$$

The case $d = 3$:

In this case the integral $P(s) = \int_1^\infty \frac{1}{(4\pi t)^{\frac{3}{2}}} e^{-st} dt$ converges

$$-\frac{dP(s)}{ds} = \int_0^\infty \frac{1}{(4\pi)^{\frac{3}{2}}} \frac{e^{-st}}{t^{\frac{1}{2}}} dt = \frac{1}{8\pi} \frac{1}{\sqrt{s}}$$

$$\Rightarrow P(s) = P(0) - \frac{\sqrt{s}}{4\pi}$$

$$\rightsquigarrow F(s) = 1 - \frac{1}{P(s)} \simeq 1 - \frac{1}{P(0)} - \frac{\sqrt{s}}{4\pi P(0)^2} = R - \frac{(1-R)^2 \sqrt{s}}{4\pi}$$

$$R = F(0) = 1 - \frac{1}{P(0)}$$

This result implies that $R \neq 1$ such that the random walk is transient.
Asymptotic form:

$$F(t) = \frac{(1-R)^2}{8\pi^{\frac{3}{2}}} \frac{1}{t^{\frac{3}{2}}}$$

2.4 Reaction-Diffusion Models

In this chapter we discuss the interplay between reaction and diffusion.

Turing ('52): A reaction-diffusion system can generate spatial-temporal patterns.

Gierer&Meinhardt: Realization by an antagonistic pair of molecular species, a slowly diffusing chemical activator and a quickly moving inhibitor

2.4.1 Protein-Concentration-Gradients

Concentration gradients play a crucial role in spacial regulation or patterning (Morphogen: Signaling molecules, cellular responses depend on its concentration)

Typical scenario

Morphogen is distributed from a local source in the cell, diffuses away from the source and degrades. Above a critical threshold expression of specific genes takes place.

The regulation via morphogen was first discussed in the context of embryonic development (morphogenesis) but there is evidence that the intracellular gradients play a role in many cellular processes.

Spatially distributed signaling cascades

System:

- activating enzyme located in the cell membrane
- deactivating enzyme freely diffusing in the cytoplasm
- 1D system (e.g. cylindrical bacteria cell)
- here: kinase located at $x = 0$, generating a phosphorylated protein at rate ν_+ (activated protein")

- The phosphatase deactivates the protein at rate $\nu_- = k_- c^*$
 c^* is the concentration of the activated protein.

The time evolution of c^* is described by the following set of equations:

$$\frac{\partial c^*(x, t)}{\partial t} = D \frac{\partial^2 c^*(x, t)}{\partial x^2} - k_- c^*(x, t)$$

Boundary equations:

$$\begin{array}{ccc} -D \frac{\partial c^*}{\partial x} \Big|_{x=0} & \overset{\text{source } x=0}{=} \nu_+ & \frac{\partial c^*}{\partial x} \Big|_{x=L} = 0 \\ \text{diffusive current and source} & & \text{no diffusive current is} \\ \text{term are balanced at } x=0 & & \text{crossing the boundary at } x=L \end{array}$$

We can easily get the stationary state of the system given by

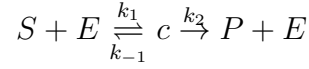
$$c^*(x) = c^*(0) \cdot \left(\frac{e^{\frac{x}{\lambda}} + e^{2\frac{x}{\lambda}} + e^{-\frac{x}{\lambda}}}{1 + e^{2\frac{x}{\lambda}}} \right); \quad \lambda = \sqrt{\frac{D}{k_-}}$$

Typically the exponential decay is rather steep, too steep to transport a signal over long distances \rightarrow cascade of protein modification cycles.

We denote the level of activated (deactivated) protein at the n th cascade c_n^* (c_n) and assume that the concentration at each cascade level is fixed $c_n^{tot} = c_n^* + c_n$.

Box: Michaelis-Menten-Kinetics

We consider the basis reaction scheme. Enzyme E is converting a substrate S into a complex C . This breaks down into a product P and the enzyme E .



Now using $S = [S]$ and similar, we get:

$$\begin{aligned}\frac{ds}{dt} &= k_{-1}c - k_1se \\ \frac{de}{dt} &= (k_{-1} + k_2)c - k_1se \\ \frac{dc}{dt} &= -(k_{-1} + k_2)c + k_1se \\ \frac{dp}{dt} &= k_2c\end{aligned}$$

The total concentration of the enzyme is constant; i.e. $e + c = e_0 = \text{const.}$
We can eliminate e using the conservatin of the enzyme:

$$\frac{dc}{dt} = -(k_{-1} + k_2)c + k_1s(e_0 - c) = -(k_{-1} + k_1s + k_2)c + k_1se_0$$

We now assume that the enzyme concentration is low, and therefore, that $s \approx \text{const.}$

We then get in the stationary state

$$c = \frac{k_1se_0}{(k_{-1} + k_1s + k_2)}$$

The production rate ist than simply given by

$$\begin{aligned}\frac{dp}{dt} &= k_2e_0 \frac{k_1s}{(k_{-1} + k_2 + k_1s)} = k_2e_0 \frac{s}{s + k_M} \\ \text{where } k_M &= \frac{k_{-1} + k_2}{k_1} \quad (\text{Michaelis constant})\end{aligned}$$

We get:

$$\begin{aligned}\frac{\partial c_1^*}{\partial t} &= D \frac{\partial^2 c_1^*}{\partial x^2} - \nu_1^-(x, t) \\ \frac{\partial c_n^*}{\partial t} &= D \frac{\partial^2 c_n^*}{\partial x^2} + \nu_n^+(x, t) - \nu_n^-(x, t) \quad n = 2, \dots, N\end{aligned}$$

where ν_n^+, ν_n^- are the activation and deactivation rates, respectively

Boundary conditions

$$\begin{aligned}-D \frac{\partial c_1^*}{\partial x} \Big|_{x=0} &= \nu_1^+ \frac{\partial c_1^*}{\partial x} \Big|_{x=L} &= 0 \\ \frac{\partial c_n^*}{\partial x} \Big|_{x=0} &= 0 = \frac{\partial c_n^*}{\partial x} \Big|_{x=L}, &n = 2, 3, \dots, N\end{aligned}$$

Assuming Michaelis-Menten Kinetics for the cascade, we have

$$\begin{aligned}\nu_n^- &= V_n^- \frac{c_n^*(x, t)}{k_n^- + c_n^*(x, t)}; \quad \nu_1^+ = V_1^+ \frac{c_1^{\text{tot}} - c_1^*(0, t)}{k_1 + c_1^{\text{tot}} - c_1^*(0, t)} \\ \nu_n^+ &= V_n^+ c_{n-1}^*(x, t) \frac{c_n^{\text{tot}} - c_n^*(x, t)}{k_n^+ c_n^{\text{tot}} - c_n^*(x, t)} \quad n = 2, 3, \dots, N\end{aligned}$$

We assume now that all parameters are independent of the cascade level

$$\begin{aligned}k_n^- &= k^-, V_n^- = V^- & c_n^{\text{tot}} &= c^{\text{tot}} & n = 1, 2, \dots, N \\ \text{and } k_n^+ &= k^+; & v_n^+ c_{\text{tot}} &= v^+ & \text{for } n = 2, 3, \dots, N\end{aligned}$$

We assume small concentrations (linear Michaelis-Menten regime)

Nondimensionalising the equations by setting

$$C_n = \frac{c_n^*}{c^{\text{tot}}}; \quad x' = \sqrt{\frac{k_-}{D}} x; \quad t' = k_+ t; \quad \gamma = \frac{k'_-}{k'_+}; \quad \text{with } k'_\pm = \frac{V_\pm}{k_\pm}$$

and dropping primes for x, k and t gives

$$\begin{aligned}\partial_t C_1 &= \gamma \frac{\partial^2 C_1}{\partial x^2} - \gamma C_1 \\ \partial_t C_n &= \gamma \partial_x^2 C_n - \gamma C_n + (1 - C_n) C_{n-1}\end{aligned}$$

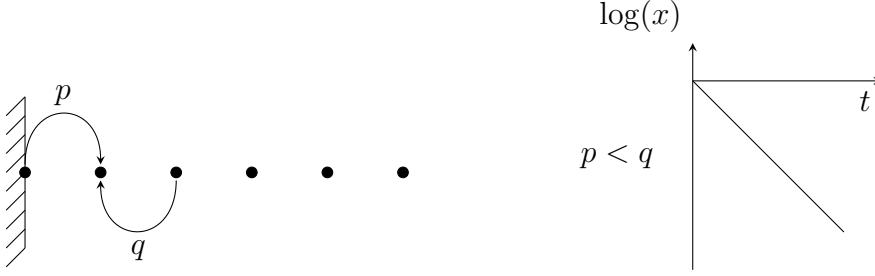
Boundary equations

$$\begin{aligned}
-\partial_x C_1|_{x=0} &= \nu(1 - C_1(x=0)); & D\partial_x C_1|_{x=L} &= 0 \\
\partial_x C_n|_{x=0} &= 0 = \partial_x C_n|_{x=L} & n &= 2, 3, \dots, N \\
\nu &= \frac{\nu_1^+}{k_1^+} \sqrt{\frac{1}{Dk_{-1}}}
\end{aligned}$$

The important parameter is γ , i.e. the ratio between deactivation and activation rates

(i) $\gamma < 1$ The signal propagates into the system

(ii) $\gamma > 1$ Localisation at the membrane



The stationary state of the system can be obtained for $\gamma > 1$. As in the single level model we get

$$C_1(x) = C_1(0)e^{-x} \quad (\text{boundary control})$$

The approximate recurrence relation (neglecting $C_n C_{n-1}$) then reads:

$$\gamma \frac{d^2 C_n}{dx^2} - \gamma C_n + C_{n-1} = 0$$

This can be solved by the polynomial ansatz

$$C_n(x) = \left(\sum_{m=0}^{n-1} Q_n^{(m)} x^m \right) e^{-x} \quad \text{for } \gamma > 1$$

For $\gamma < 1$ this solution breaks down near $x = 0$. Nevertheless we get

$$C_n(x) \approx \frac{C_1(0)}{(n-1)!(2\gamma)^{n-1}} x^{n-1} e^{-x}$$

for the tail of the profile

2.4.2 Theory of Turing Pattern Formation

Two-component system in two dimensions. Chemical concentrations $u(\underline{x}, t)$ and $v(\underline{x}, t)$ with $\underline{x} \in \mathbb{R}^2$ $\left(= \begin{pmatrix} x \\ y \end{pmatrix} \right)$, $t \in \mathbb{R}^+$. We assume an area Ω where $0 \leq x \leq L$, $0 \leq y \leq L$.

The standard reaction-diffusion (RD) model takes the form:

$$\begin{aligned} \frac{\partial u}{\partial t} &= D_u \nabla^2 u + f(u, v) \\ \frac{\partial v}{\partial t} &= D_v \nabla^2 v + g(u, v) \end{aligned}$$

The nonlinear functions f, g describe the chemical reactions, D_v, D_u the diffusion for the two species. No flux boundary conditions

$$\underline{n} \cdot \underline{\nabla} u = 0 = \underline{n} \cdot \underline{\nabla} v \quad \text{for } \underline{x} \in \partial\Omega$$

\underline{n} denotes the outward normal on the boundary.

We assume that there exists a homogeneous stationary state (u^*, v^*) for which $f(u^*, v^*) = g(u^*, v^*) = 0$

Turing's idea: Stable stationary state in absence of diffusion, unstable in presence of diffusion. We linearize the equations (*) about the homogeneous state (u^*, v^*) by setting $U = u - u^*$, $V = v - v^*$

$$\frac{\partial}{\partial t} \begin{pmatrix} U \\ V \end{pmatrix} = \frac{\partial}{\partial t} \begin{pmatrix} U \\ V \end{pmatrix} = \mathbb{L} \begin{pmatrix} U \\ V \end{pmatrix} = \begin{pmatrix} f_u & f_v \\ g_u & g_v \end{pmatrix}_{u^*, v^*} \begin{pmatrix} U \\ V \end{pmatrix} + \begin{pmatrix} D_u & 0 \\ 0 & D_v \end{pmatrix} \begin{pmatrix} \nabla^2 U \\ \nabla^2 V \end{pmatrix}$$

with $f_x = \frac{\partial f}{\partial x}$

The general solution of the linear system is given by

$$\underline{U}(\underline{x}, t) = \sum_{\underline{k}} \underline{c}_{\underline{k}} e^{i \underline{k} \underline{x}} e^{\lambda(\underline{k}) t}$$

where $\underline{c}_{\underline{k}} e^{i \underline{k} \underline{x}}$ and $\lambda(\underline{k})$ from an eigenvalue pair.

Substituting the general solution into the linearized equation, we get

$$\left| A - D k^2 - \lambda(\underline{k}) \mathbb{1} \right| = 0$$

with

$$A = \begin{pmatrix} f_u & f_v \\ g_u & g_v \end{pmatrix}_{u^*, v^*} \quad D = \begin{pmatrix} D_u & 0 \\ 0 & D_v \end{pmatrix}$$

We obtain the following quadratic equation for λ :

$$\lambda^2 + [(D_u + D_v)k^2 - f_u - f_v] \lambda + D_u D_v k^4 - k^2 (D_v f_u + D_u g_v) + f_u g_v - f_v g_u = 0$$

In absence of diffusion ($D_u = D_v = 0$) this reduces to:

$$\lambda^2 - [f_u + g_v] \lambda + f_u g_v - f_v g_u = 0$$

Stability in absence of diffusion is obtained for

$$f_u + g_v < 0, \quad f_u g_v - f_v g_u > 0$$

Instability in the **stationary** state means that there exists a $\underline{k} \neq \underline{0}$ for which $\lambda(\underline{k}) = 0$. (stationarity of $\underline{U}(\underline{x}, t) = \underline{U}(\underline{x})$)

For $\lambda = 0$ we get:

$$D_u D_v k^4 - k^2 (D_v f_u + D_u g_v) + f_u g_v - f_v g_u = 0$$

This equation will have a positive solution for k^2 if

$$D_v f_u + D_u g_v > 0$$

Therefore, the conditions of a Turing instability are given by

$$\begin{aligned} f_u + g_v < 0 \quad f_u g_v - f_v g_u > 0 & \text{ (stability in absence of diffusion)} \\ \text{and } D_v f_u + D_u g_v > 0 & \text{ (instability in presence of diffusion)} \end{aligned}$$

Remarks: The conditions given above define the parameterspace where a Turing instability can occur.

· Note that the wave numbers are discrete in finite systems

$$|k| = \frac{\pi}{L} \sqrt{n_x^2 + n_y^2} \quad n_x, n_y \in \mathbb{Z}$$

Example: We consider the nondimensionalized RD-system

$$\begin{aligned} \frac{\partial u}{\partial t} &= D \nabla^2 u + \kappa(u + av - uv^2 - cuv) \\ \frac{\partial v}{\partial t} &= \nabla^2 v + \kappa(-u + bv + uv^2 + cuv) \end{aligned}$$

This equation has a unique homogeneous stationary state at $(u, v) = (0, 0)$
 Linearizing the equation leads to the characteristic equation:

$$\left| \begin{pmatrix} \kappa - Dk^2 & \kappa a \\ -\kappa & -\kappa - k^2 \end{pmatrix} - \lambda(k) \mathbb{1} \right| = 0$$

$$\leadsto (\kappa - Dk^2 - \lambda)(b\kappa - k^2 - \lambda) + a\kappa^2 = 0$$

For $k = 0$ (homogeneous solution)

$$\lambda^2 - (1 + b)\kappa\lambda + (b + a)\kappa^2 = 0$$

with roots:

$$\lambda = \frac{\kappa}{2} \left[(1 + b) \pm \sqrt{(1 - b)^2 - 4(b + a)} \right]$$

The fixpoint is stable for $b < -1$; $b + a > 0$

Turing instability ($k \neq 0$ for $\lambda(k) = 0$)

$$Dk^4 - \kappa k^2(Db + 1) + \kappa^2(b + a) = 0$$

$$\leadsto \left(k^2 - \frac{\kappa(Db + 1)}{2D} \right)^2 = \left(\frac{\kappa(Db + 1)}{2D} \right)^2 - \frac{\kappa^2(b + a)}{D}$$

At onset of the instability, the discriminant for k^2 vanishes

$$[\kappa(Db + 1)]^2 = 4D\kappa^2(b + a) \leadsto a = \frac{(Db - 1)^2}{4D}$$

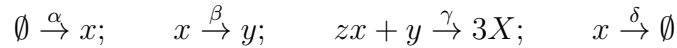
The critical wavenumber is $k_c = \frac{\kappa(Db+1)}{2D}$

Such a solution exists if $Db + 1 > 0$

2.4.3 Stochastic pattern formation

1) Turing instability in the Brusselator model

Reminder: Brusselator model is an idealized model of an idealized auto catalytic reaction, described by:



$$\frac{du}{dt} = \alpha - (\beta + 1)u + u^2v \quad (u = [x]; \gamma = \delta = 1)$$

$$\frac{dv}{dt} = \beta u - u^2v \quad (v = [y])$$

Here we consider a spatially extended version of the Brusselator model, given by the RD system

$$\begin{aligned}\frac{du}{dt} &= D_u \nabla^2 u + \alpha - (\beta + 1)u + u^2 v \\ \frac{dv}{dt} &= D_v \nabla^2 v + \beta u - u^2 v\end{aligned}$$

where D_u, D_v are the diffusion coefficients of the species x and y . As usual we linearize the system about the homogeneous steady state solution, given by $u^* = \alpha, v^* = \frac{\beta}{\alpha}$, by using the ansatz:

$$u(\underline{x}, t) = u^* + \xi(\underline{x})e^{\lambda t}; \quad v(\underline{x}, t) = v^* + \eta(\underline{x})e^{\lambda t}$$

In first order of ξ and η we get:

$$\lambda \begin{pmatrix} \xi \\ \eta \end{pmatrix} = \begin{pmatrix} \beta - 1 + D_u \nabla^2 & \alpha^2 \\ -\beta & -\alpha^2 + D_v \nabla^2 \end{pmatrix} \begin{pmatrix} \xi \\ \eta \end{pmatrix}$$

The system has eigensolutions of the form:

$$\xi(\underline{x}) = \hat{\xi}(\underline{k})e^{-i\underline{k}\underline{x}}, \quad \eta(\underline{x}) = \hat{\eta}(\underline{k})e^{-i\underline{k}\underline{x}}$$

Inserting this into the linearized equation, we effectively replace $\nabla^2 \rightarrow -k^2$ and get the characteristic equation:

$$\begin{aligned}(\beta - 1 - D_u k^2 - \lambda)(\alpha^2 + D_v k^2 + \lambda) - \alpha^2 \beta &= 0 \\ \leadsto \lambda_{\pm}(\underline{k}) &= \frac{1}{2} \left[\Gamma(\underline{k}) \pm \sqrt{\Gamma(\underline{k})^2 + 4\Lambda(\underline{k})} \right]\end{aligned}$$

where

$$\Gamma(\underline{k}) = \beta - 1 - \alpha^2 - (D_u + D_v)k^2, \quad \Lambda(\underline{k}) = (\beta - 1 - D_u k^2)(\alpha^2 + D_v k^2) - \alpha^2 \beta$$

Stability for $k = 0$:

$$\begin{aligned}(\Gamma(0) = \beta - 1 - \alpha^2, \Lambda(0) = (\beta - 1)\alpha^2 - \alpha^2 \beta) \\ \lambda_{\pm}(0) = \frac{1}{2} [\beta - 1 - \alpha^2 \pm i\alpha]\end{aligned}$$

We require $\Re(\lambda_{\pm}) < 0 \leadsto \underline{\underline{\beta < 1 + \alpha^2}}$

In order to obtain a parameter regime where $\Re(\lambda_{\pm}) > 0$ in the presence of

noise, $\Lambda(k)$ has to be positive since $\Gamma(k)$ is monotonously decreasing with k . Therefore the critical wave number k_c for a Turing instability is given by $\Lambda(k_c) = 0$

$$\leadsto [(\beta - 1)D_v - \alpha^2 D_u] k_c^2 \approx \alpha^2$$

Taken together, we obtain a Turing instability if

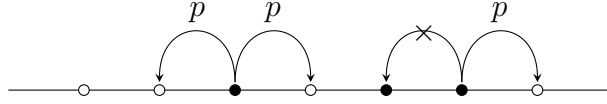
$$1 + \frac{D_u}{D_v} \alpha^2 < \beta < 1 + \alpha^2$$

This implies that $D_u < D_v$! If β is taken as bifurcation parameter, we get Turing instability at a critical value $\beta = 1 + \frac{D_u}{D_v} \alpha^2$

For $\beta > \beta_c$ spatially periodic eigenmodes will grow with wavenumbers around k_c .²

2.5 Transport by many molecular motors

2.5.1 The symmetric exclusion process (SEP)



Evolution of the density at a given site n :

Let $P_{n,m}(t)$ be the joint probability that sites n, m are occupied, $P_{n,\bar{m}}$ the probability that n is occupied but m isn't and similar.

For the SEP the single-particle density evolves as:

$$\frac{dP_n}{dt} = \sum_m (P_{\bar{n},m} - P_{n,\bar{m}})$$

where the hopping rate $p = 1$. The sum runs over all neighboring sites of n . The joint probabilities fulfill the relation

$$P_{n,m}(t) + P_{n,\bar{m}}(t) = P_n(t) \quad \& \quad P_{n,m}(t) + P_{\bar{n},m}(t) = P_m(t)$$

$$\frac{dP_n}{dt} = \sum_n (P_m - P_n)$$

²G. Meacci, Karsten Kruse q-bio/0504017: Min-Oscillations

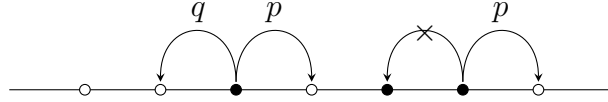
→ The evolution of the density is the same as for symmetric diffusion of a single particle, irrespective of the particle density.
The differences to single particle diffusion show up for the dynamics of a given tracer particle. There the typical displacement grows as:

$$\sqrt{\langle x^2 \rangle} = At^{\frac{1}{4}} \text{ with } A = \left(\frac{2}{\sqrt{\pi}} \frac{1-c}{c} \right)^{\frac{1}{2}}$$

2.5.2 The Asymmetric Exclusion Process (ASEP)

The ASEP is a stochastic process that combines exclusion, stochasticity and directionality, and thereby the essential characteristics of the motor dynamics, except their finite runlength.

A particle hops to the right with rate p and to the left with rate q



We consider $p > q$ and, for convenience, $p + q = 1$. The main qualitative features are observed for any strength of the relative bias. Therefore, often $p = 1$ (TASEP for Totally Asymmetric Exclusion Process) is chosen.

Steady states

A state of the ASEP is specified by the location of all particles. There is a configuration \mathcal{C} . The probability $P(\mathcal{C}, t)$ to find a configuration \mathcal{C} at time t evolves according to:

$$\frac{dP(\mathcal{C}, t)}{dt} = \sum_{\mathcal{C}'} \left(P(\mathcal{C}', t) W(\mathcal{C}' \rightarrow \mathcal{C}) \right) - P(\mathcal{C}, t) \sum_{\mathcal{C}'} W(\mathcal{C} \rightarrow \mathcal{C}')$$

In a steady state one obviously gets:

$$\sum_{\mathcal{C}'} P_S(\mathcal{C}') W(\mathcal{C}' \rightarrow \mathcal{C}) = P(\mathcal{C}) \sum_{\mathcal{C}'} W(\mathcal{C} \rightarrow \mathcal{C}')$$

For an equilibrium system the stationary solution is given by

$$P_S(\mathcal{C}) = P_{eq}(\mathcal{C}) = \frac{1}{Z} e^{-\beta E(\mathcal{C})}$$

This is not true for non-equilibrium processes, where the stationary master equation has to be solved. For non-equilibrium system the detailed balance condition does not hold in general.

Steady states on a ring

The steady state on a ring can be obtained by arranging particles into "islands".



Here, we have $N = 15$, $I(\mathcal{C}) = 3$ and $M = 6$.

Now in a given time interval dt the probability of learning \mathcal{C} is given by $I(\mathcal{C})P_S(\mathcal{C})dt$, since only the rightmost particle of an island may hop.

The configurations \mathcal{C}' that may have led to \mathcal{C} differ by a single step of an arbitrary particle. Obviously there are $I(\mathcal{C})$ of such configurations.

$$\leadsto \sum_{\mathcal{C}'} P_S(\mathcal{C}') W(\mathcal{C}' \rightarrow \mathcal{C}) = \sum_{\mathcal{C}'} P_S(\mathcal{C}')$$

If all configurations have the same weight we get:

$$\sum_{\mathcal{C}'} P_S(\mathcal{C}') = I(\mathcal{C}) P(\mathcal{C})$$

and the stationary condition holds.

Then the weight of a configuration is given by

$$P_S(\mathcal{C}) = \binom{N}{M}^{-1} \quad \text{since } \binom{N}{M} \text{ is the number of allowed configurations.}$$

The current between two sites is given by the relative weight of the local configuration $\bullet \circ$

It is given by

$$\begin{aligned} J &= \frac{\binom{N-2}{M-1}}{\binom{N}{M}} \\ &= \frac{\# \text{ configurations for } M-1 \text{ particles on the remaining } N-2 \text{ sites}}{\# \text{ configurations}} \\ &= \frac{M}{N} \frac{N-M}{N-1} \end{aligned}$$

In the limit $N, M \rightarrow \infty$, $\frac{M}{N} = \rho$ we get $J = \rho(1 - \rho)$

This result agrees to the most naive approach, a simple product ansatz, since:

$$J = \langle n_i(1 - n_{i+1}) \rangle = \langle n_i \rangle - \langle n_i n_{i+1} \rangle \underset{\text{PA}}{\approx} \langle n_i \rangle^\rho - \langle n_i \rangle^\rho \langle n_{i+1} \rangle^\rho = \rho(1 - \rho)$$

Open systems

We now consider a system that is coupled to two particle reservoirs.



The particle dynamics is described by the ASEP rules in the bulk. They may enter the system at site 1 with rate α and leave it at site N with rate β . We introduce the occupation number $n_i = \{0, 1\}$ ($n_i = 0(1)$: site i is empty (filled))

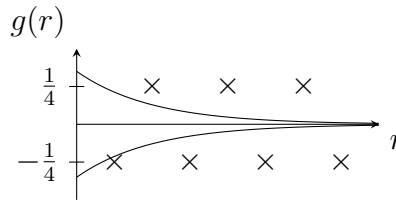
The particle number evolves as

$$\frac{dn_i(t)}{dt} = n_{i-1}(t)(1 - n_i(t)) - n_i(t)(1 - n_{i+1}(t))$$

Averaging over different histories, we get:

$$\frac{d\langle n_i(t) \rangle}{dt} = \langle n_{i-1}(1 - n_i) \rangle - \langle n_i(1 - n_{i+1}) \rangle$$

Remark: Please note that this **exact** expression relates densities to two-point correlation functions $\langle n_i n_{i+1} \rangle$ & $\langle n_{i-1} n_i \rangle$. This implies that a hierarchy of correlation functions has to be solved in order to calculate exact expressions of the density.



$$g(i, r) = \langle n_i n_{i+r} \rangle - \rho^2$$

The equation above holds for the time evolution of the density in the bulk. The complete set of equations is given by

$$\frac{d\langle n_i \rangle}{dt} = \begin{cases} \alpha\langle 1 - n_1 \rangle - \langle n_1(1 - n_2) \rangle & i = 1 \\ \langle n_{i-1}(1 - n_i) \rangle - \langle n_i(1 - n_{i+1}) \rangle & 1 < i < N \\ \langle n_{N-1}(1 - n_N) \rangle - \beta\langle n_N \rangle & i = N \end{cases}$$

The steady state of the open system is in general non-trivial. Most elegantly it can be obtained by a matrix method.

The key idea is to write the probability of a given configuration \underline{n} as a product of matrices.

$$P_N(\underline{n}) = \frac{1}{Z_N} \langle W | \prod_{i=1}^N n_i D + (1 - n_i) E | V \rangle$$

where D, E are matrices and $\langle W |, | V \rangle$ auxiliary vectors, and Z_N denotes the normalization constant.

Example: $\circ \circ \bullet \circ \rightsquigarrow P(0010) = \frac{1}{Z_4} \langle W | E E D E | V \rangle$

The normalisation constant Z_N makes sure that the sum of all weights is normalized, $\sum_{\underline{n}} P(\underline{n}) = 1$. It is given by

$$Z_N = \langle W | (D + E)^N | \rangle = \langle W | C^N | E \rangle \text{ where } C = D + E$$

By using the matrix representation we get:

$$\langle n_i \rangle = \frac{1}{Z_N} \langle W | C^{i-1} D C^{N-i} | V \rangle$$

as average value of the density at site i , since $\langle n_i \rangle$ is the relative weight of all configurations with an occupied site i . Similarly the current between site i and $i + 1$ is given by

$$\langle J_i \rangle = \frac{1}{Z_N} \langle W | C^{i-1} D E C^{N-i-1} | V \rangle$$

As a result of mass conservation in the bulk we have $\langle J_i \rangle = \langle J \rangle = \text{const.}$

This implies that:

$$\alpha \langle E C^{N-1} \rangle = \langle D E C^{N-2} \rangle \dots$$

From the bulk we get $(DE)C = C(DE)$. It turns out that the simplest solution $DE = E + D$ which fulfills the commutation relation is correct. Therefore,

we get $\langle J_i \rangle = J = \frac{Z_{N-1}}{Z_N}$

The set of equations is completed by the boundaries via $DE = D+E$; $\langle W|E = \alpha^{-1}\langle W|$; $D|V\rangle = \beta^{-1}|V\rangle$. Relative weights of a 2-site system:

$$\begin{aligned}\langle W|EE|V\rangle &= \frac{1}{\alpha^2} \langle W|V\rangle & \langle W|ED|V\rangle &= \frac{1}{\alpha\beta} \langle W|V\rangle \\ \langle W|DE|V\rangle &= \langle W|D+E|V\rangle = \left(\frac{1}{\alpha} + \frac{1}{\beta}\right) \langle W|V\rangle & \langle W|DD|V\rangle &= \frac{1}{\beta^2} \langle W|V\rangle\end{aligned}$$

We already expressed the current of a N -site system by

$$J_N = \frac{Z_{N-1}}{Z_N} = \frac{\langle W|C^{N-1}|V\rangle}{\langle W|C^N|V\rangle}$$

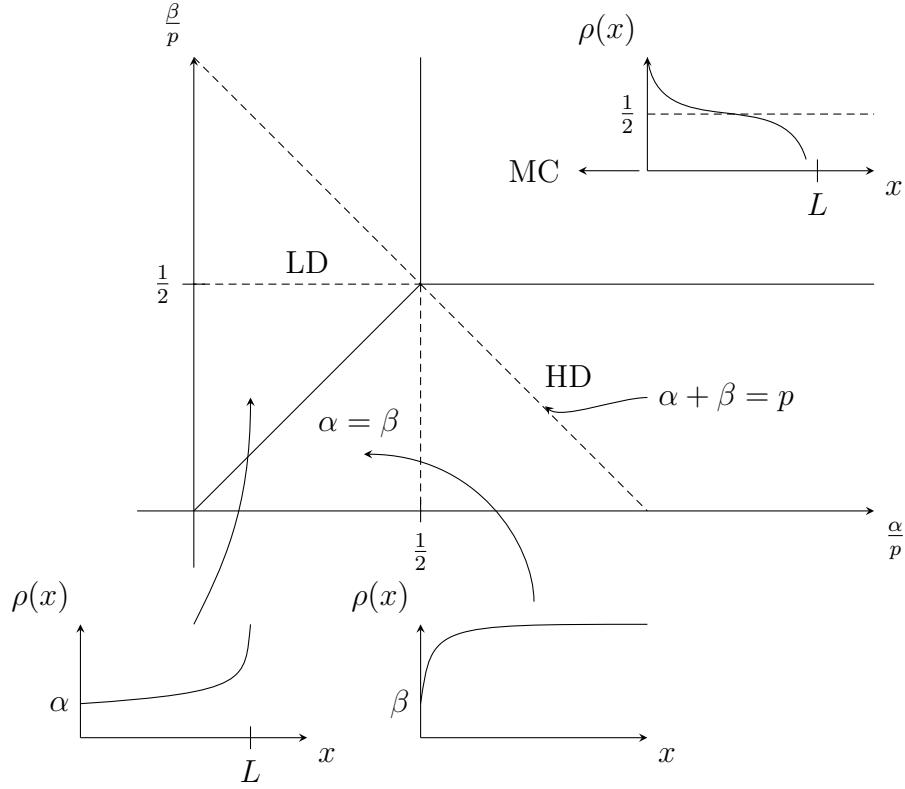
It is therefore the most important task to compute an exact expression for C^N , i.e. to express the sum in "normal order". The derivation of the exact result is difficult and won't be given here. Instead we will simply quote the result:

$$\begin{aligned}(D+E)^N &= \sum_{p=1}^N p \frac{(2N-1-p)!}{N!(N-p)!} \sum_{q=0}^p E^q D^{p-q} \\ \leadsto \frac{\langle W|C^N|V\rangle}{\langle W|V\rangle} &= \sum_{p=0}^N p \frac{(2N-p-1)!}{N!(N-p)!} \frac{\beta^{-p-1} - \alpha^{-p-1}}{\beta^{-1} - \alpha^{-1}}\end{aligned}$$

For infinite systems ($N \rightarrow \infty$), we get:

$$J = \begin{cases} \frac{1}{4} & \alpha \geq \frac{1}{2}; \beta \geq \frac{1}{2} & \text{maximum current phase} \\ \alpha(1-\alpha) & \alpha < \frac{1}{2}; \alpha < \beta & \text{low density phase} \\ \beta(1-\beta) & \beta < \frac{1}{2}; \beta < \alpha & \text{high density phase} \end{cases}$$

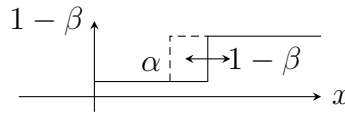
phase diagram:



The domainwall picture of the ASEP

The domain-wall theory describes phenomenologically the competition between two domains composed by the two reservoirs. For $\alpha < \frac{1}{2}; \beta < \frac{1}{2}$ two domains coexist. The density in the left reservoir is given by α , the flow by $\alpha(1 - \alpha)$.

Analogously, we have a density $(1 - \beta)$ and a flow $\beta(1 - \beta)$ for the right domain. The two domains are separated by a shock:



The domain wall is displaced to the left by the particle from left reservoir. The displacement is given by:

$$\Delta m = J_{\alpha} \Delta t = \Delta x (1 - \beta - \alpha) \Rightarrow \frac{\Delta x}{\Delta t} = \frac{\alpha(1 - \alpha)}{1 - \beta - \alpha}$$

Analogously we get for the domain-wall motion to the right that:

$$\frac{\Delta x}{\Delta t} = \frac{\beta(1 - \beta)}{1 - \beta - \alpha}$$

Therefore, the drift velocity for the random walker is given by $v = \frac{J_\beta - J_\alpha}{\rho_\beta - \rho_\alpha}$

$$v = \frac{\beta(1 - \beta) - \alpha(1 - \alpha)}{1 - \beta - \alpha} = \frac{\beta(1 - \beta - \alpha) - \alpha(1 - \alpha - \beta)}{1 - \beta - \alpha} = \beta - \alpha$$

This simple result shows that for $\alpha < \beta$ the domain wall is shifted to the right, since the domain-wall-velocity is positive and vice versa. For $\alpha = \beta$ the domain-wall-motion is purely diffusive. If we identify $p = \frac{J_\beta}{\rho_\beta - \rho_\alpha}$ as hopping rate to the right and $q = \frac{J_\alpha}{\rho_\beta - \rho_\alpha}$ as hopping rate to the left, we get the following stationary state of the random walk ($p < q$, HD):

$$p_n = \left(\frac{p}{q}\right)^{n-1} p_1 = \left(\frac{J_\beta}{J_\alpha}\right)^{n-1} p_1$$

Obviously the probabilities of the stationary random walk are exponentially distributed for $\alpha \neq \beta$. The fluctuations of the domain-wall positions are described by a localization length χ given by:

$$\left(\frac{J_\beta}{J_\alpha}\right) = e^{-\frac{n}{\chi}} \quad \rightsquigarrow \quad \left|\ln\left(\frac{J_\beta}{J_\alpha}\right)\right|^{-1} = \chi$$

This can be rewritten as

$$\chi^{-1} = \left|\chi_\beta^{-1} - \chi_\alpha^{-1}\right|$$

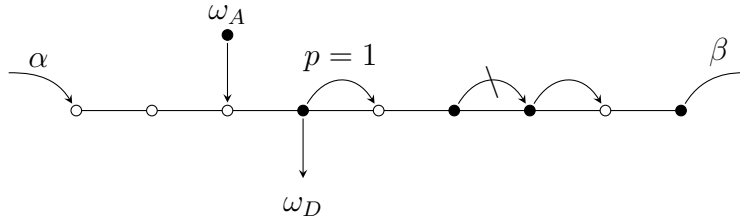
where $\chi_x^{-1} = -\ln[4x(1-x)]$ for $x < \frac{1}{2}$ and $\chi_x^{-1} = 0$ for $x \geq \frac{1}{2}$

The stationary densities can be used in order to construct the density profiles. They have the form

$$\begin{aligned} \rho(x) &= \rho_\beta - \Delta\rho e^{-\frac{x}{\chi}} && \text{HD} \\ \text{or } \rho(x) &= \rho_\alpha + \Delta\rho e^{-\frac{L-x}{\chi}} && \text{LD} \\ \alpha &= \beta && \text{linear density profile} \end{aligned}$$

Unidirectional traffic of molecular motors

The model is defined as follows:



The time-evolution of the density takes the form:

$$\begin{aligned} 1 < i < N & \quad \frac{d\langle \tau_i \rangle}{dt} = \langle \tau_{i-1}(1 - \tau_i) \rangle - \langle \tau_i(1 - \tau_{i+1}) \rangle + \omega_A \langle (1 - \tau_i) \rangle - \omega_D \langle \tau_i \rangle \\ 1 : & \quad \frac{d\langle \tau_1 \rangle}{dt} = -\langle \tau_1(1 - \tau_2) \rangle + \alpha \langle 1 - \tau_1 \rangle - \omega_D \langle \tau_1 \rangle \\ N : & \quad \frac{d\langle \tau_N \rangle}{dt} = \langle \tau_{N-1}(1 - \tau_N) \rangle + \omega_A \langle (1 - \tau_N) \rangle - \beta \langle \tau_N \rangle \end{aligned}$$

$$\rho_{eq} = \frac{\omega_A}{\omega_A + \omega_D}$$

Mean-Field analysis of the model

$$\langle \tau_{i\pm 1} \rangle = \rho(x) \pm \frac{1}{N} \frac{\partial \rho}{\partial x} + \frac{1}{2N^2} \frac{\partial^2 \rho}{\partial x^2} + \mathcal{O}((\Delta x)^3)$$

Keeping leading order terms in $\Delta x = \frac{1}{N}$, one obtains:

$$\frac{\partial \rho}{\partial \tau} = -(1 - 2\rho) \frac{\partial \rho}{\partial x} - \omega_D N [k - (1 + k) \rho]$$

where $\tau = \frac{t}{N}$ and $k = \frac{\omega_A}{\omega_D}$. For the open system we are interested in the case where $\Omega_A = \omega_A N$ & $\Omega_D = \omega_D N$ are finite for $N \rightarrow \infty$. This condition implies a balance between bulk- and boundary reservoirs.

The boundary conditions are $\rho(x = 0) = \alpha$ and $\rho(x = 1) = 1 - \beta$. The analysis of the mean-field-equations is performed in terms of characteristics which are defined for a quasi-linear equation.

$$a(x, \tau, \rho) \frac{\partial \rho}{\partial \tau} + b(x, \tau, \rho) \frac{\partial \rho}{\partial x} = c(x, \tau, \rho)$$

by the equations:

$$\frac{\partial x}{\partial \tau} = \frac{b(x, \tau, \rho)}{a(x, \tau, \rho)} \quad \frac{\partial \rho}{\partial \tau} = \frac{c(x, \tau, \rho)}{a(x, \tau, \rho)}$$

For this model the characteristics are given by:

$$\frac{\partial x}{\partial \tau} = (1 - 2\rho) \quad \frac{\partial \rho}{\partial \tau} = \Omega_D [k - (1 + k) \rho]$$

The characteristics are curves along which information about the solution propagates from the boundary condition. In the absence of creation and annihilation of particles the characteristics propagate at constant speed. Here the density of the pattern is changing in time and thereby the speed of the characteristics. When two characteristic lines meet one may observe a shock. The speed of the shock is given by

$$v_S = \frac{\rho_2(1 - \rho_2) - \rho_1(1 - \rho_1)}{\rho_2 - \rho_1} = 1 - (\rho_1 + \rho_2)$$

Steady state solution of the mean-field-equation

The stationary state mean-field-equation is given by:

$$(1 - 2\rho) \frac{\partial \rho}{\partial x} - \Omega_D [k - (1 + k) \rho] = 0$$

In order to determine the solution of this first-order-differential-equation, we have to integrate independently from the left and right boundary.

The solution from the left boundary $\rho(0) = \alpha$ is given by:

$$x = \frac{1}{\Omega_D} \int_{\alpha}^{\rho_l(x)} ds \frac{1 - 2\rho}{k - (1 + k) \rho} = \frac{1}{\Omega_D (1 + k)} \left[2(\rho_l + \alpha) + \frac{k - 1}{1 + k} \ln \left| \frac{k - (1 - k) \rho_l}{k - (1 + k) \alpha} \right| \right]$$

and from the right boundary condition by

$$1 - x = \frac{1}{\Omega_D (1 + k)} \left[2 (1 - \beta - \rho_r) + \frac{k - 1}{1 + k} \ln \left| \frac{k - (1 + k) (1 - \beta)}{k - (1 + k) \rho_r} \right| \right]$$

At given position the solution is realized that corresponds to the lower value of the current.

The discussion simplifies considerably if $k = 1$, i.e. $\omega_A = \omega_D$. In this case, the stationary mean-field-equations read:

$$(2\rho - 1) (\partial_x \rho - \Omega) = 0$$

The solution of this equation is given by $\rho = \frac{1}{2} = \rho_{eq}$ or $\rho(x) = \Omega x + c$.

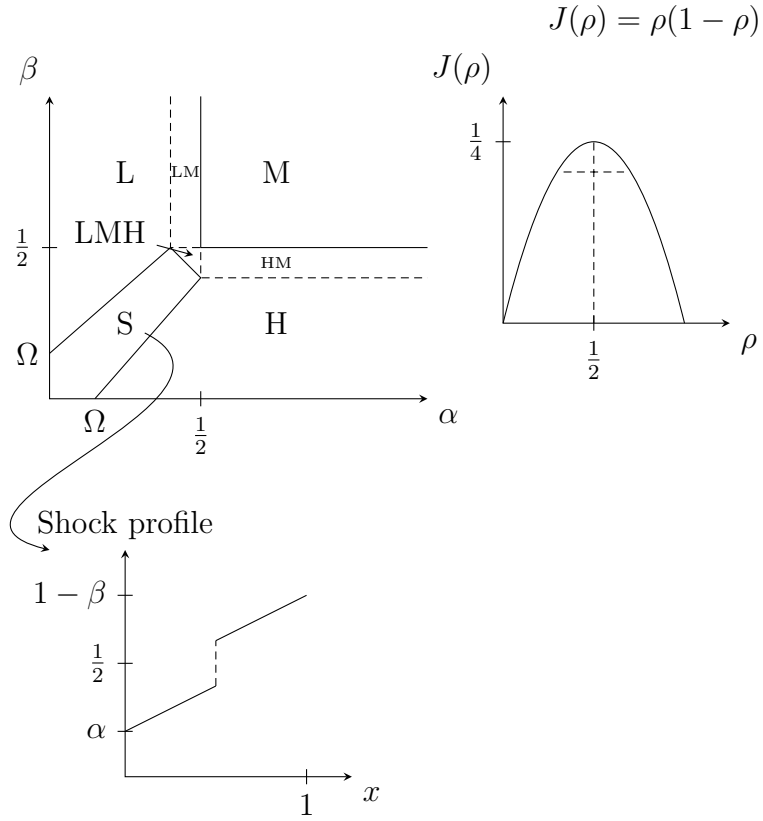
The phase diagram can be constructed by using the minimal flow criterion.

First we observe a shock if a position exists where the shock has a vanishing velocity, i.e. where the $v_S = 1 - \rho_l(x_S) - \rho_r(x_S) = 0$. For the piecewise linear solution we get:

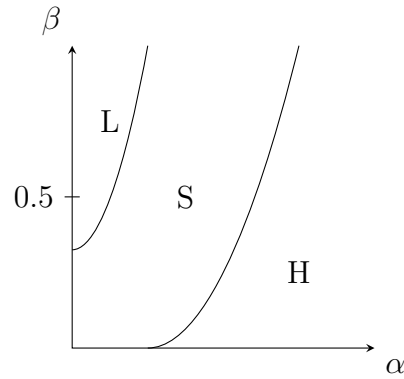
$$x_S = \frac{\beta - \alpha}{2\Omega} + \frac{1}{2}$$

The height of the shock is given by:

$$\Delta = \rho_r(x_S) - \rho_l(x_S) = 1 = 1 - (\alpha + \beta) - \Omega = \Omega_C - \Omega$$



The case $k \neq 1$ is different, since a maximal current phase is not observed, because the bulk reservoir destroys a maximum current domain. In this case the solution is non-linear and has to be computed numerically. The phase diagram has the following form:



Phase boundaries: $(\alpha < \frac{1}{2} \& \beta < \frac{1}{2})$

Low-density Phase: The left solution propagates through the system, i.e. $\rho_l(1) < \beta$

$$\leadsto \Omega_D (1 + D) = \left[2(\beta - \alpha) + \frac{k-1}{1+k} \ln \left| \frac{k - (1+k)\beta}{k - (1+k)\alpha} \right| \right]$$

High-density phase: The right solution propagates through the system or $\rho_r(0) \geq 1 - \alpha$

$$\Omega_D (1 + k) = 2(\alpha + 1) + \frac{k-1}{1+k} \ln \left| \frac{k - (1+k)(1-\beta)}{k - (1+k)(1-\alpha)} \right|$$

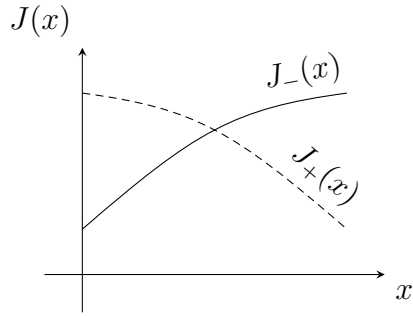
In case of $\alpha > \frac{1}{2}$ or $\beta > \frac{1}{2}$ the second order terms are of importance. There is no shock between the solution at the right boundary and the bulk solution. We can therefore effectively consider α or $\beta = \frac{1}{2}$ in order to obtain the shock position if existent.

While higher order terms are important in order to construct the density and flow profile, the fluctuations of the shock can be obtained by a modified version of the domain wall theory. Now the "hopping rates" are given by:

$$\omega_l(i) = \frac{J_-(i)}{\Delta(i)}, \omega_r(i) = \frac{J_+(i)}{\Delta(i)}$$

where ω_l (ω_r) denote the hopping rates to the left (right) and $J_-(i)$ [$J_+(i)$] the flux in the low (high) density domain at site i . $\Delta(i)$ is the height of the shock at position i .

The mechanism of the localization of the shock is illustrated by the following picture



The bias of the Random walk changes the orientation at the position of the shock

\leadsto The shock is trapped

From a continuum approximation one obtains that the relative width of the shock scales as $N^{-\nu}$ with $\nu = \frac{1}{2}$.

2.5.3 Brownian ratchet model of a processive motor

- motors have different internal states (ATP-cycle)
- states in a cycle $i = 1, 2, \dots, M$
- motors move in a periodic potential $V_i(x)$, where the index refers to the internal state

Symmetric Potential: $V_i(-x) = V_i(x + \Delta x)$ for all x , Δx arbitrary but fixed (if such a Δx does not exist: asymmetric Potential) We can write a Fock-Planck-equation:

$$\frac{\partial p_i(x, t)}{\partial t} = -\frac{\partial J_i(x, t)}{\partial x}$$

$p_i(x, t)$ = probability density for a motor to be in a state i at position x .
 $J_i(x, t)$ is the corresponding flux of probability

$$J_i(x, t) = \frac{1}{\gamma} \left[-V'_i(x) - k_B T \frac{\partial}{\partial x} \right] p_i(x, t)$$

where $\gamma = \frac{k_B T}{D}$ (Einstein relation).

Now: Add transitions between states

$$\frac{\partial p_i(x, t)}{\partial t} = -\frac{\partial J_i(x, t)}{\partial x} + \sum_{j=1}^M [\omega_{ij}(x)p_j(x, t) - \omega_{ji}(x)p_i(x, t)]$$

where ω_{ij} denotes the rates at which the motors switch from j to i .

Two-state model

$$\begin{aligned} \frac{\partial p_1}{\partial t} + \frac{\partial J_1(x, t)}{\partial x} &= -\omega_1(x)p_1(x, t) + \omega_2(x)p_2(x, t) \\ \frac{\partial p_2}{\partial t} + \frac{\partial J_2(x, t)}{\partial x} &= \omega_1(x)p_1(x, t) - \omega_2(x)p_2(x, t) \end{aligned}$$

We consider l -periodic potentials $V_1(x), V_2(x)$ where $V_i(x) = V_i(x + l)$ where $V_i(x) = V_i(x + l)$ and introduce the reduced probabilities and fluxes:

$$\hat{P}_j(x, t) = \sum_{n=-\infty}^{\infty} p_j(x + nl, t) \quad , \quad \hat{J}_j(x, t) = \sum_{n=-\infty}^{\infty} J_j(x + nl, t)$$

The total flux of probability can then be written as:

$$\hat{J}(x, t) = -\frac{1}{\gamma} \left[V_1'(x) \hat{p}_1(x, t) + V_2'(x) \hat{p}_2(x, t) + k_B T \frac{\partial \hat{p}(x, t)}{\partial x} \right]$$

with $\hat{p} = \hat{p}_1 + \hat{p}_2$

Now we introduce $\lambda(x) = \frac{\hat{p}_1(x)}{\hat{p}(x)}$

$$\leadsto V_{\text{eff}}'(x) \hat{p}(x) + k_B T \frac{\partial \hat{p}(x)}{\partial x} = -\hat{J}_0 \gamma \quad \hat{p}(x) \text{ is the only variable}$$

where $V_{\text{eff}} = \int_0^x [\lambda(y) V_1'(y) + (1 - \lambda(y)) V_2'(y)] dy$

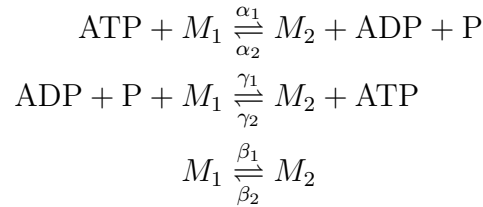
1) Thermal equilibrium \rightarrow detailed balance is satisfied

$$\begin{aligned} \frac{\omega_1(x)}{\omega_2(x)} &= e^{\frac{V_1(x) - V_2(x)}{k_B T}} = \frac{\hat{p}_2(x)}{\hat{p}_1(x)} \\ \Rightarrow \lambda(x) &= \frac{\hat{p}_1(x)}{\hat{p}_1(x) + \hat{p}_2(x)} = \frac{1}{1 + \frac{\hat{p}_2(x)}{\hat{p}_1(x)}} \\ &= \frac{1}{1 + \exp\left(\frac{V_1(x) - V_2(x)}{k_B T}\right)} \quad (l \text{ periodic}) \end{aligned}$$

$\Rightarrow V_{\text{eff}}(x)$ is an l -periodic function and, therefore, there is no net motion in a particular direction.

2) ATP-hydrolysis

Scheme:



ATP-hydrolysis: Gain of chemical energy $\Delta\mu$

$$\begin{aligned} \leadsto \frac{\alpha_1}{\alpha_2} &= e^{\frac{V_1 - V_2 + \Delta\mu}{k_B T}} \\ \frac{\gamma_1}{\gamma_2} &= e^{\frac{V_1 - V_2 - \Delta\mu}{k_B T}} \\ \frac{\beta_1}{\beta_2} &= e^{\frac{V_1 - V_2}{k_B T}} \end{aligned}$$

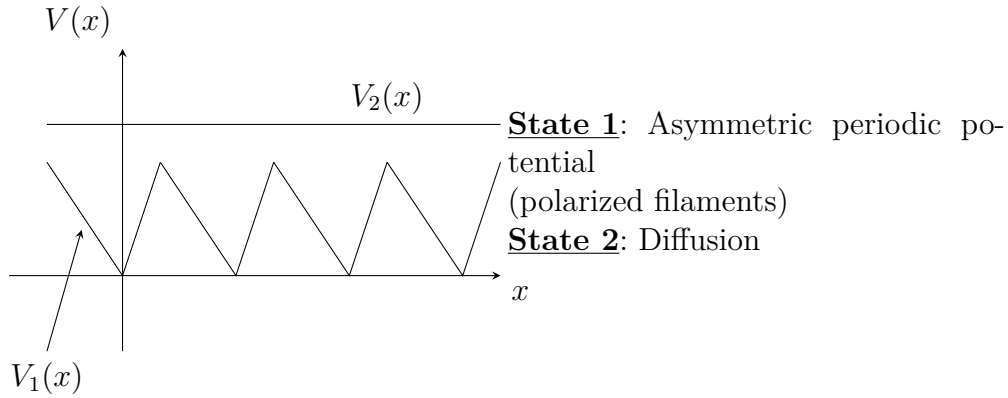
With this we get for the transition rates

$$\omega_1 = \alpha_1 + \beta_1 + \gamma_1 = \alpha_2 e^{\frac{V_1 - V_2 + \Delta\mu}{k_B T}} + \gamma_2 e^{\frac{V_1 - V_2 - \Delta\mu}{k_B T}} + \beta_2 e^{\frac{V_1 - V_2}{k_B T}}$$

$$\omega_2 = \alpha_2 + \beta_2 + \gamma_2 \rightarrow \text{detailed balance is broken!}$$

Detailed balance is broken. The solution of the FP-equation has to be determined numerically.

What is needed in order to generate driven motion \rightarrow asymmetric potential



Mechanism: Forward drift since it is more likely to return to state at a forward directing slope