Theoretische Biophysik

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Inhaltsverzeichnis

Literatur

„A first course in system biology“, Eberhard o. Voit, Garland Science

„Physical biology of the cell“, Rob Phillips et al., Garland Science

„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 <u>nodes</u> (or vertices) and <u>edges</u>. Nodes represent the interacting components (molecules, species, subpopulations) and edges their interactions (chemical reactions, competition in evolution).

1.2.2 Examples of networks

(A) Directed network

(B) Indirected network

(C) Bidirectional network

(D) Signaling network

- - - - - inhibiting

·········· stimulating
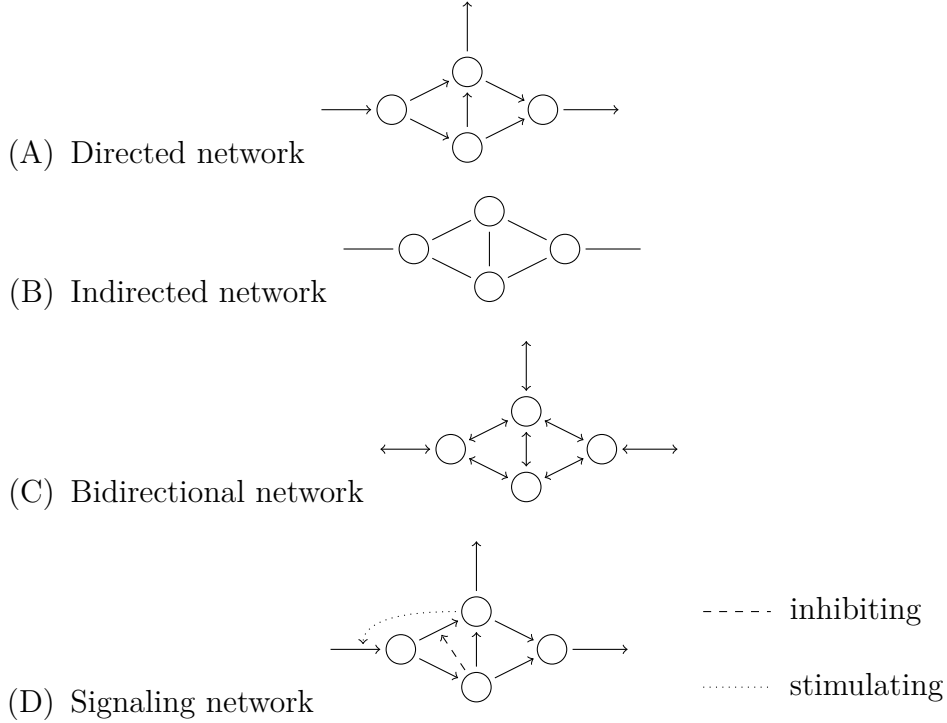
1.2.3 The properties of graphs

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

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

$\deg(N_1) = \deg(N_2) = \deg(N_4) = 2$

$\deg(N_3) = 3$

$\deg(N_5) = 1$
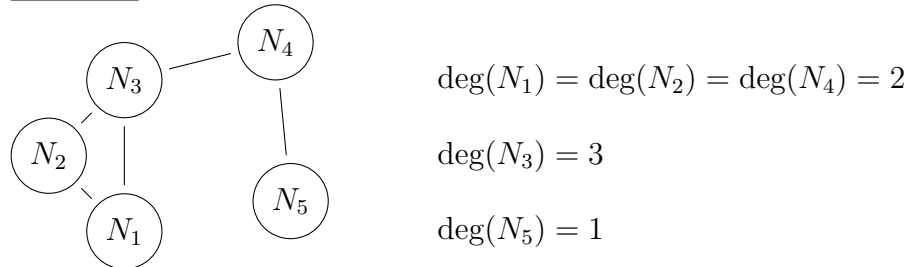
In case of directive graphs it's useful to distinguish between in-degree $\deg_{in}(N_i)$ and out-degree $\deg_{out}(N_i)$ which refer to the number of in- and outgoing edges.

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:

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

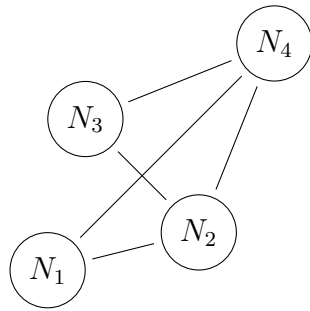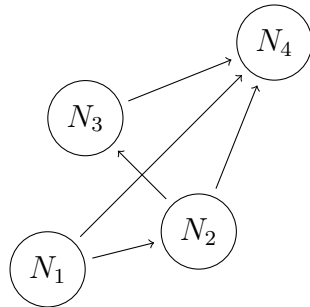$$A = \begin{pmatrix} 0 & 1 & 0 & 1 \\ 0 & 0 & 1 & 1 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 \end{pmatrix}$$

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:

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

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

Remark: In real biological networks $C_\mathcal{G}$ is typically low. There exists only a relatively small number of hubs, i.e. nodes that are highly connected to dense clusters.
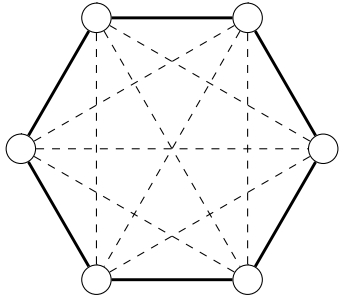
----- possible connection
——— connection
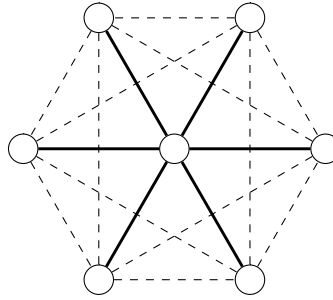
----- possible connection
——— connection

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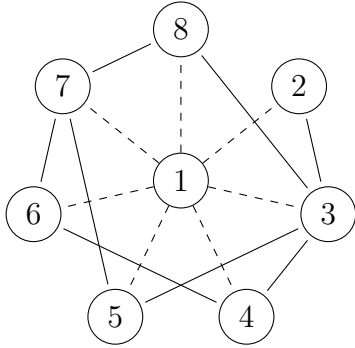Scale-free networks are dominated by a few hubs and many sparsely connected nodes

  – 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" networks[1] 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 $\sim \deg(N) \to \gamma = 3$

  – Variations of the mechanism lead to other values of γ

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[1]Barabasi Rev. Mod. Phys

1.2.6 Dependencies among network components

– Causality analysis: True cause must be neccessary 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 acces. 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 vertain 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.

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

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

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

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

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$\sum\limits_{i=1}^{\Omega} p_i = 1.$

Properties:

(1) Entropy is maximum for equal probabilities

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

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

$\mathcal{S}(p)$
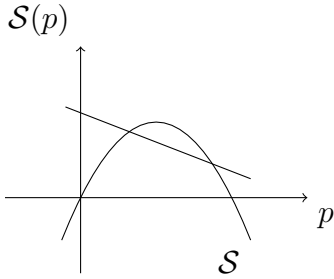
$$x = \lambda a + (1 - \lambda b) \qquad \lambda \in]0,1[$$
$$\rightarrow f(x) = \mathcal{S}(\lambda a + (1-\lambda)b) > \lambda \mathcal{S}(a) + (1-\lambda)\mathcal{S}(b)$$

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 $b = p_2 \qquad \leadsto \mathcal{S}(\frac{p_1+p_2}{2}) \geq \frac{1}{2}\left(\mathcal{S}(p_1) + \mathcal{S}(p_2)\right)$

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

$$\mathcal{S}\left(\frac{\sum\limits_{k=1}^{\Omega} p_k}{\Omega}\right) = \mathcal{S}\left(\frac{\Omega-1}{\Omega} \frac{\sum\limits_{i=1}^{\Omega-1} p_k}{\Omega-1} + \frac{1}{\Omega} p_\Omega\right)$$

$$\geq \frac{\Omega-1}{\Omega} \mathcal{S}\left(\frac{\sum\limits_{k=1}^{\Omega-1} p_k}{\Omega-1}\right) + \frac{1}{\Omega} \mathcal{S}(p_\Omega)$$

$$\geq \frac{\Omega-1}{\Omega} \frac{1}{\Omega-1} \sum\limits_{k=1}^{\Omega-1} \mathcal{S}(p_k) + \frac{1}{\Omega} \mathcal{S}(p_\Omega) = \frac{1}{\Omega} \sum\limits_{k=1}^{\Omega} \mathcal{S}(p_k)$$

The identity leads to:

$$H_S(p_1, \ldots, p_\Omega) = -\sum\limits_{k=1}^{\Omega} p_k \log_2(p_k) = \sum \mathcal{S}(p_k)$$

$$\leq \Omega \mathcal{S}\left(\frac{1}{\Omega} \sum\limits_k p_k\right) = \Omega \mathcal{S}\left(\frac{1}{\Omega}\right) = -\sum\limits_{k=1}^{\Omega} \frac{1}{\Omega} \log_2\left(\frac{1}{\Omega}\right)$$

$$= H_S\left(\frac{1}{\Omega}, \ldots, \frac{1}{\Omega}\right)$$

(2) Entropy has the property that

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

i.e. it does not change if we add states with probability 0.
This property is given, since $p\ln(p) \underset{p \to 0}{=} 0$.

(3) <u>Entropy changes for conditional probabilities</u>
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

$$\sum\limits_k P(A_k|B_l) = 1$$

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

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

$$H_I(AB) = H(r_{11}, r_{12}, \ldots, r_{\Omega\mu})$$
$$= H(c_{11}q_1, c_{12}q_2, \ldots, c_{\Omega\mu}q_\mu)$$

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:

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

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:

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

$$H_S(A, B) = -k_s \sum_{kl} c_{kl} q_l \ln(c_{kl} q_l) \qquad P_{kl} = P(A_k, B_l) = c_{kl} q_l$$

$$= -k_S \left(\sum_{kl} q_l \left[\ln(c_{kl}) + \ln(q_l) \right] \right)$$

$$= \sum_l q_l \underbrace{\left(-k_S \sum_k c_{kl} \ln(c_{kl}) \right)}_{H_S(A|B_l)} - k_S \sum_l \left(q_l \ln(q_l) \underbrace{\sum_k c_{kl}}_{=1} \right)$$
$$\underbrace{\phantom{- k_S \sum_l \left(q_l \ln(q_l) \sum_k c_{kl} \right)}}_{H_S(B)}$$

$$= \langle H_S(A|B_l) \rangle_B + H_S(B)$$

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

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

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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:

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

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.
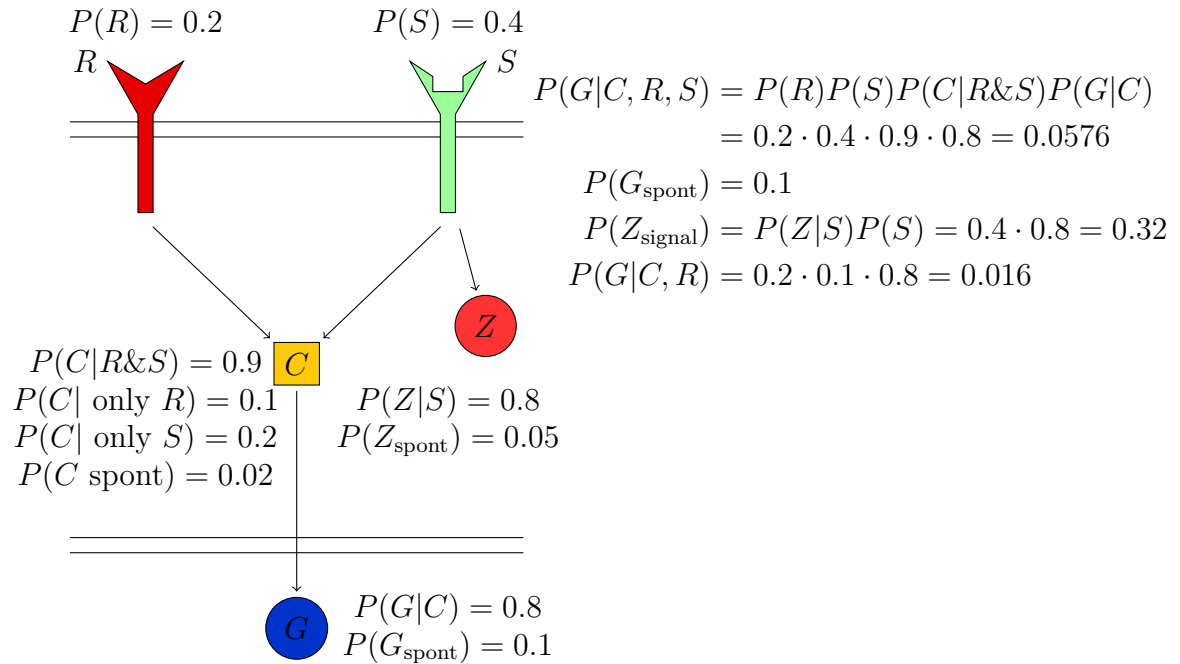$P(\text{hypothesis})$ is called the prior probability. It represents the state of knowledge about the hypothesis before we analysed the data.
$P(\text{data}|\text{hypothesis})$ is called the likelihood function which modifies the prior.
$P(\text{hypothesis}|\text{data})$ is called posterior, which represents the state of knowledge after about the truth of the hypothesis given the data.
$\rightarrow$ recipes in parameter estimation!

1.2.8 Signaling Networks

$P(R) = 0.2$ $P(S) = 0.4$

R S

$P(G|C, R, S) = P(R)P(S)P(C|R\&S)P(G|C)$
$$= 0.2 \cdot 0.4 \cdot 0.9 \cdot 0.8 = 0.0576$$
$$P(G_{\text{spont}}) = 0.1$$
$$P(Z_{\text{signal}}) = P(Z|S)P(S) = 0.4 \cdot 0.8 = 0.32$$
$$P(G|C, R) = 0.2 \cdot 0.1 \cdot 0.8 = 0.016$$

Z

$P(C|R\&S) = 0.9$ C
$P(C| \text{ only } R) = 0.1$
$P(C| \text{ only } S) = 0.2$ $P(Z|S) = 0.8$
$P(C \text{ spont}) = 0.02$ $P(Z_{\text{spont}}) = 0.05$

G $P(G|C) = 0.8$
$P(G_{\text{spont}}) = 0.1$

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

$\rightarrow$ the trigger same signal cascade of individually or collectively activated
$\rightarrow$ genomic response.

Typically signaling is not deterministic, examples:

$\rightarrow$ spontaneous trigger of the cascade with small probability

$\rightarrow$ 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.
Bayesion interference is mostly applied if the probability tables are not known
a priori.

– A Bayesion 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; $\mathrm{Par}_j(X_i)$

- States of parents: "On"(1); "Off"(0) or other values x_j

- configurations of a network witch n nodes

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

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 contditional 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
    $\rightarrow$ run an optimization scheme $\rightarrow$ the outcome of the measurements serf 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 glucolisis).
Compounds of interest in metabolic networks are represented as nodes, enzymatic reactions and transitions as edges.
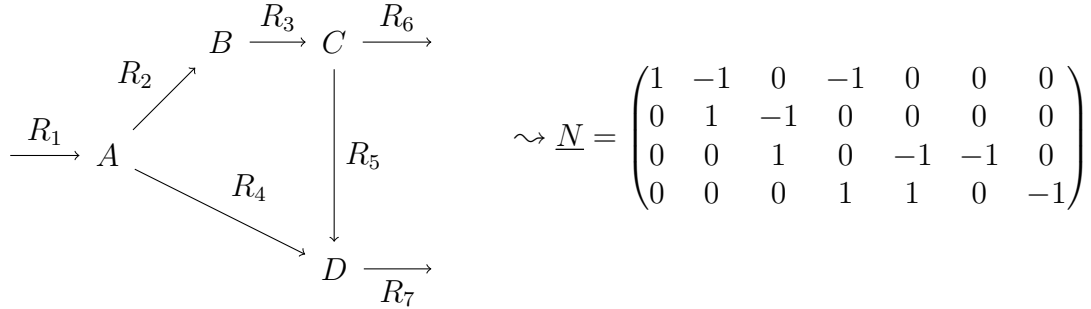
1.3 Stoichiometric networks
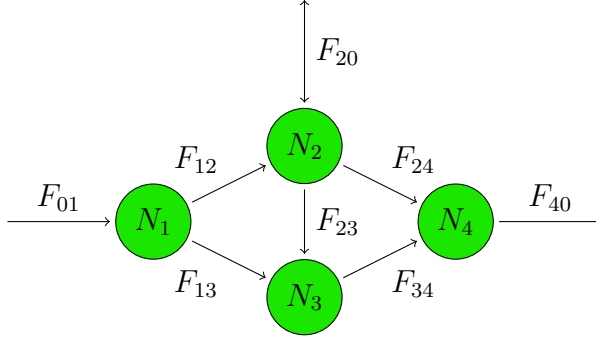
We consider a stationary state, i.e. incoming and outgoing fluxes balance eacht other at a given node.

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.

$$\rightsquigarrow \underline{N} = \begin{pmatrix} 1 & -1 & 0 & -1 & 0 & 0 & 0 \\ 0 & 1 & -1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & -1 & -1 & 0 \\ 0 & 0 & 0 & 1 & 1 & 0 & -1 \end{pmatrix}$$

± 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:

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

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

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

1.3.1 Reconstruction of metabolic networks

$\to$ the reconstruction of (metabolic) networks in case of unknown edges is very labor intensive

$\to$ Metabolites can be obtained with mass-spectroscopy

$\to$ Pathways can be obtained from the presence of genes, homologies with other organisms etc.

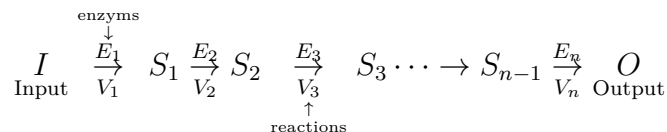$\to$ The combined knowledge is used in order to fill the missing links

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 contriubutes to the control of the steady state flux.

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

1.3.3 Generic metabolic pathway

$$I \underset{V_1}{\overset{E_1}{\rightarrow}} S_1 \underset{V_2}{\overset{E_2}{\rightarrow}} S_2 \underset{V_3}{\overset{E_3}{\rightarrow}} S_3 \cdots \rightarrow S_{n-1} \underset{V_n}{\overset{E_n}{\rightarrow}} O$$

where E_i are enzyms, I is Input, O is Output, V_i are reactions.

Steady state:

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

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

Small pertubations: We are interested in small pertubations 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:

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

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

1.3.4 Metabolite Control Coefficient

$$c_{v_i}^{S_k} = \frac{v_i}{S_k}\frac{\partial S_k}{\partial v_i} = \frac{\partial \ln(S_k)}{\partial \ln(v_i)}$$
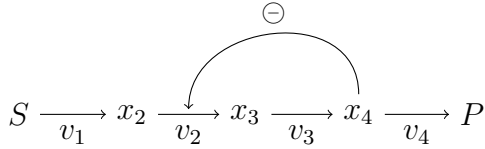
The influence of an enzyme on a flux or on a metabolite concentration can be very different. The impact of S_k on v_i is measured by the **elasticity coefficient**

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

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

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

1.3.5 Example

$$S \xrightarrow[v_1]{} x_2 \xrightarrow[v_2]{} x_3 \xrightarrow[v_3]{} x_4 \xrightarrow[v_4]{} P$$

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

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

The other elasticities are 0.

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

$$c_{v_1}^J \epsilon_{x_2}^{v_1} + c_{v_2}^J \epsilon_{x_2}^{v2} = -0.9 c_{v_1}^J + 0.5 c_{v_2}^J = 0 \qquad c_{v_4}^J = 0.38$$

Solving the set of equations, we get:

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

The information can be used in order to identify the bottle necks of the pathway and manipulate, e.g. the enzyme concentration of 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: $P_{t+1} = 2 P_t$

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

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 degradated.

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

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

$M_n = \#$ of new blood cells $\qquad\qquad g =$ production rate per degradated blood cell

$R_n = \#$ of circulation blood cells $\qquad\qquad\qquad f =$ fraction of degradated cells

Steady state?

$\rightarrow$ 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: $R_n = R_{n-1} = R_{n-2} = R$

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

We get a non-trivial stationary state if

$$Rf = fgR \quad \rightsquigarrow g = 1$$

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 then in terms of the number of bacteria.

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

$$\dot{x} = y \qquad\qquad \dot{x} = \frac{d}{dt}x$$
$$\dot{y} = -x$$

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 bei described by

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

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

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

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

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

In case of $u(t) = 0$, we have a homogeneous system, which has a fixpoint if
$\underline{\underline{A}}\underline{x} = 0$
If $\operatorname{rank}(\underline{\underline{A}}) = n$, it follows that $\det(\underline{\underline{A}}) \neq 0$. Then the solution of the linear system is unique and given by $\underline{x} = 0 \quad \forall t$.
If $\det(\underline{\underline{A}}) = 0$, 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:

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

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

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

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

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

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

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

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

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

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

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

The proof follows from Taylorexpansion of the rhs.

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

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

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

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

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

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

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

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

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

Or, integrating from t_0 to t:

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

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

<u>Remarks</u>:

1) This is the formal solution of the linear system with constant coefficient. For big linear systems, this solution is difficult to obtain explicitely, since it involves an infinite number of matrix multiplications

2) The homogeneous solution $x_n(t)$ depents 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 dpends on $\underline{\underline{H}} = e^{\underline{\underline{A}}t}$. If $\underline{\underline{H}}(t)$ is given, we can calculate the time evolution for arbitrary pertubations of $\underline{u}(t)$ and

Example: Linear system in 1D

$$\dot{x} = ax + u$$

$$u(t) = \begin{cases} 0 & t \leq 0 \\ u & t > 0 \end{cases}; \qquad a \in \mathbb{R}$$

$$\rightsquigarrow x(t) = x_0 e^{at} + \int_0^t u e^{a(t-\tau)} d\tau$$

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:

$$\dot{x}_1 = x_2$$
$$\dot{x}_2 = -\frac{g}{l} \sin(x_1)$$

Obviously the rhs of the 2nd equation is non-linear and there fore the whole system.

(ii) The forced harmonic oszillatro:

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

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

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

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

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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 $\dot{x} = \sin(x)$
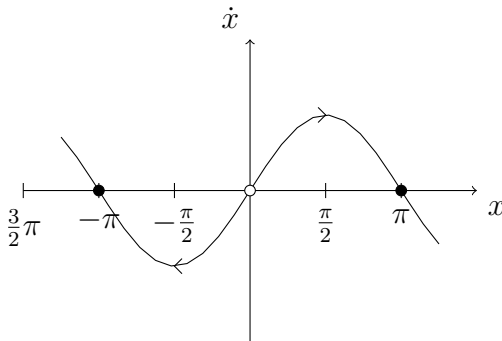This system can be solved analytically by seperation of variables:

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

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

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

The result is obviously difficult to interprete. 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.

$\bullet$ stable ficed point - flow is oriented toward the FP
$\circ$ 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 $x = \pi$.

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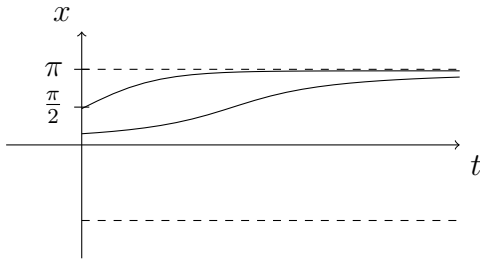
Fixed points and stability

We now generalize our system and consider $\dot{x} = f(x)$ Again, we get
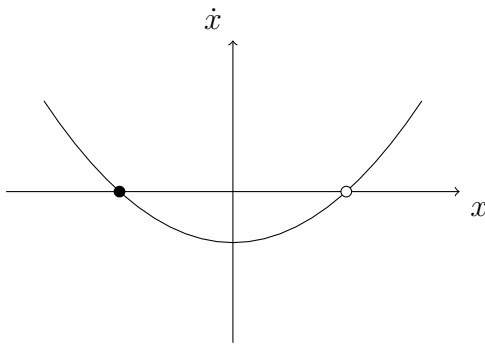
For the qualitative analysis of the trajectory. We consider x(t) as a "phase fluid", flowing with velocity $\underline{\dot{x}(t) = f(x(t))}$

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 ifferent 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: $\dot{N} = rN \rightsquigarrow N(t) = N_0 e^{rt}$

    $\rightarrow$ unrestricted growth

More realistic: Finite resources have to be considered:

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

maximum slope at $N - \frac{k}{2}$
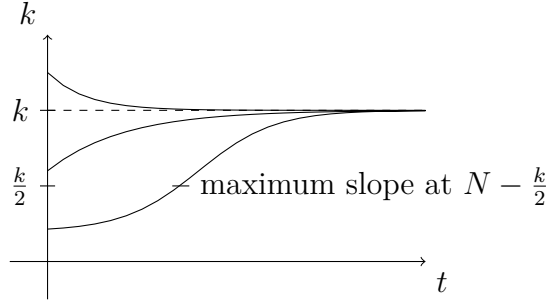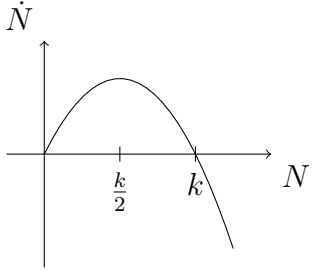
Linear stability analysis

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

$$f(x^* + \eta) = \underset{=0}{f(x^*)} + \eta\frac{df}{dx}(x^*) + \mathcal{O}(\eta^2)$$

$$\rightsquigarrow \dot{x} = \dot{\eta} = \eta\frac{df}{dx}(x^*) + \mathcal{O}(\eta^2)$$

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

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

This equation is linear in $\eta(t)$ and called **linearization** about x^*. The pertubation $\eta(t)$ grow 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 ist that we obtain a time scale $\frac{1}{\left|\frac{df}{dx}(x^*)\right|}$ which governs the exponential growth or decay. <u>Remark</u>: In cases where $\frac{df}{dx}f(x^*) = 0$ nothing can be said

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

$(0,0)$ is stable $(0,0)$ is unstable

all stable

$(0,0)$ is halfstable
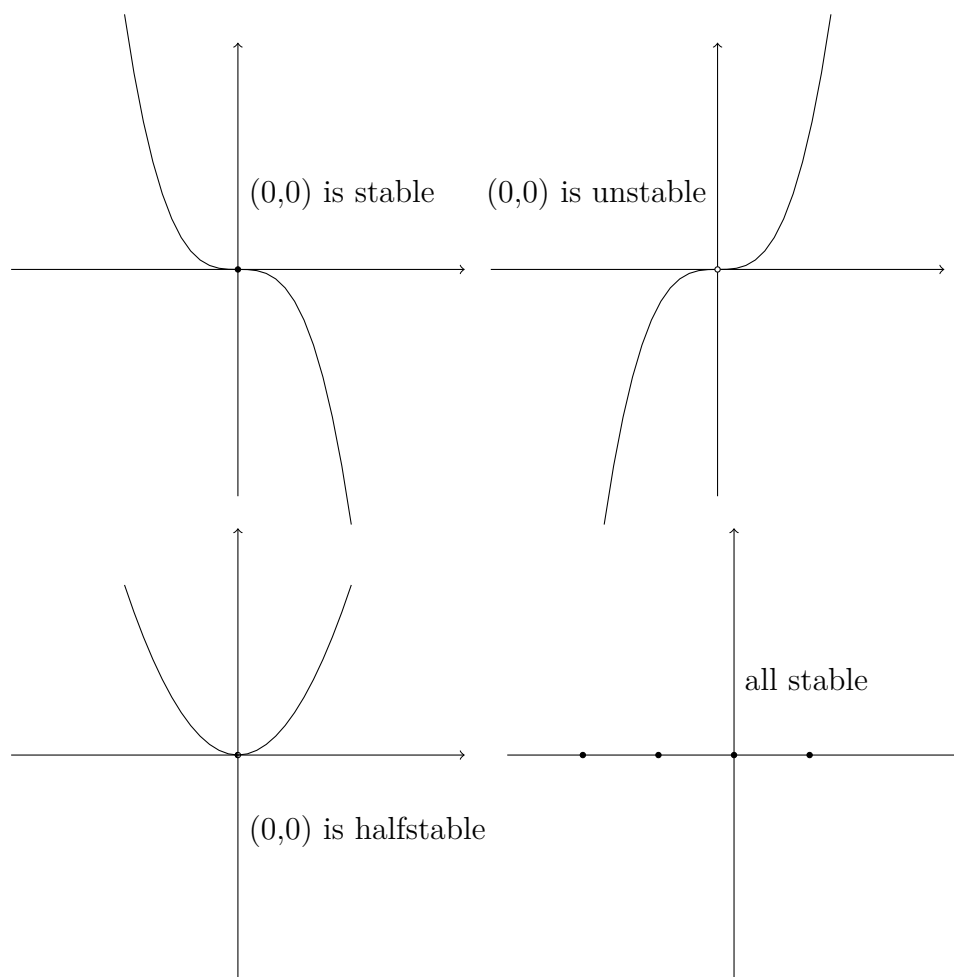
So far we did not consider the existence and uniqueness of the solutions. The importance of that issue is illustrated by the following example:

<u>Example</u>: Consider $\dot{x} = \sqrt[3]{x}$ and use tie 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 $c = 0 \quad \rightsquigarrow \quad x(t) = \left(\frac{2}{3}t\right)^{\frac{3}{2}}$ is also a solution!
In case of a non-unique solution our analysis obiously fails!
So, we have to ask, which conditions are neccessary to obtain a unique solution.

Exsitence 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: $\dot{x} = 1 + x^2; \quad x(0) = x_0$. 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 $t \to \frac{\pi}{2}$, 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.

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

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

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

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stable fixpoint

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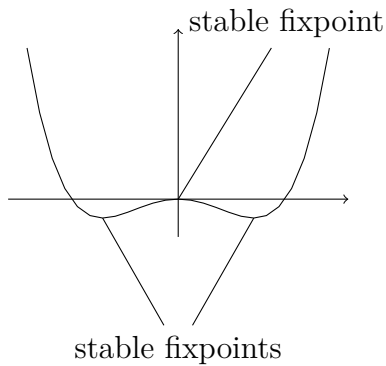
Bifurcations: 1D flows are simle: Either they converge to a fixed point or head on to $\pm\infty$. The most interesting aspect of 1D flows is their parameter dependence.

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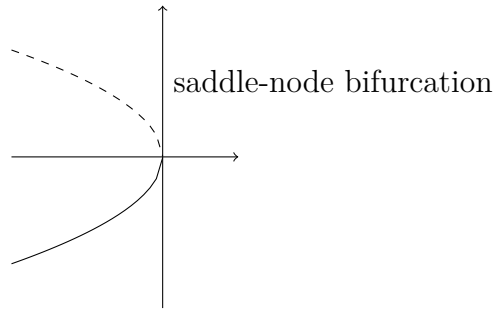
Saddle-Node-Bifurcation

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

one stable and
one unstable fixpoint   half-stable fixpoint   no fixpoint
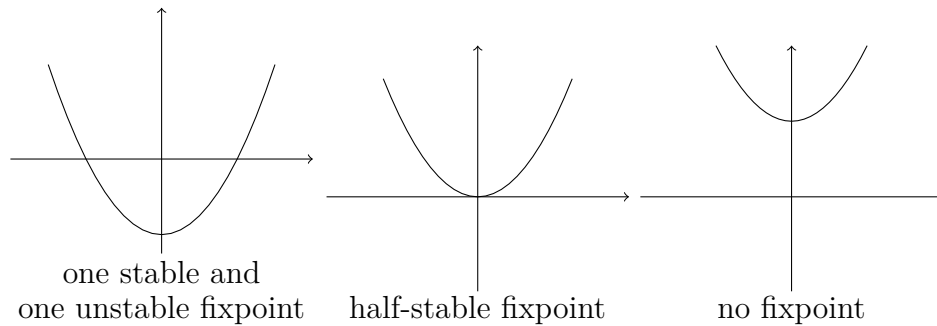
The fixpoints are located on the curve $r = -x^2$
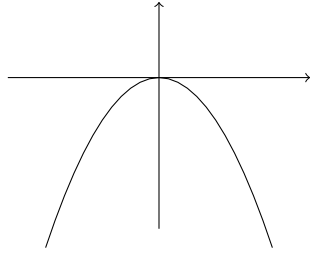
Typically the axes are inverted since r is the independent variable
Bifurcation diagram:

saddle-node bifurcation

<u>Example</u>: 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 curces e^{-x} and $r - x$ intersect upon variation of r we get:
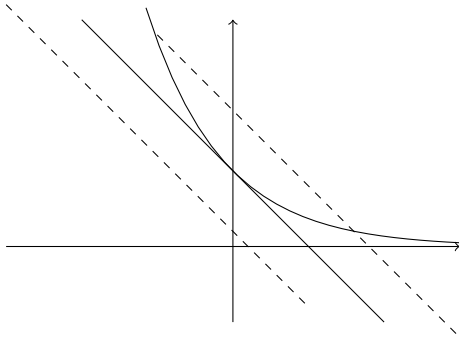
Normal forms: The form $\dot{x} = r \pm x^2$ is prototypical for saddle-node bifurcations. This can be understood from the following argument:
We consider $\dot{x} = f(x, r)$ near the bifurcation point at $x = x^*$ and $r = r_c$.

$$\rightsquigarrow \dot{x} = f(x, r) = f(x^*, r_c) + (x - x^*) \frac{\partial f}{\partial x}\Big|_{(x^*, r_c)} + (r - r_c) \frac{\partial f}{\partial r}\Big|_{(x^*, r_c)} + \frac{1}{2}(x - x^*)^2 \frac{\partial^2 f}{\partial x^2}\Big|_{(x^*, r_c)} + \cdots$$

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.

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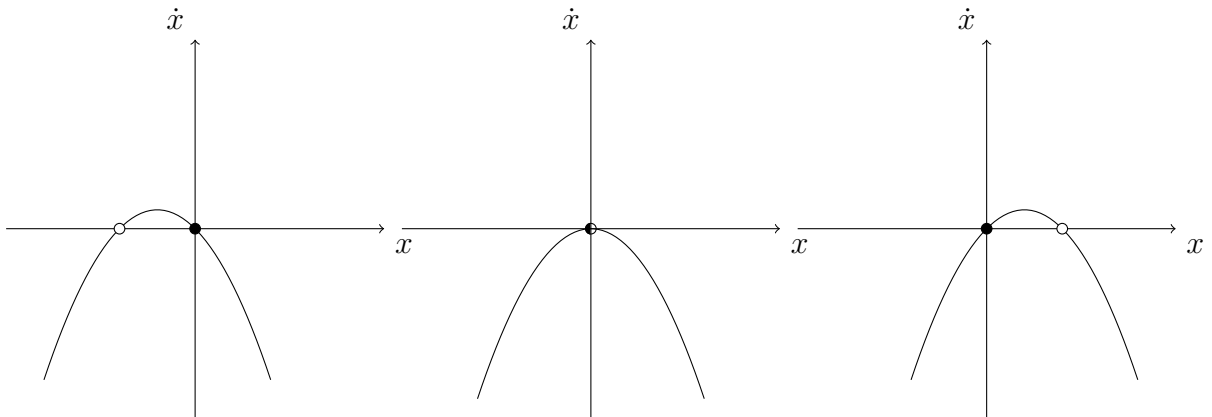We also have $\frac{\partial}{\partial x} f \Big|_{(x^*, r_c)} = 0$ by the tangency condition. Therefore, we are left with:

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

where $a = \frac{\partial f}{\partial r} \Big|_{(x^*, r_c)}$ and $b = \frac{\partial^2 f}{\partial x^2} \Big|_{(x^*, r_c)}$
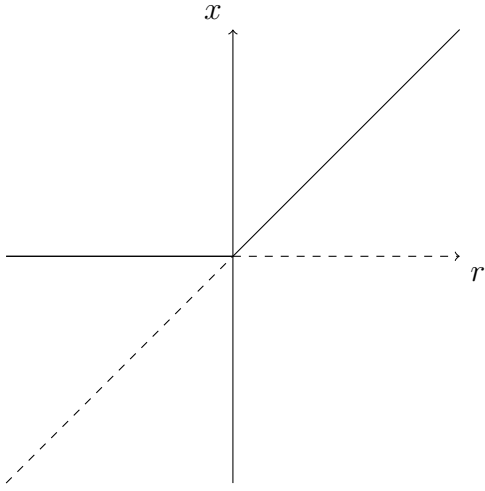
Transcritical bifurcation

Normal form of a transcritical bifurcation

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

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

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

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:

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

This leads to:

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

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

$\Rightarrow$ The non-zero fixed point is given at $(1 - ab) + \frac{1}{2}ab^2x = 0$
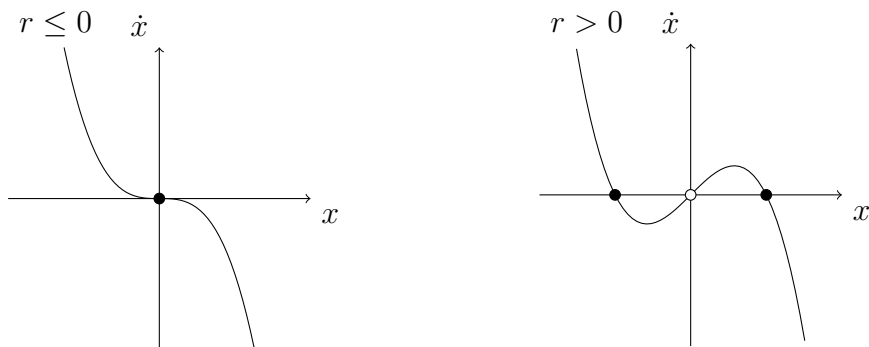
$$\Rightarrow x^* = \frac{2(ab - 1)}{ab^2}$$

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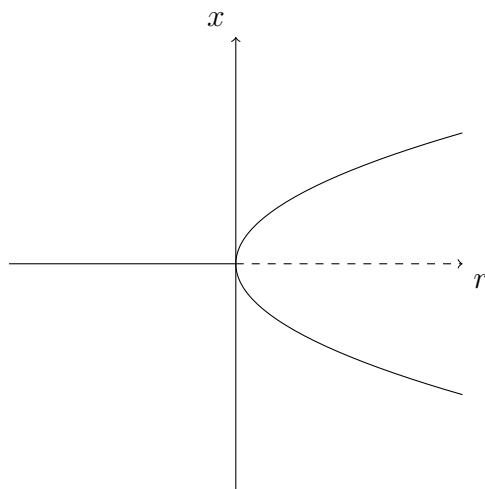
Supercritical Pitchfork bifurcation

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

Note that this equation is invariant under the exchange of the variable $x \to -x$. We get the following vector fileds for different values of r
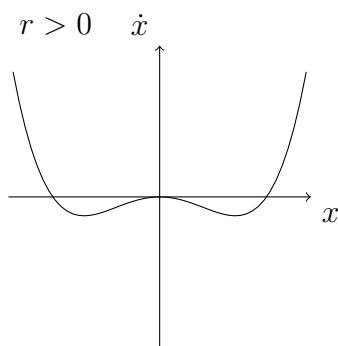
$r \leq 0 \quad \dot{x}$

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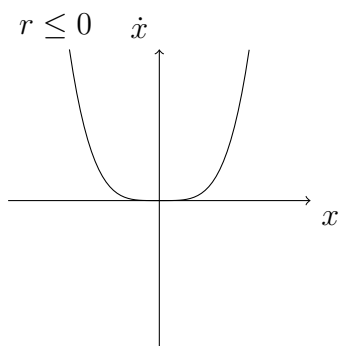
At $r = 0$ we observe a transition from a single stable Fixpoint at $x^* = \pm\sqrt{r}$. The fixpoint at $x^* = 0$ gets unstable.
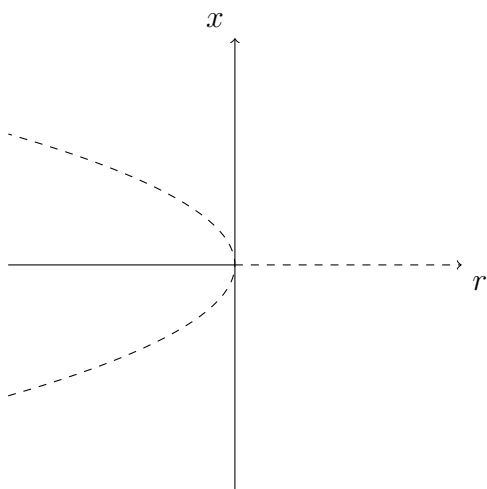
Bifurcation diagram:

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

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$r \leq 0$ $\dot{x}$

x

$r > 0$ $\dot{x}$

x

Subcritical pitchfork bifurcation

Normal form: $\dot{x} = rx + x^3 \leftarrow$ the cubix term is destabilizing.
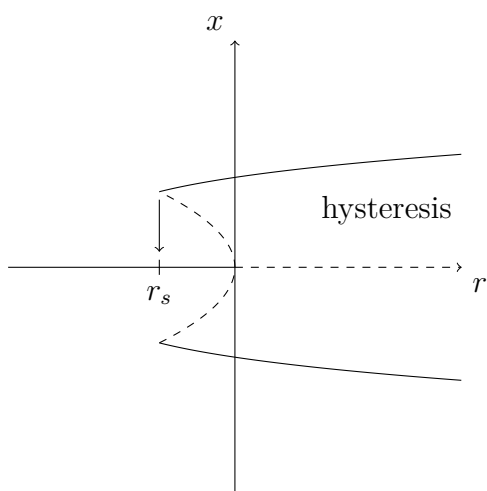
<u>Bifurcation diagram</u>

x

r

The nonzero fixed points are located at $x^* = \pm\sqrt{r}$. The 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: $\dot{x} = xr + x^3 - x^5$. The system has still the $x \to -x$ symmetry.

Remark:

1) In the range $r_s < r < 0$ two qualitatively different stable fixed points exist. The fixed points at the origin is <u>locally</u> 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 allowsus to get periodic solutions in a 1D-system.

<u>Example</u>: Vector filed corresponding to $\dot\theta = \sin(\theta)$
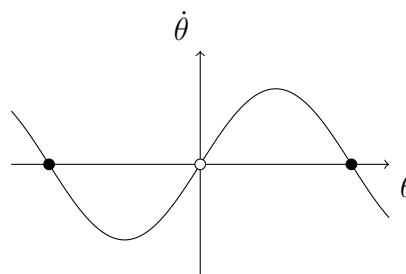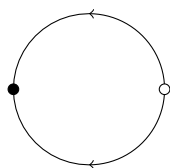
A vector field on a circle is a rule that assigns a unique velocity vector to a point on the circle. Therefore $f(\theta)$ has to be a periodic function. There is for example no unique velocity for $\dot\theta = \theta$ since $\theta = 0$ and $\theta = 2\pi$ correspond to the same point on a circle but to different velocities.

<u>**Uniform oscillator**</u>: A point on a circle is often called phase or angle. And

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

<u>Nonuniform oscillator</u>: $\dot\theta = \omega - a\sin(\theta) \quad , a, \omega > 0$

In this realization of the oscillator its velocity is not constant anymore.
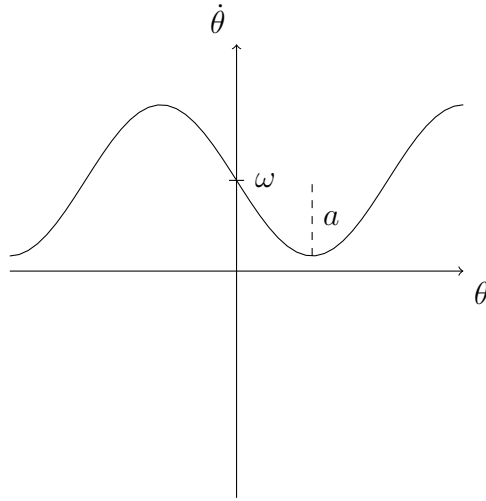
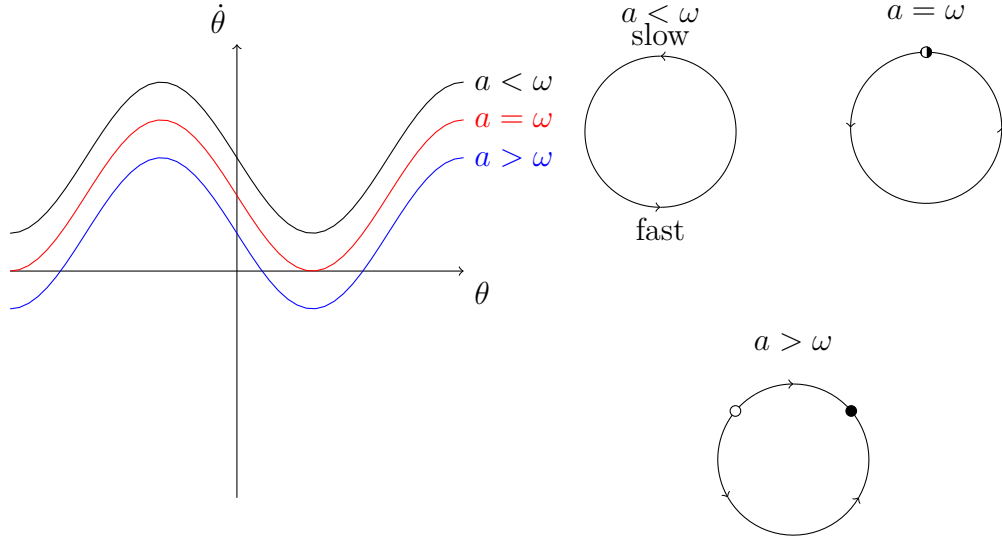We now discuss the parameter space of the system:
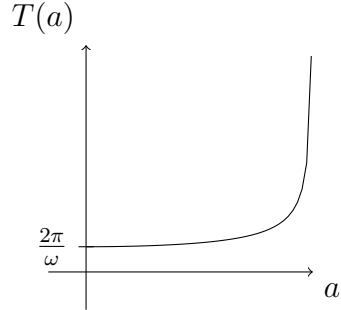
$a = 0$ We return to the uniform oscillator

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

<u>Bottleneck</u>: If $\omega > 0$ but $\omega - a << 1$ the system slows down considerably. The phase point $\theta(t)$ takes a long time to passt 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

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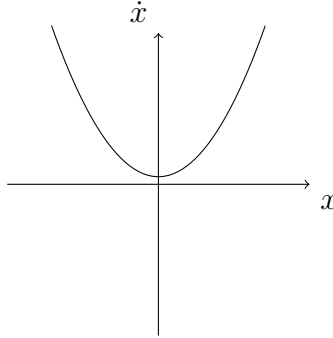
$$T \approx \frac{\pi\sqrt{2}}{\sqrt{\omega}} \frac{1}{\sqrt{\omega - a}} \approx (a_c - a)^{-\frac{1}{2}}$$

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:

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

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

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

$$\dot{x} = ax + by$$
$$\dot{y} = cx + dy$$

This system can be rewritten as:

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

Linearity implies that $\underline{x} = c\underline{x}_1 + c\underline{x}_2$ 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

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

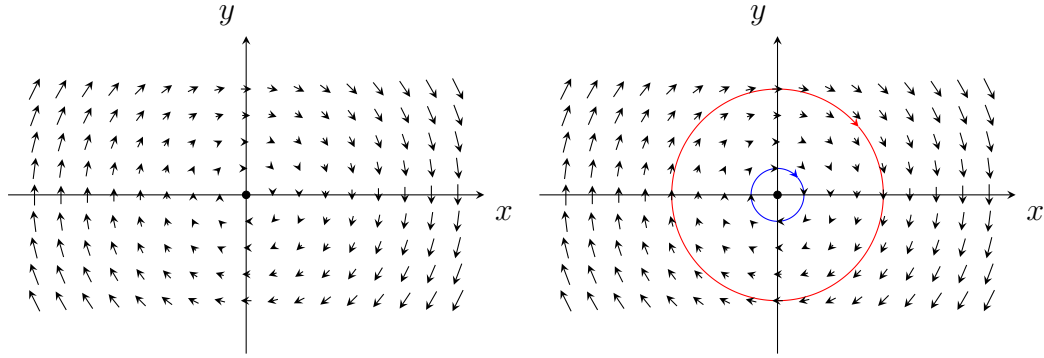Again, we obtain a vectorfield which we want to analyse in the following:
At the x-axis (i.e. $v = 0$) we get:

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

Similarly, we get:

$$\dot{x} = v \quad \text{at the } v\text{-axis}$$
$$\dot{v} = 0$$

Usign similar arguments we get:

<u>Classification of linear systems</u>:

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:

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

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

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

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

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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 sytem.
We obtain the following classification of fixed points:
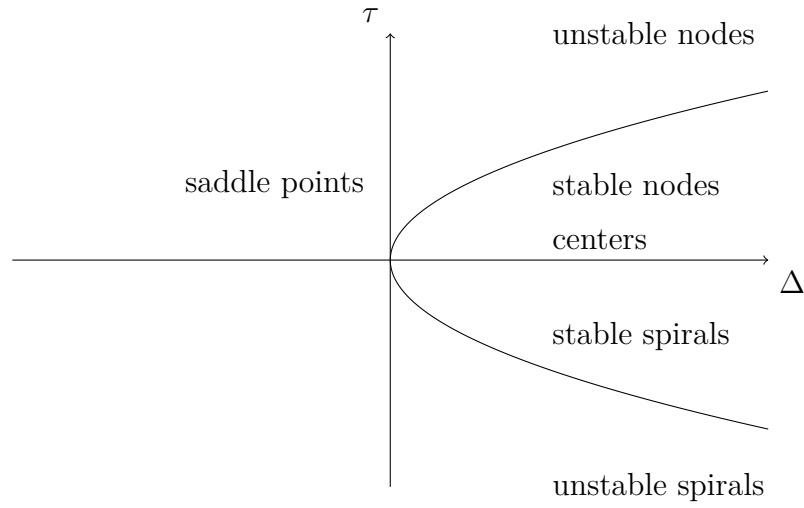
The classification can be obtained by using the following equations

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

$\Delta < 0$: 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, $\tau^2 - 4\Delta < 0$)
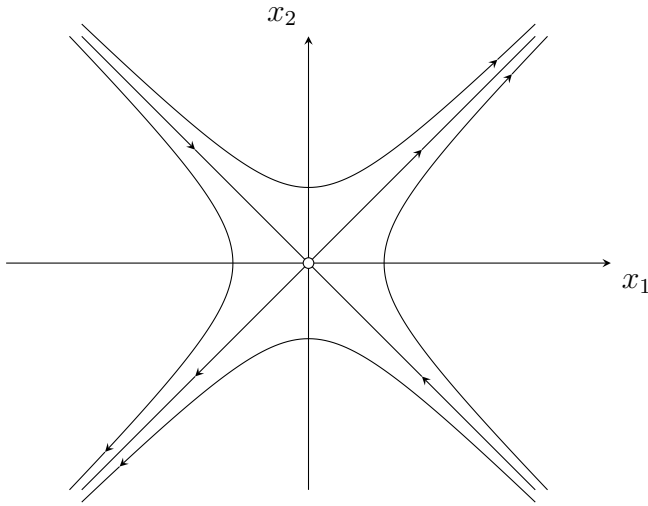$\tau < 0$: Both eigenvalues have negative real parts $\to$ stable spirals
$\tau > 0$: unstable nodes and spirals
$\tau = 0$: stable
$\Delta = 0$: At least one of the eigenvalues is zero $\to$ origin is not an isolated fixed point
Phase plane: From now on we consider non-linear two-dimensional systems
Phase-Portrait: Vectorfield:

$$\underline{x}_1 = f_1(x_1, x_2)$$
$$\underline{x}_2 = f_2(x_1, x_2)$$

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

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

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

where

$$k_1 = \underline{f}\left(\underline{x}_n\right)\Delta t \qquad\qquad k_2 = \underline{f}\left(\underline{x}_n + \frac{1}{2}\underline{k}_1\right)\Delta t$$

$$k_3 = \underline{f}\left(\underline{x}_n + \frac{1}{2}\underline{k}_2\right)\Delta t \qquad\qquad k_4 = \underline{f}\left(\underline{x}_n + \underline{k}_3\right)\Delta t$$

Example: We consider the system

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

Fixed point: $\dot{x} = 0, \dot{y} = 0 \quad \Rightarrow \quad y = 0; x = -1$ corresponds to a fixed point
The solution of $\dot{y} = -y$ is given by $y(t) = y_0 e^{-t}$
$\underset{t \to \infty}{\rightsquigarrow} y(t) = 0 \underset{t \gg 1}{\rightsquigarrow} \dot{x} = x+1$ This equation has exponentially growing solution,
which indicates, that the fixed point is unstable.
The phaseportrait can be construted 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 $\dot{y} = 0$.

$$\dot{y} = 0 \rightsquigarrow \text{ horizontal flow}$$
$$\dot{x} = 0 \rightsquigarrow \text{ vertical flow.}$$
$$\text{We have } x + e^{-y} = 0 \rightsquigarrow y = \ln\left(-\frac{1}{x}\right)$$
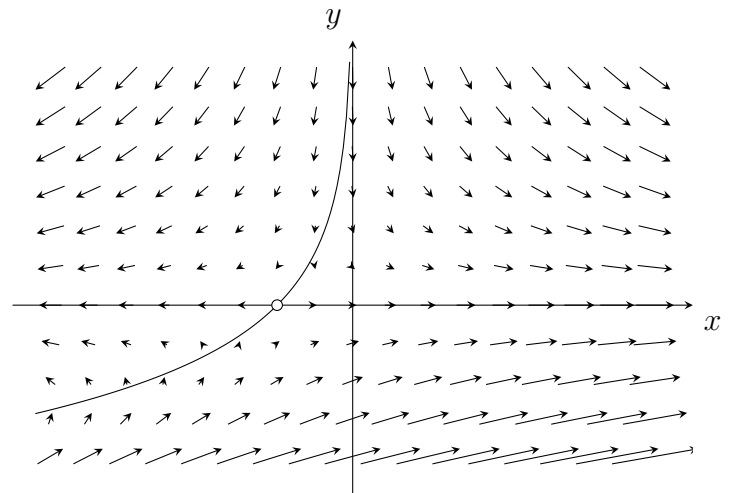
Existence, uniqueness and topological consequences

Theorem: Consider the initial value problem $\dot{\underline{x}} = \underline{f}(\underline{x}); \underline{x}(0) = \underline{x}_0$
Suppose that $\underline{f}$ is continuous and that all its partial derivatives $\frac{\partial f_i}{\partial x_j}$, $i, j = 1, 2, \ldots, n$ are continuous for $\underline{x}$ in some open connected set $D \in \mathbb{R}^n$. Then for $\underline{x}_0 \in D$, 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:

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

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

$$\Pi(r) \sim \frac{1}{\sqrt{2\pi N}}\left(\frac{r}{N}\right)^{-r-\frac{1}{2}}\left(\frac{N-r}{N}\right)^{-N+r-\frac{1}{2}} p^r q^{N-r}$$

$$= \frac{1}{\sqrt{2\pi N}}\exp\left(-\left(r+\frac{1}{2}\right)\ln\left(\frac{r}{N}\right) - \left(N-r+\frac{1}{2}\right)\ln\left(\frac{N-r}{N}\right) + r\ln(p) + (N-r)\ln(q)\right)$$

Now, assuming that $1 << y << Np$, 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:

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

where we have considered symmetric hopping <u>rates</u> (<u>not</u> 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:

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

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 Mster-equations is given by:

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

$$= \left(\gamma\left(e^{ik} + e^{-ik}\right) - 2\right)P(k,t) \qquad (**)$$

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

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

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:

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

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

$$f'(x) = \lim_{\Delta x \to 0}\frac{f(x + \Delta x) - f(x)}{\Delta x} \qquad \text{and}$$

$$f''(x) = \lim_{\Delta x \to 0}\frac{f'(x + \Delta x) - f'(x)}{\Delta x}$$

$$= \lim_{\Delta x \to 0}\frac{f(x + 2\Delta x) - f(x + \Delta x) - f(x + \Delta x) + f(x)}{(\Delta x)^2}$$

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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

$$P(k,t) = \int\limits_{-\infty}^{\infty} P(x,t)e^{ikx}dx; \; P(x,t) = \frac{1}{2\pi} \int\limits_{-\infty}^{\infty} P(k,t)e^{-ikx}dk$$

$$\rightsquigarrow \frac{\partial P(k,t)}{\partial t} = -Dk^2 P(k,t) \; \Rightarrow \; P(k,t) = P(k,0)e^{-k^2 Dt}$$

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

Inverting the Fouriertransform we obtain:

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

<u>Central limit theorem</u> (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 $y_N = \sum\limits_{n=1}^{N} x_n$ 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:

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

(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 $P_N(k) = P_0(k)\left[p(k)\right]^N$. For $P_0(x) = \delta_{x,0}$ we get $P_0(k) = 1 \& P_N(k) = \left[p(k)\right]^N$. The distribution in real space is then given by

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

We now find that

$$p(k) = \int\limits_{-\infty}^{\infty} p(x)e^{ikx}dx = \int\limits_{-\infty}^{\infty} p(x)\left[1 + ikx - \frac{1}{2}k^2x^2 + \mathcal{O}(x^3)\right]dx$$

$$= 1 + ik\langle x \rangle - \frac{1}{2}k^2\langle x^2 \rangle + \cdots$$

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

$$P_N(y) \approx \frac{1}{2\pi} \int\limits_{-\infty}^{\infty} \left[1 + ik\langle x \rangle - \frac{1}{2}k^2\langle x^2 \rangle\right]^N e^{-iky}dk$$

$$= \frac{1}{2\pi} \int\limits_{-\infty}^{\infty} \exp\left[N\ln\left(1 + ik\langle x \rangle - \frac{1}{2}k^2\langle x^2 \rangle\right)\right]e^{-iky}dk$$

$$\underset{\mathcal{O}(\langle x \rangle^2, \langle x^2 \rangle)}{\approx} \frac{1}{2\pi} \int\limits_{-\infty}^{\infty} \exp\left[N\left(ik\langle x \rangle - \frac{k^2}{2}\left(\langle x^2 \rangle - \langle x \rangle^2\right)\right)\right]e^{-iky}dk$$

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.

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

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:

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

$$= ar(\frac{1}{z} - 1)F + a(1-z)\frac{\partial F}{\partial z} + bg(z-1)F + b(z^2 - z)\frac{\partial F}{\partial z}$$

$$= (1-z)(a-bz)\frac{\partial F}{\partial z} + (1-z)\left(\frac{ar}{z} - bg\right)F$$

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

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

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

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

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

$$-\frac{dz}{a - bz} = \frac{d\log(F)}{\frac{ar}{z} - bg} \rightsquigarrow$$