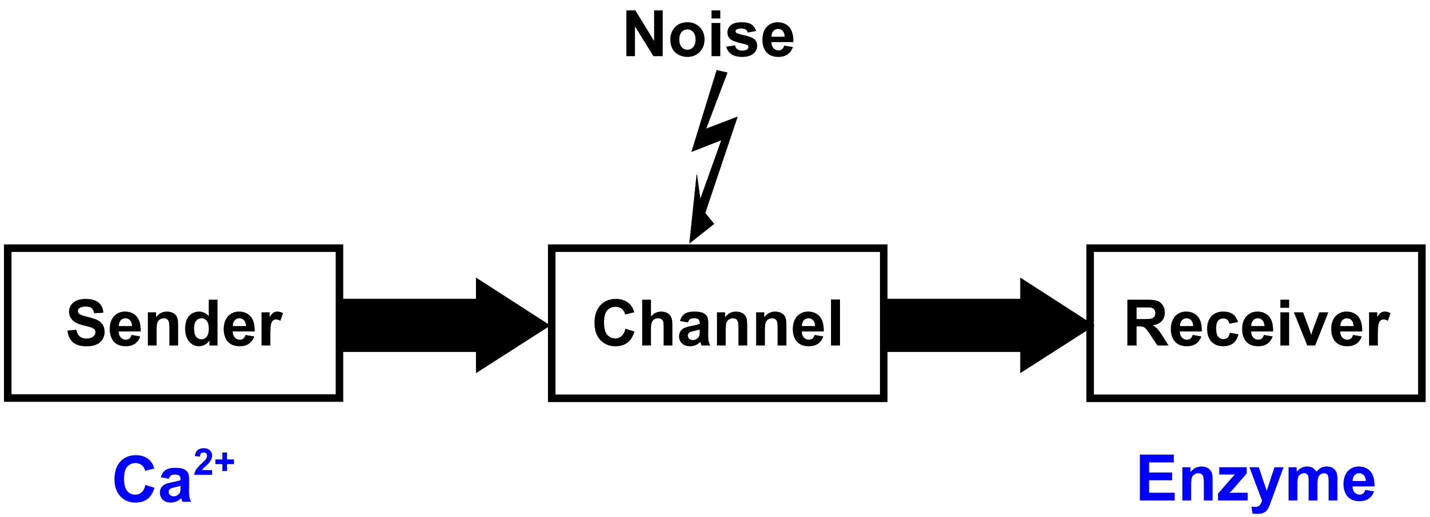
Seminar
Information processing in living systems

Dr. Jürgen Pahle
UdS, Saarbrücken
27.4.2012

Information theory

- Claude E. Shannon (1916-2001)
  "Mathematical Theory of Communication" (1948)
- Information theory can answer questions about limits of faithful information transfer over a given (noisy) channel etc.

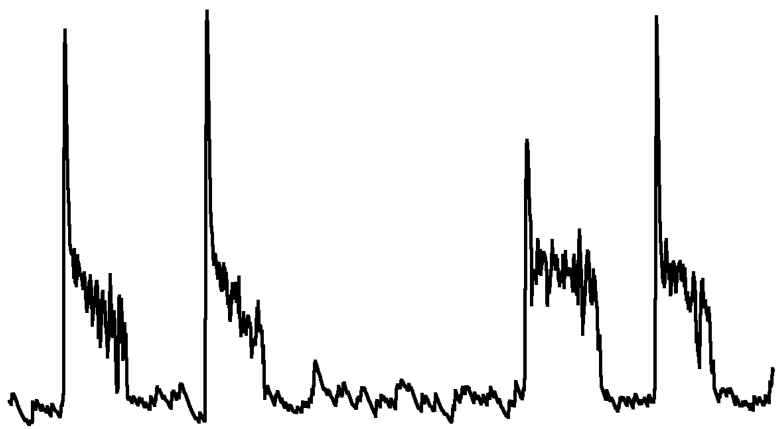


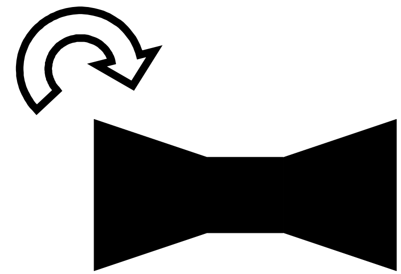
Signal transduction via Calcium

Hormones (angiotensin II, vasopressin etc.)

Nucleotides (ATP, UTP)

Ca^{2+}-signal





bow tie structure

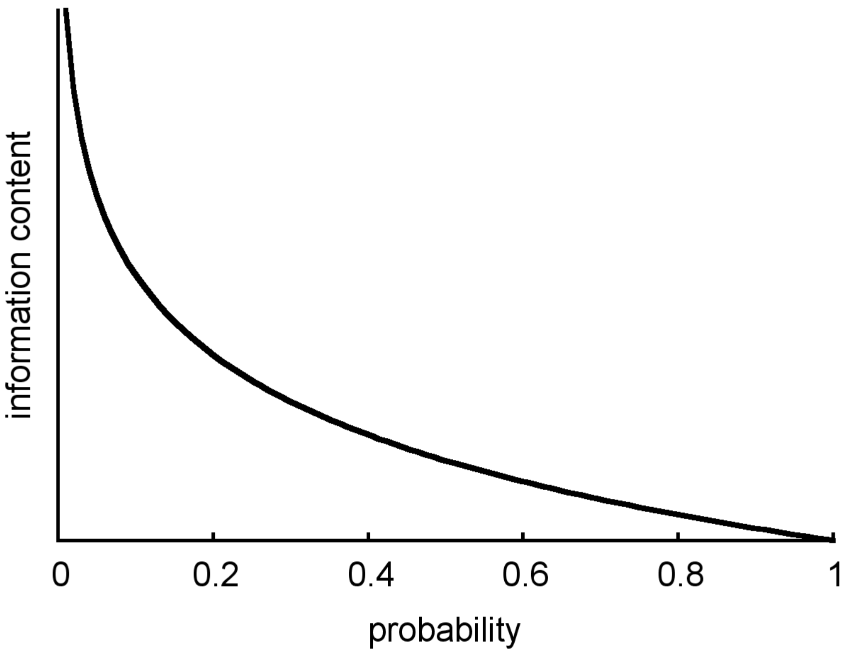
calcium code?

Target proteins (calmodulin, phosphorylase b kinase, etc.)

Transcription factors (NF-κB, etc.)

How to quantify information?

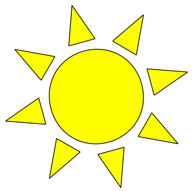
Information content of an event
→ uncertainty
(negative log of probability)



Average uncertainty of all possible events
→ so-called entropy

Information = decrease in uncertainty

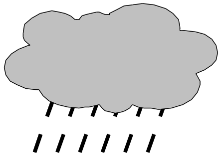
Weather example



50%

Probability(sunny) = ½

→ Uncertainty(sunny) = 1.0



50%

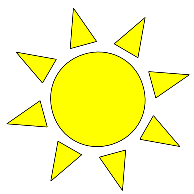
Probability(rainy) = ½

→ Uncertainty(rainy) = 1.0

On average (entropy of the weather)

→ 1.0 [bit/day]

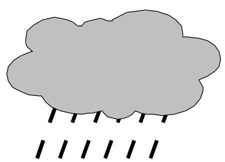
Weather example



100%

Probability(sunny) = 1.0

→ Uncertainty(sunny) = 0.0



0%

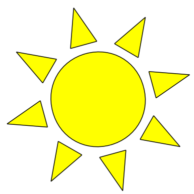
Probability(rainy) = 0

→ Uncertainty(rainy) = 0.0 per convention

On average (entropy of the weather)

→ 0.0 [bit/day]

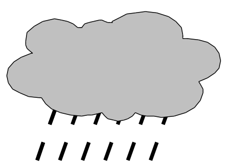
Weather example



80%

Probability(sunny) = 0.8

→ Uncertainty(sunny) = 0.32



20%

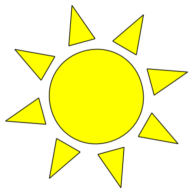
Probability(rainy) = 0.2

→ Uncertainty(rainy) = 2.32

On average (entropy of the weather)

→ 0.64 [bit/day]

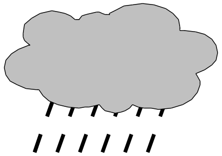
Weather example (London)



220/365

Probability(sunny) = 0.603

→ Uncertainty(sunny) = 0.73



145/365

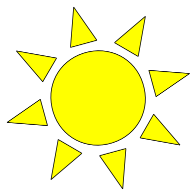
Probability(rainy) = 0.397

→ Uncertainty(rainy) = 1.33

On average (entropy of the weather in London)

→ 0.97 [bit/day]

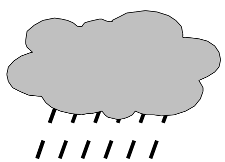
Weather example



p%

Probability(sunny) = p

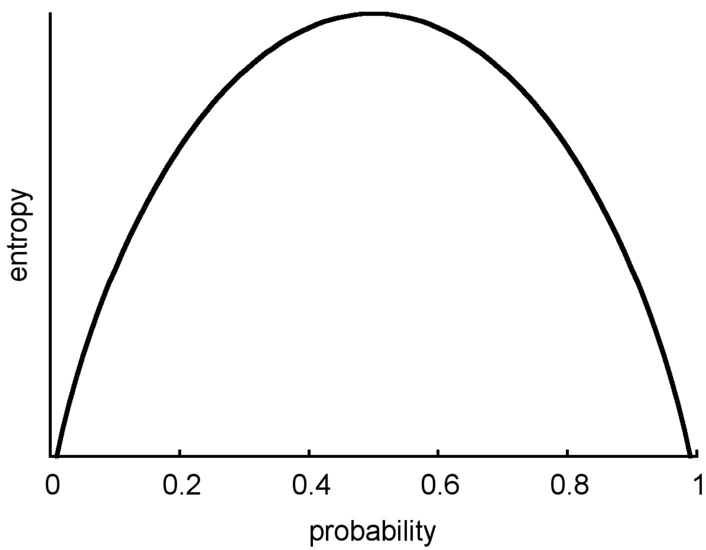
→ Uncertainty(sunny) = - $\log_2(p)$



(1-p)%

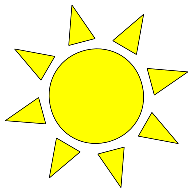
Probability(rainy) = 1-p

→ Uncertainty(rainy) = - $\log_2(1-p)$



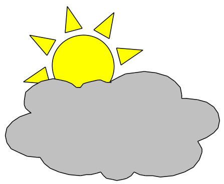
On average (entropy of the weather) [bit/day]

Weather example



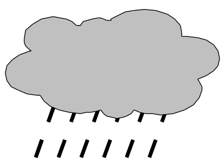
Probability(sunny) = 0.25

→ Uncertainty(sunny) = 2.0



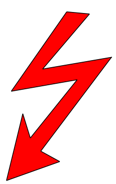
Probability(cloudy) = 0.25

→ Uncertainty(cloudy) = 2.0



Probability(rainy) = 0.25

→ Uncertainty(rainy) = 2.0



Probability(thunderstorm) = 0.25

→ Uncertainty(thunderstorm) = 2.0

On average (entropy of the weather)

→ 2.0 [bit/day]

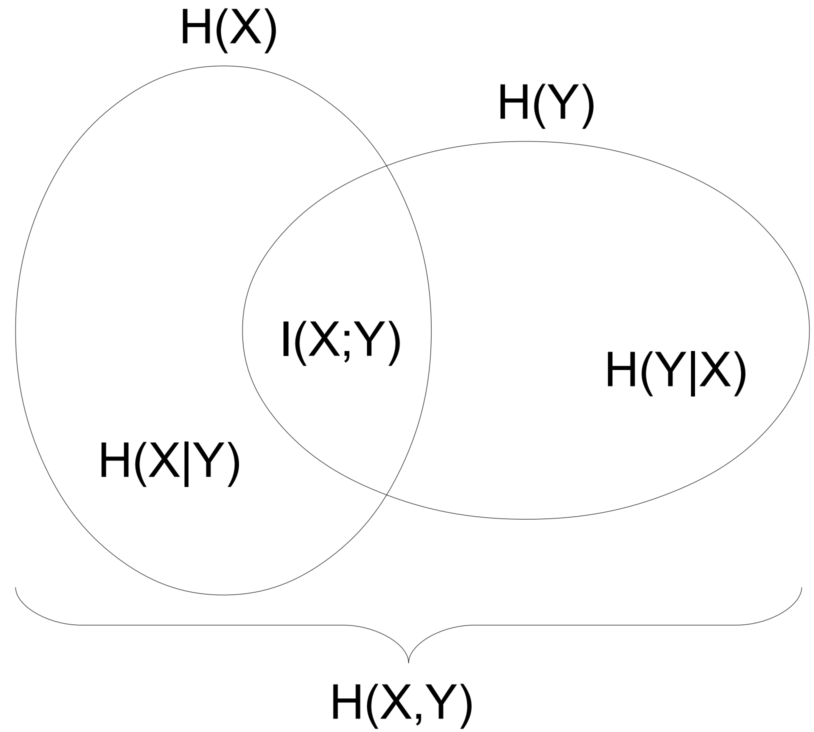
Entropy and Mutual information

$$H(X) = -\sum_{x} p(x) \log p(x)$$

Entropy

$$D(p\|q) = \sum_{x} p(x) \log \frac{p(x)}{q(x)}$$

Relative Entropy /
Kullback-Leibler Divergence

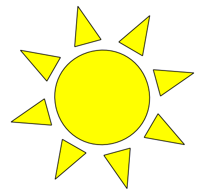
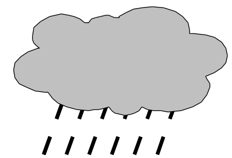
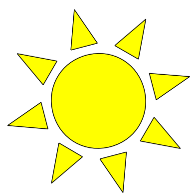
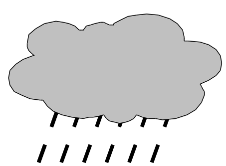


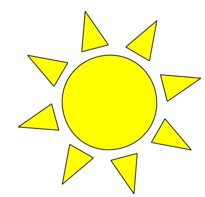
$$I(X;Y) = \sum_{x,y} p(x,y) \log \frac{p(x,y)}{p(x)\,p(y)}$$

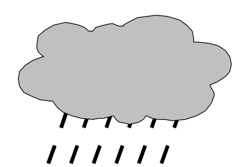
Mutual
Information

"Reduction of uncertainty about X
due to the knowledge of Y"

Weather dynamics

		
	0.75	0.25
	0.5	0.5

 ⅔

 ⅓

Markov process

- Markov process can not remember former states, only current state determines future
- *Markovian* modeling is used in a variety of fields:
  - Communication:
    Telephone system (Hidden Markov models)

  - Hard disks

  - Language recognition
  - PageRank algorithm of Google
  - Biological modeling: Population dynamics, etc.
  - Games of chance (chutes and ladders)

Information/Entropy-rate

The information gained by observing tomorrow's weather, when the today's weather is known:

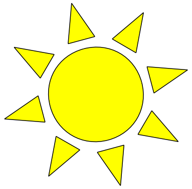
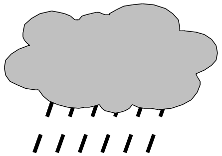
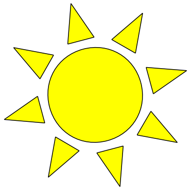
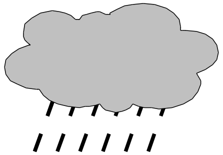
Entropy(tomorrow's weather | today's weather)
→ conditional probabilities

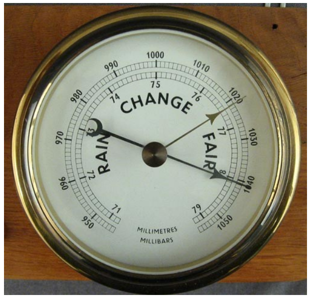
In our example:

Entropy(tomorrow's weather) = 0.92 [bit/day]

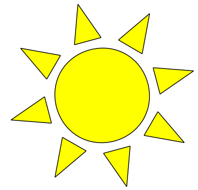
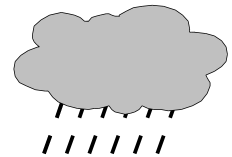
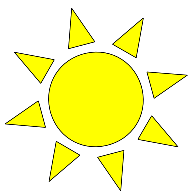
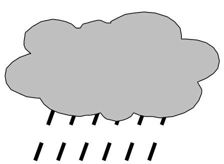
Entropy(tomorrow's weather | today's weather) = 0.87 [bit/day]

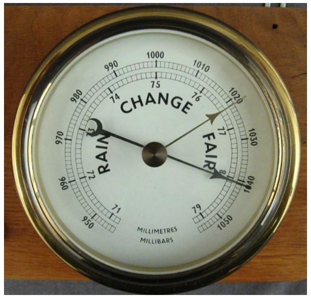
Weather dynamics

			
	high	0.9	0.1
	low	0.6	0.4
	high	1	0
	low	0	1



Weather dynamics (London)

1.3.2010, 12:00: 1012 hPa → slightly low			
	high	0.9	0.1
	low	0.6	0.4
	high	1	0
	low	0	1



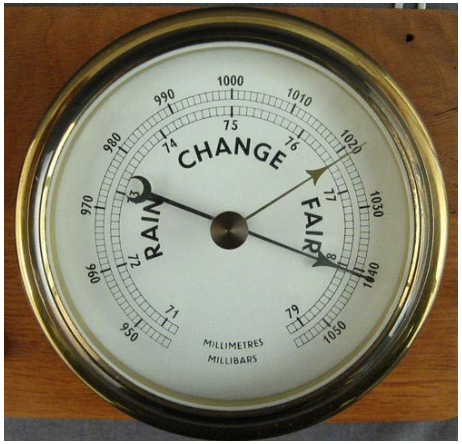
Information provided by the barometer

Information =

Uncertainty (without barometer)

minus

Uncertainty (with barometer)



Assumption Probability(high) = Probability(low) = 0.5

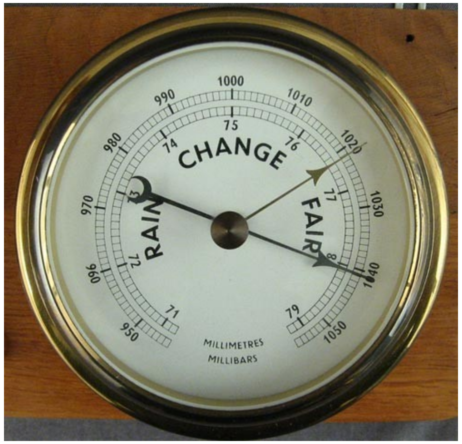
Information provided by the barometer

Information =

Uncertainty (without barometer)

minus

Uncertainty (with barometer)



Assumption Probability(high) = Probability(low) = 0.5

Information = 0.39 [bit/day]

Transfer Entropy

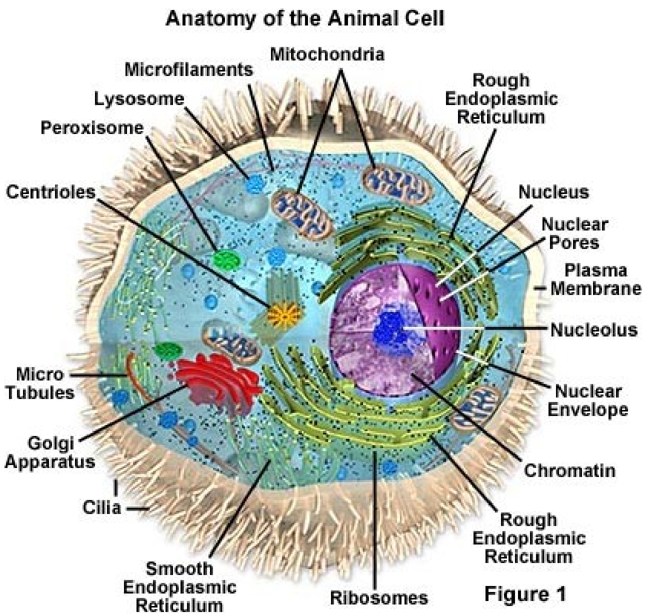
Quantifies the information transferred by calculating how much uncertainty is lost (or information gained) about a dynamic stochastic process, when the value of the driving signal is known

Kullback-Leibler-form

T. Schreiber (2000), Phys. Rev., 85(2), 461-4

$$T_{J \to I} = \sum p\left(i_{n+1}, i_n^{(k)}, j_n^{(l)}\right) \log\left(\frac{p\left(i_{n+1} | i_n^{(k)}, j_n^{(l)}\right)}{p\left(i_{n+1} | i_n^{(k)}\right)}\right)$$

How-To (Biochemical modeling)



- Compartments (nucleus, cytosol, ...)
- Species (proteins, small molecul., ions,...)
- Reactions (decay, ...)
- Kinetics (velocity of reactions)

$$\frac{\mathrm{d}G_\alpha}{\mathrm{d}t} = k_1 + k_2 \cdot G_\alpha - \frac{k_3 \cdot PLC \cdot G_\alpha}{(K_4 + G_\alpha)} - \frac{k_5 \cdot [Ca^{2+}] \cdot G_\alpha}{(K_6 + G_\alpha)} \qquad G_\alpha(t_0) = 0.01\ nmol$$

$$\frac{\mathrm{d}PLC}{\mathrm{d}t} = k_7 \cdot G_\alpha - \frac{k_8 \cdot PLC}{(K_9 + PLC)} \qquad PLC(t_0) = 0.01\ nmol$$

$$\frac{\mathrm{d}[Ca^{2+}]}{\mathrm{d}t} = k_{10} \cdot G_\alpha - \frac{k_{11} \cdot [Ca^{2+}]}{(K_{12} + [Ca^{2+}])} \qquad [Ca^{2+}](t_0) = 0.01\ nmol$$

Simulation:

- How does the system change over time?

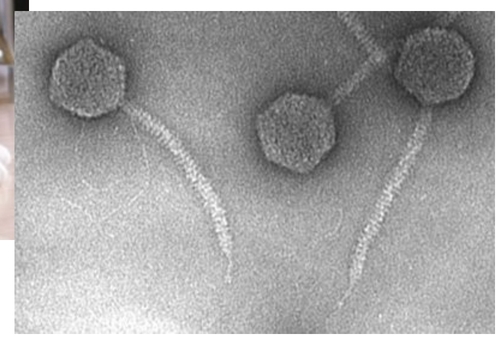
Analysis of the model:

- Which parts influence the behavior most?
- Which states are stable (steady state, oscillations)?

Reasons for stochastic modeling

- Small particle numbers on single cell level (e.g. signal transduction, gene expression)
  → discreteness of the system, random fluctuations
- Bi-stable systems:

Calico cat

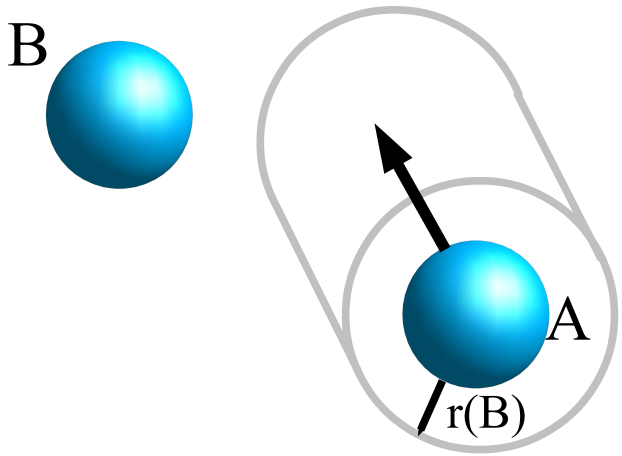


λ phage

- Stochasticity as an important property of the system: noise-sustained oscillations, stochastic resonance, etc.
- Extinction of species
- Rare events

images: commons.wikimedia.org

Basis of the Stochastic Approaches



$$a_\mu(x)\cdot dt = c_\mu \cdot h_\mu(x)\cdot dt$$

specific probabilistic reaction rate
product of

probability of collision
(~ average relative speed * collision cross-section area / volume) and

probability of reaction after collision
(collision energy larger than threshold)

number of different combinations of substrate particles

Chemical Master Equation (CME)

$$\frac{\partial P(x,t|x_0,t_0)}{\partial t} = \sum_{j=1}^{M} \left[a_j(x-\nu_j) * P(x-\nu_j,t|x_0,t_0) - a_j(x) * P(x,t|x_0,t_0) \right]$$

"probability flux"
to x from other states

"probability flux"
from x to other states

- ν_j is stoichiometric vector of reaction j
- More important for the simulation methods is the so-called Reaction Probability Density Function
  - When will the next reaction take place?
  - Which reaction will it be?

$$P(\tau,\mu) = \begin{cases} a_\mu \exp(-a_0 \tau) & \text{if } 0 \leqslant \tau < \infty \wedge \mu = 1,\dots,M \\ 0 & \text{otherwise} \end{cases}$$

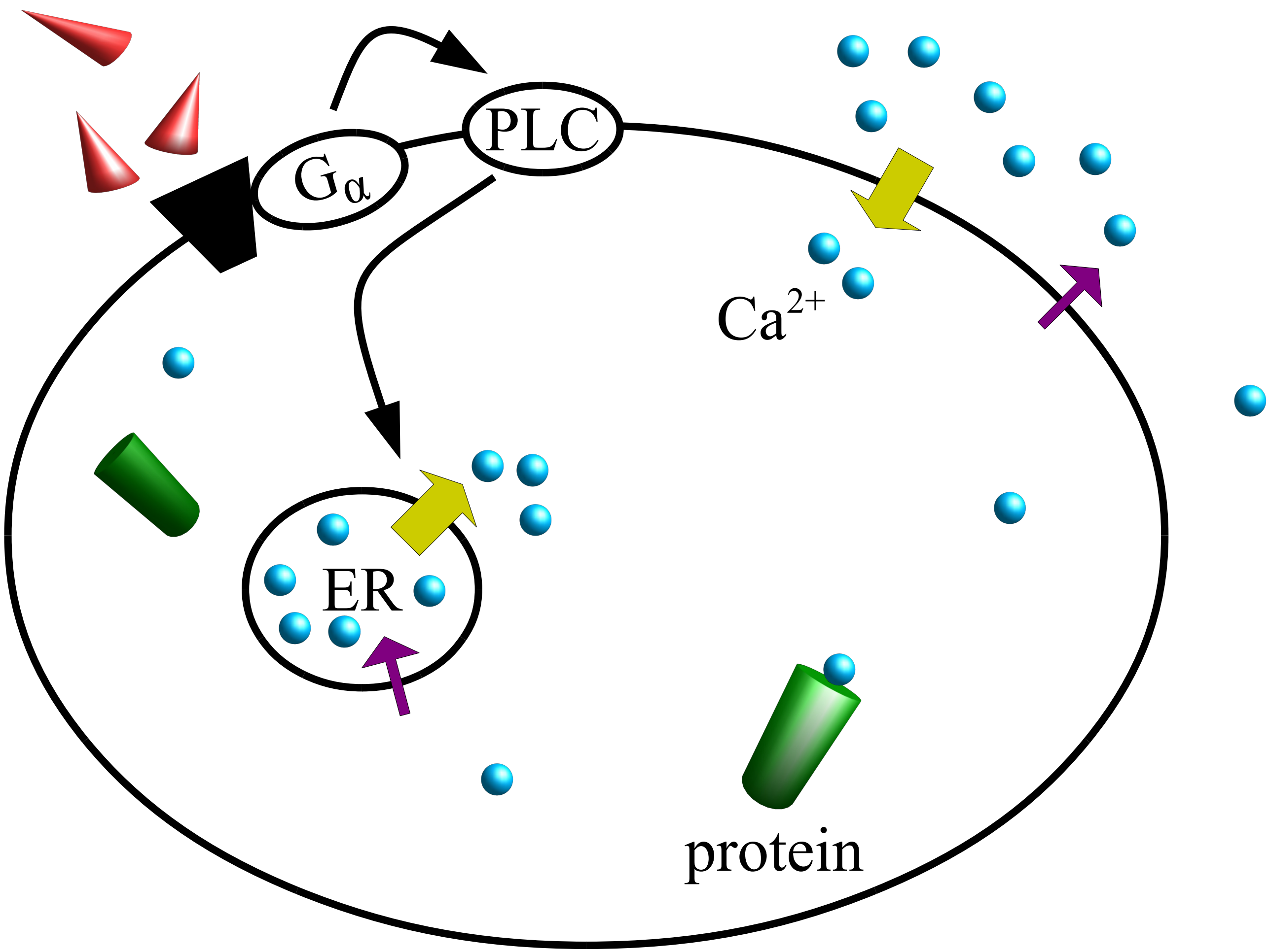
Stochastic Simulation *(Gillespie 1976)*

1) Calculate probabilities for all reactions
2) Calculate stochastic time step t (exponentially distributed, sum of all reaction prob.) $\tau = \frac{1}{a_0} \ln(r_1)$
3) Monte Carlo Simulation: The reaction to be realized is chosen by "playing roulette", discrete distribution

$$\sum_{\alpha=1}^{\mu-1} \frac{a_\alpha}{a_0} \leqslant r_2 \leqslant \sum_{\alpha=1}^{\mu} \frac{a_\alpha}{a_0}$$

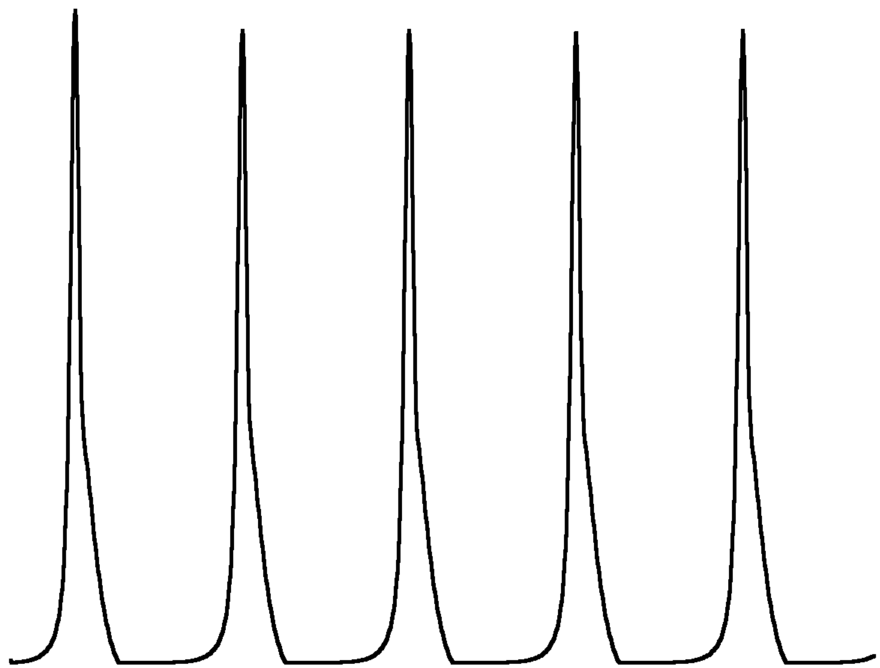
4) Instantiate the reaction: Change particle numbers according to stoichiometry

Signal transduction via Ca^{2+}-ions



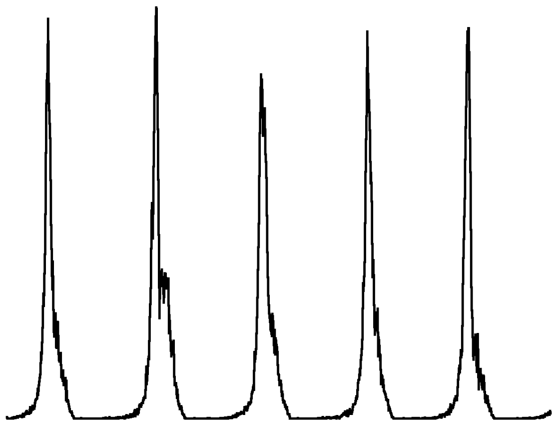
Calcium dynamics (simulated deterministically)

spiking

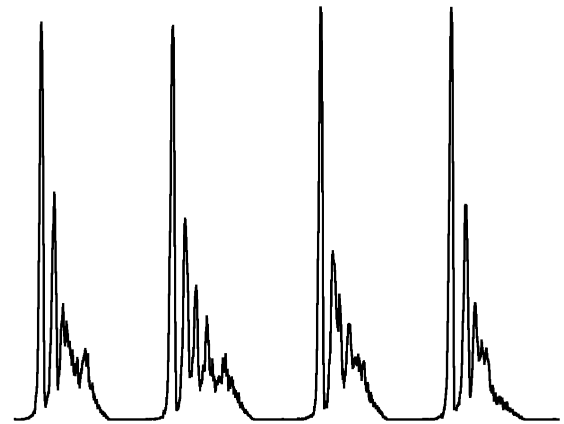


Calcium dynamics ***(simulated)***

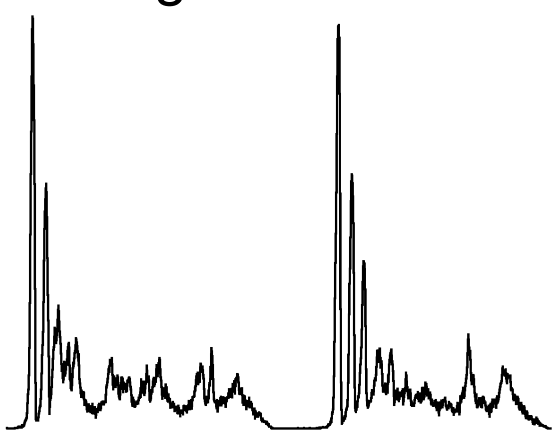
spiking



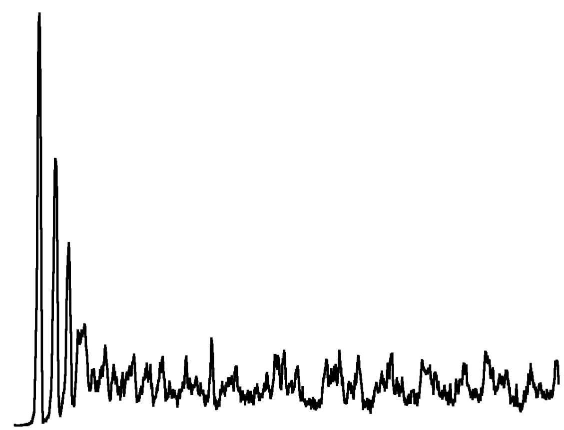
bursting



irregular/chaotic



overstimulation



Presentations & Write-ups

- What is/are the main question/s of the article?
- Have these questions been adequately answered?
- Summarize and **explain** the most important steps taken in the approach.
- Are there errors, inconsistencies, omissions?

- Would there be alternative approaches? Which ones? Why did the authors choose theirs?
- If approximations are involved, under which circumstances are they valid? When do they break?
- How does this work fit into the bigger field of research? Do the authors refer to closely related work?
- ...

Literature

Information Theory

- Cover and Thomas (1991) *Elements of Information Theory*. John Wiley & Sons, Inc., ISBN 0-471-06259-6
- Shannon (1948) A Mathematical Theory of Communication. *Bell System Technical Journal* **27**:379-423, 623-656

(Computational) Systems Biology

- Klipp et al. (2009) *Systems Biology - A Textbook*. WILEY-VCH, ISBN 978-3-527-31874-2

To agree on...

- Presentation days (14th and 15th June 2012, from 14:30)
- Opponents assignments
  - Pahle 2008 (Thorsten Klingen): Ugur Kira, Abirami Veluchamy
  - Gourevitch 2007 (Zeinab M.P.Aghdam): Thorsten Klingen, Pramod Kaushik Mudrakarta
  - Niven 2007 (Azim Dehghani Amirabad): Thorsten Klingen, Zeinab M.P.Aghdam
  - Staniek 2008 (Ugur Kira): Zeinab M.P.Aghdam, Azim Dehghani Amirabad
  - Ziv 2007 (Pramod Kaushik Mudrakarta): Daria Gaidar, Ugur Kira
  - Tkacik 2008 (Abirami Veluchamy): Azim Dehghani Amirabad, Daria Gaidar
  - Waltermann 2011 (Daria Gaidar): Abirami Veluchamy, Pramod Kaushik Mudrakarta