Theoretical Neuroscience Lecture Notes

26th February 2002

Part II
Neuroscience

N 1 The Single Neuron

Goal: quantitive modeling of the behaviour of neurons and networks there of.

→ understanding of the system (what mechanisms are at work? What effects do they have? Which phenomena are unimportant?)

- Neurons have electrical and chemical signals
- signal processing involves complex spatio-temporal processes

→ synapses translate electrical signals into chemical and vice versa

- transmission properties may change on short time scales (ms)
- depressive / fascilitating synapses (Markram)
- transmission properties can also change on longer time scales (mins / hrs) - *Long-Term-Potentiation (LTP), Long-Term-Depression (LTD), Hebbian Learning*

→ dendritic trees: passive (diffusive) spread of *post-synaptic-potentials (PSP)* - excitatory (EPSP) or inhibitory (IPSP)

- PSPs are theoretically well understood
- spread over the dendritic tree are so called *"hot spots"*, which work as amplifiers for the incoming currents
- active backpropagation of action potentials (Sakman)

→ soma: firing threshold, production of action potentials
→ axon: propagation of action potentials; the axon uses saltatory conduction for speeding up transmission

- mutliple biochemical mechanismsare involved: different ions, voltage-gated channels and ionic pumps

- simplification is necessary

→ different neurons have established (compartmental model, Hodgkin-Huxley-Model, integrate-and-fire-neuron, analog neuron, McCulloch-Pitts neuron (binary))

N 1.1 Electrical properties of the cell membrane

- the cell membrane consists of a double layer of lipid molecules plus protein complexes which serve as channels and ionic pumps
- different ions exist in the extracellular and intracellular space. In general their concentrations c_i and c_o differ: the system is not in an equilibrial state.[1]

Examples:

- Squid giant axon

K^+	$c_i = 400\frac{mmol}{l}$	$c_o = 10\frac{mmol}{l}$
Na^+	$c_i = 49\frac{mmol}{l}$	$c_o = 410\frac{mmol}{l}$
Cl^-	$c_i = 40\frac{mmol}{l}$	$c_o = 540\frac{mmol}{l}$

- spinal moto-neuron of the cat

K^+	$c_i = 150\frac{mmol}{l}$	$c_o = 5.5\frac{mmol}{l}$
Na^+	$c_i = 15\frac{mmol}{l}$	$c_o = 150\frac{mmol}{l}$
Cl^-	$c_i = 9\frac{mmol}{l}$	$c_o = 125\frac{mmol}{l}$

This disquilibrium is maintained by ion pumps, e.g. $Na^+ - K^+$pump. $3\,Na^+$ions are moved from $i \to o$, $2\,K^+$ions are moved from $o \to i$

- the different ion concentrations yield a separation of electric charges: the interior of the cell is negative with respect to the exterior of the cell
- the polarization of the membrane leads to a force F on the charges Q or to an electric field E, such that

$$E = \frac{F}{Q} \Leftrightarrow F = EQ \tag{N 1.1}$$

→ How is the electric field generated by the other charges?

- inside and outside the cell there are electric potentials ϕ_i and ϕ_o, respectively, for which $\frac{F}{Q}d = Ed = -(\varphi_i - \varphi_o) = V$ where φ_i and φ_o is the electric potential voltage. The difference of the potentials is called the *electric voltage* V, neurophysiological: membrane potential V. Membrane potentials are found in the range from $-90mV$ ... $+50mV$. The resting state of the cell V_R amounts nearly $-65mV$.

[1] c_i^* is the concentration of the specific ion *inside* the cell-soma, c_o^* is the concentration *outside* of the cell.

N 1.1.1 interlude: Physical units

There are 7 basic units:

meter m	–	length
kilogram kg	–	mass
second s	–	time
ampere A	–	electric current
kelvin K	–	absolute temperature
candela cd	–	luminosity intensity
mol	–	amount of substance

Other units are derived from these. I.e.:

$$\begin{aligned}
\text{force} \quad &: \quad 1 \text{ Newton} = 1N = 1\frac{kg\,m}{s^2} \\
& \quad\; F = ma \\
\text{charge} \quad &: \quad 1 \text{ coulomb} = 1As \\
& \quad\; I = \frac{dQ}{dt},\ I = \frac{Q}{t} \Leftrightarrow It = Q \\
\text{voltage} \quad &: \quad 1V = 1\frac{kg\,m^2}{A\,s^3} \\
\text{electric resistance} \quad &: \quad 1Ohm = 1\Omega = 1\frac{V}{A} = 1\frac{kg\,m^2}{A^2s^3} \\
\text{capacity} \quad &: \quad 1 \text{ Farad} = 1F = 1\frac{A^2s^4}{kg\,m^2} \\
& \quad\; \tau = RC \;\; [\tau] = 1\frac{kg\,m^2}{A^2s^3}\frac{A^2s^4}{kg\,m^2} = 1s
\end{aligned}$$

N 1.1.2 Currents

- **ionic currents:** The movement of ions across the cell membrane corresponds to <u>electric currents</u> I.
  - **leak currents:** due to
    - ... the membrane potential
    - ... concentration differences of an ion X (c_i^*, c_o^*)

    there are leak currents I_L^*across the membrane. For $c_i^* = c_o^* = const.$, the currents depend only on the voltage $VI_L^* = I_L^*(V)$. The total leak current across the membrane is $I_L^{tot}(V) = \sum_x I_L^*(V)$.
  - **pump currents:** even in the resting state of a neuron, V_R , the leak currents, do not vanish - $I_L^*(V_R) \neq 0$. They must be compensated by ionic pumps; currents I_p^* constant; For these holds $I_p^* = -I_L^*(V_R)$. The total pump current is $I_p^{tot} = \sum_x I_p^* = -I_L^{tot}(V_R) > 0$ (because on average, positive charges move $i \to 0$)

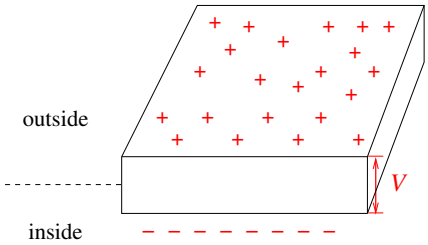
- **gating currents** are currents across channes which are transmitter- or voltage-gated, $I_g = I_g(V) \rightarrow$ action potentials!
- **other currents** are external currents applied by neuroscientists

Mind that electric charges are connected to voltage and current is connected to the *change* of voltage.

In N 1.1 q is a charge in an already existing electric field for a given voltage V. How does V come about?

<u>Electric charges</u> give rise to forces on other charges, electric fields and electric potentials.

The general relationship $Q \leftrightarrow V$ is complicated (so called Poisson Equation in electrodynamics)



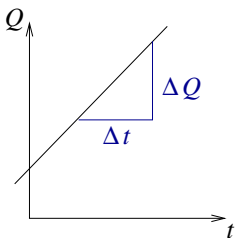
$$Q = -CV \qquad \text{(N 1.2)}$$

Figure N 1.1: capacitor / membrane

either: $\begin{cases} C: & \text{Capacitance } (1F) \\ Q: & \text{Charge } (1C = 1As) \end{cases}$ for a certain patch of membrane/whole

or: $\begin{cases} C: \frac{\text{capacitance}}{\text{membrane area}} & \frac{1F}{cm^2} \\ Q: \frac{\text{charge}}{\text{membrane area}} & \frac{1C}{cm^2} \end{cases}$

The current across the membrane is the charge moving across the membrane per time unit:



$$I(t) = \frac{\triangle Q}{\triangle t} \qquad \text{(N 1.3a)}$$

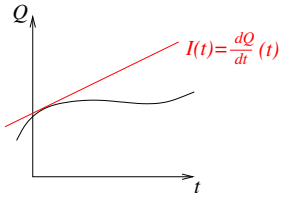
Computing the derivative of both sides of N 1.2 yields:

$$\begin{array}{rrcl} & Q(t) & = & -CV(t) \\ \Leftrightarrow & \frac{dQ(t)}{dt} & = & -C\frac{dV(t)}{dt} \\ \Leftrightarrow & I(t) & = & -C\frac{dV(t)}{dt} \end{array}$$

$$C\frac{dV}{dt}(t) + I(t) = 0 \qquad \text{(N 1.4a)}$$

Instead of $\frac{dV}{dt}(t)$:

$$CV(t) + I(t) = 0 \tag{N 1.4b}$$



$$I(t) = \frac{dQ}{dt}(t) \tag{N 1.3b}$$

Figure N 1.2: The change of voltage at time t is I, the current

N 1.4a is a <u>differential equation</u> for $V(t)$:

$CV(t) = -I(t) \rightarrow$ change depends on the state of the system

$\downarrow$

change of the variable we are interested in

$$I(t) \begin{array}{cc} \swarrow & I_P^* \\ \leftarrow & I_L^*(V) \\ \nwarrow & I_R(V) \end{array}$$

Our goal: compute $V(t)$ from N 1.4a and solve the differential equation. Equation N 1.4a is the starting point for a number of neural models, including:

- the integrate-and-fire neuron
- the Hodgkin-Huxley model

which differ in $I(t)$.

N 1.2 Integrate-and-Fire Neuron

In order to obtain a particular model, the currents in N 1.4a have to be specified.

- Simplified model, we assume: the spatial structure of the neuron is neglected. In particular, the membrane potential does <u>not</u> depend on a spatial variable. At time t, the neuron is described by a single number $V(t)$: <u>point neuron</u> (no special structure). Equation N 1.4a is suitable for this: it is an ODE for $V(t)$.
- We do <u>not</u> consider different kinds of ions.
- <u>currents:</u>

1. leak currents / pump currents. We consider a current

$$I_{L,P}(V) := \underbrace{I_L^{tot}(V)}_{\text{total leak current}} + \underbrace{I_P^{tot}}_{\text{total pump current}} \tag{N 1.5}$$

For $V = V_R$ we had $I_L^{tot}(V_R) = -I_P^{tot}$.
At resting state they must compensate $\Rightarrow$

$$I_{L,P}(V_R) = I_L^{tot}(V_R) - I_L^{tot}(V_R) = 0$$

- no current at the resting potential
This gives us a model for the leak current:

$$I_L(V) : \; I_{L,P}(V) = \frac{1}{R}(V - V_R) \tag{N 1.6}$$

where R is the <u>total resistance</u> of the neuron, which is constant.
<u>Ohms law is valid:</u> $U = RI$; $R = const \Rightarrow U = I$

2. external currents: (synaptic, electrode) written as $-I(t)$ (coming from the inside). $I(t)$ does not depend on V.

ODE N 1.4a $\Rightarrow$

$$\begin{aligned} C\tfrac{dV(t)}{dt} + \quad & I_{L,P}(V) \quad = I(t) \quad [I(t) \text{ is nonlinear}] \\ \Leftrightarrow C\tfrac{dV(t)}{dt} + \quad & \underbrace{I_{L,P}(V)}_{\frac{V-V_R}{R}} \qquad -I(t) = 0 \\ & \qquad\qquad \text{where } V \text{ is linear} \end{aligned} \tag{N 1.7}$$

Further simplification:

$$\begin{aligned} \tilde{V} &= V - V_R \\ \frac{d\tilde{V}(t)}{dt} &= \frac{d}{dt}(V - V_R) = \frac{dV}{dt} \\ \frac{d\tilde{V}(t)}{dt} + \frac{\tilde{V}(t)}{R} &= I(t) \end{aligned}$$

$\tilde{V}$: derivation from the resting potential

$\tilde{V} > 0$: depolarisation

$\tilde{V} < 0$: hyperpolarisation

For further simplification we substitute $\tilde{V}$ with V:

$$c\frac{dV}{dt} + \frac{V}{R} = I \tag{N 1.8}$$

- Equivalent circuit [Eccles 1957]

$$C = 3 * 10^{-9} F$$

$$R = 8 * 10^{5} \Omega$$

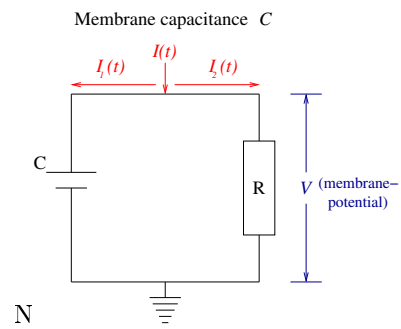


Figure N 1.3: membrane capacitance

N 1.2.1 Kirchhoff's rule

Currents compensate each other at each point in an electric circuit (otherwise, charges would accumulate).

$$I(t) = \underbrace{I_1(t)}_{C\frac{dV}{dt}} + \underbrace{I_2(t)}_{\frac{V}{R}} = C\frac{dV}{dt} + \frac{V}{R} \tag{N 1.8}$$

ODE, $V(t)$ results as a solution of N 1.8. Often an initial condition is supplied: $V(t_0) = V_0$, eg. $V(0) = 0$. The model is <u>linear</u> and <u>solvable</u> - the solution can be written down.

N 1.2.2 Membrane time constant

N 1.8 $\Rightarrow \frac{dV}{dt} + \frac{V}{RC} = \frac{I}{C}$

$RC = \tau$ - membrane time constant

<u>here:</u> $\tau = 2.4$ms (see "Physical units")

The *membrane time constant* determines the speed at which the membrane potential changes upon current injection.

$$\Rightarrow \frac{dV}{dt} + \frac{V}{\tau} = \frac{I}{C} \tag{N 1.9}$$

Our model is not complete, because it is not capable of prodicing spikes! $\rightarrow$ Here gating currents are not considered.

N 1.2.3 Empirical observation

For a constant electrode current $I(t) \equiv I_0 = const.$, a biological neuron produces a spike train,

$$\text{(N 1.9)} \Rightarrow \quad \frac{dV}{dt} = \frac{I_o}{C} - \frac{V}{\tau} \tag{N 1.10}$$

where I_o, C and τ are constant. We consider a fixed value for $V \rightarrow$ everything is constant. The curve above is not a solution because $0 > \frac{dV}{dt} > 0$ is not possible $\rightarrow$ no spikes can be produced. Then the r.b.s of N 1.10 is <u>fixed</u>

- either > 0 or < 0 or $= 0$

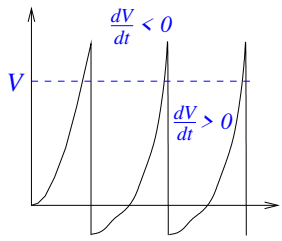


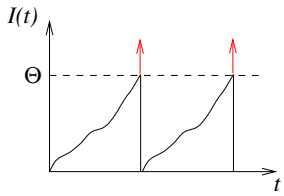
Figure N 1.4: spike train

- Therefore, the left side of the equation cannot be both positive and negative as it is required for an action potential. $V(t)$ in the figure cannot be a solution of N 1.10. The ODE N 1.9 does <u>not</u> produce spikes.

→ additional condition for spiking: firing threshold Θ

$$V(t) \geq \Theta \Rightarrow V(t^+) = 0$$

$$t^+ = \lim_{\varepsilon \to 0} (t + \varepsilon) \tag{N 1.11}$$



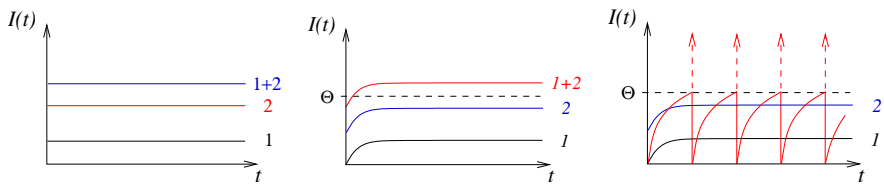
$I(t)$ arbitrary - not constant!

Figure N 1.5: Threshold Θ

Upon reaching the threshold V is set back to 0: "spike"; the spike itself is <u>not</u> modeled!

- complete integrate-and-fire neuron: $\begin{cases} \text{N 1.8 or N 1.9 ODE, subthreshold behaviour} \\ \text{N 1.11 } - \text{spikes} \end{cases}$

  disadvantage: The complete model is <u>nonlinear</u> (because of the threshold)



(a) currents, a neuron is stimulated with

(b) linear response of the neuron

(c) with the threshold the behaviour changes

Figure N 1.6: Stimulation of a neuron and nonlinear response in an environment with threshold

- some models include a <u>refractory period</u> during which the neuron cannot fire (<u>absolute refractory period</u>) or during which it is harder to elicit an action potential (<u>relative refractory period</u>). This is done by making the threshold time dependant

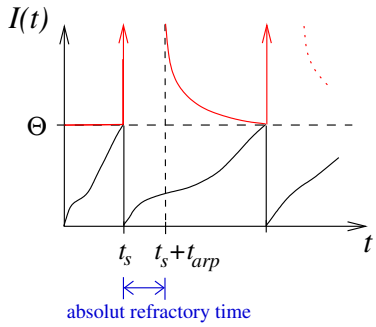


Figure N 1.7: Θ is pushed to infinity and decreases

$$\Theta(t) = \begin{cases} \infty, \; t_s \leq t \leq t_s + t_{ars} \\ \Theta_o + \frac{1}{[t-(t_s+t_{arp})]^n} \end{cases} \quad , \; t > t_{s(\text{pike})} + t_{a(\text{bsolut})\, r(\text{efractory})\, p(\text{eriod})}$$

When hitting Θ_o the potential goes to infinity. A new action potential is building up during $[t_s, \, t_{arp}]$ until it reaches Θ again.

N 1.3 Integrate-and-fire neuron: subthreshold behaviour

Consider an IaF neuron below its firing threshold. - Only N 1.9 is needed for the description, eq. N 1.11 plays no role.

<u>Linear system</u> $\rightarrow$ solutions can be written down for neurons $I(t)$.

N 1.3.1 $I(t) = 0$ (Exercise 4.3 a)

In the first case, there is <u>no</u> input current, $I(t) = 0$. N 1.9 $\rightarrow \frac{dV(t)}{dt} + \frac{V(t)}{\tau} = 0$. Initial value:

$$V(t_0) = V_0 \tag{N 1.14}$$

solution $\begin{array}{l} \nearrow M_2: \text{ separation of variables} \\ \searrow M_3: \text{ eq. M 3.3} \end{array}$

$$V(t) = V_0 e^{-\frac{1}{\tau}(t-t_0)} \tag{N 1.15}$$

Exponential decay towards $V = 0$, the resting potential.

N 1.3.2 $I(t) \neq 0$ (Exercise 4.3 b)

for $I(t) \neq 0$, N 1.9 is an inhomogenous linear ODE.

$$\frac{dV(t)}{dt} = -\frac{1}{\tau}V(t) + \frac{I(t)}{C} \tag{N 1.9}$$

$$\text{M 3}: \; \frac{dx(t)}{dt} = a(t)x(t) + b(t)$$

Initial condition:

$$V(t_0) = V_0 \tag{N 1.14}$$

We apply the variation of constants formula (M 3.4)

$$\varphi(t) = e^{\int_{t_0}^{t} a(\bar{t})d\bar{t}}$$

<u>here</u>:

$$\varphi(t) = e^{-\frac{1}{\tau}(t-t_0)}$$

and

$$x(t) = \varphi(t)\left\{x_0 + \int_{t_0}^{t} \frac{1}{\varphi(\tilde{t})} b(\tilde{t})d\tilde{t}\right\}$$

<u>here</u>:

$$\begin{aligned} V(t) &= e^{-\frac{1}{\tau}(t-t_0)} && * && \left\{V_0 + \int_{t_0}^{t} e^{\frac{1}{\tau}(t-t_0)} \frac{I(\tilde{t})}{C} d\tilde{t}\right\} \\ &= V_0 e^{-\frac{1}{\tau}(t-t_0)} && + && \frac{1}{C}\int_{t_0}^{t} e^{\frac{1}{\tau}(\bar{t}-t_0)-\frac{1}{\tau}(\bar{t}-t_0)} I(\tilde{t})d\tilde{t} \\ &= \underbrace{V_0 e^{-\frac{1}{\tau}(t-t_0)}}_{\text{Membrane potential at a spike}} && + && \underbrace{\frac{1}{C}\int_{t_0}^{t} e^{-\frac{1}{\tau}(\bar{t}-t_0)} I(\tilde{t})d\tilde{t}}_{\text{Membrane potential for an arbitrary input current in the substhreshold case}} \end{aligned} \tag{N 1.16}$$

For the special initial condition:

$$V(0) = 0 \tag{N 1.17}$$

N 1.16 results in:

$$\begin{aligned} V(t) &= \frac{1}{C}\int_0^t e^{-\frac{1}{\tau}(t-\bar{t})} I(\tilde{t})d\tilde{t} \\ &= \frac{1}{C} e^{-\frac{1}{\tau}\int_0^t e^{\frac{1}{\tau}\tilde{t}} I(\bar{t})d\bar{t}} \end{aligned} \tag{N 1.18}$$

Below threshold:

$$V(t) = I_0 R(1 - e^{-\frac{t}{\tau}}) \tag{N 1.19}$$

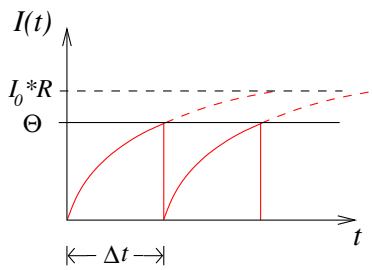


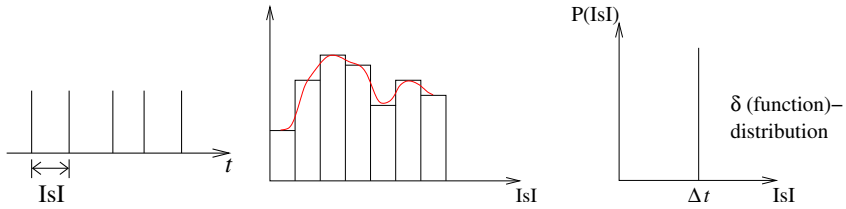
Figure N 1.8: $I_0 R > 0$

We know:

- the neuron fires periodically
- time $\triangle t$ to reach the threshold

$$\begin{array}{rrcl} & \Theta & = & I_0 R(1-e^{-\frac{\triangle t}{\tau}}) \\ \Leftrightarrow & \frac{\Theta}{I_0 R} & = & 1-e^{-\frac{\triangle t}{\tau}} \\ \Leftrightarrow & e^{-\frac{\triangle t}{\tau}} & = & 1-\frac{\Theta}{I_0 R} \\ \Leftrightarrow & \triangle t & = & -\tau \ln(1-\frac{\Theta}{I_0 R}) \end{array} \qquad \text{(N 1.21)}$$

Time between spikes: <u>interspike interval</u>



(a) Interspike interval

(b) Interspike interval distribution

(c) delta function distribution

Figure N 1.9: Interspike interval

$\triangle t$ is defined only for $1-\frac{\Theta}{I_0 R} > 0 \Leftrightarrow I_0 > \frac{\Theta}{R}$. Only in this case the neuron fires.

Firing frequency

$$f(I_0) = \frac{1}{\triangle t(I_0)} = -\frac{1}{\tau \log(1-\frac{\Theta}{I_0 R})} \qquad \text{(N 1.22)}$$

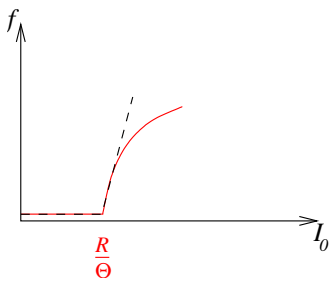


Figure N 1.10: N 1.22 is sometimes approximated by a linear function (dotted line)

Example 1 constant current

$$I(t) \equiv I_0$$
$$\hookrightarrow \text{Exercise 4_3}$$

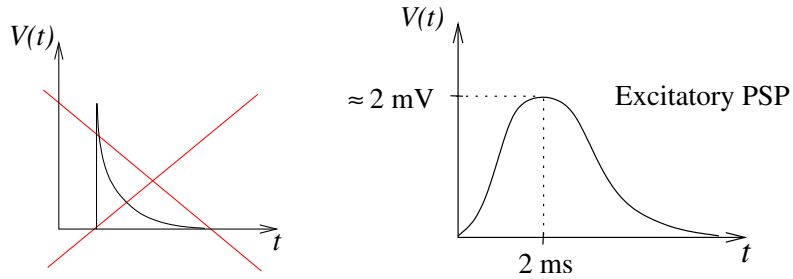
$$V(0) = 0$$

$\Rightarrow$N 1.18

$$\begin{aligned} V(t) &= \tfrac{1}{C}\int_0^t e^{-\frac{1}{\tau}(t-\tilde{t})} I_0 d\tilde{t} \\ &= I_0 R\left\{1 - e^{\frac{t}{\tau}}\right\} \\ [\tau &= RC] \end{aligned} \tag{N 1.19}$$

This means: our membrane potential goes up.

Example 2



(a) Post synaptic potentials look different

(b) Spinal motoneuron of the cat (Curtis & Eccles 1959)

Figure N 1.11: Postsynaptic potentials (PSP)

A current which yields neural responses looking like PSPs is

$$I(t) = kte^{-\alpha t}\,(\alpha > 0) \tag{N 1.20}$$

Neural response $\rightarrow$cf. exercise 5_2.
Let $\beta = \frac{1}{\tau} - \alpha$

$$\begin{aligned} \beta \neq 0: \quad V(t) &= \frac{ke^{-\frac{t}{\tau}}}{\beta c}\left\{te^{\beta t} - \frac{e^{\beta t} - 1}{\beta}\right\} \\ \beta = 0: \quad V(t) &= \frac{kt^2}{2C}e^{-\frac{t}{\tau}} \end{aligned}$$

N 1.4 IaF-Neuron including firing threshold

Complete Model N 1.9 linear ODE and N 1.11 threshold.

A solution $V(t)$ can be obtained in only one case: $I(t) \equiv I_0 = const.$

$$\triangle t = -\tau \ln(1 - \frac{\Theta}{I_0 R}) \tag{N 1.21}$$

Firing frequency $f(I_0) = \frac{1}{\triangle t} = -\frac{1}{\tau \ln(1 - \frac{\Theta}{I_0 R})}$

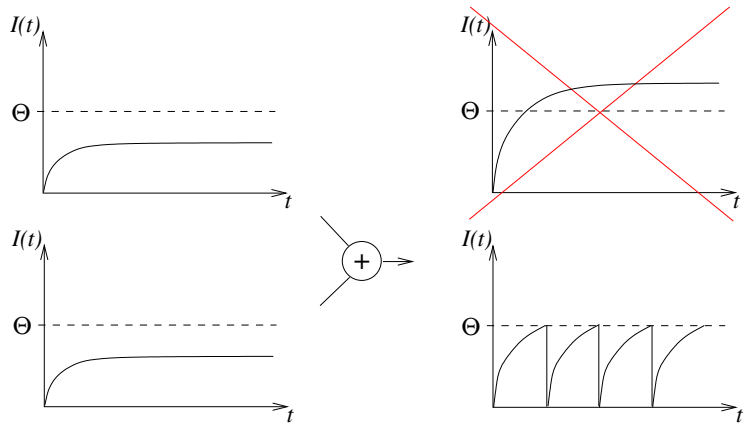


Figure N 1.12: IaF-Neuron: consideration of the firing threshold

N 1.4.1 General currents

In general, interspike interval distributions cannot be written down explicitly. even for periodic currents, i.e. $I(t) = I_0 \sin \omega t$, no closed expression exists. ISI's have to be computed numerically "spike by spike", by iterating the ODE N 1.9 and solving the threshold condition N 1.11, $V(t) \geq \Theta$.

N 1.4.2 Dimensionless variables

Consider again the IaF neuron

$$C\frac{dV(t)}{dt} + \frac{V(t)}{R} = I(t) \tag{N 1.8}$$

$$V(t) \geq \Theta \Rightarrow V(t^*) = 0 \tag{N 1.11}$$

Here the quantities have physical units, e.g.,
V, Θ in V(olt) or mV
$I(t)$ in A(mpere) or mA

t in s(econds) or ms

It is convenient, to study the system dynamics with variables which do not have units (<u>dimensionles variables</u>). A suitable transformation <u>reduces</u> the number of <u>system parameters</u> (here: R, C, Θ) thereby giving a better overview of the dynamics.

$$\begin{array}{rcll} a\frac{dx}{dt} + & b & x = 0 & |: a \\ \frac{dx}{dt} + & \underbrace{\frac{b}{a}}_{c} & x = 0 & \end{array}$$

Step 1 time: let t be measured in units of the membrane time constant $\tau = RC$

$$t' = \frac{t}{\tau}$$

t' has no dimension any more $\rightarrow t'$ is a dimensionless variable.

$$\begin{aligned} \frac{dV(t)}{dt} \quad &\rightarrow \quad \frac{dV(t')}{dt'} \\ \text{e.g.} \quad V(t) &= V_0 \frac{t^2}{\tau^2} \\ V(t') &= V_0 t'^2 \end{aligned}$$

Composition of functions:

$$\begin{aligned} V(t) &= V(t'(t)) \\ t'(t) &= \frac{t}{\tau} \\ V(t') &= V_0 t'^2 \end{aligned}$$

chain rule applied:

$$\begin{aligned} \frac{dV}{dt} &= \frac{dV}{dt'}\frac{dt'}{dt} \\ t' \rightarrow \tilde{t} \quad & \quad V(t) = V(\tilde{t}(t)) \\ \frac{dV(t)}{dt} &= V'(\tilde{t}(t))\tilde{t}'(t) \leftarrow \text{chain rule} \end{aligned}$$

$$\begin{aligned} \tfrac{dV}{dt} &= \tfrac{dV}{dt'} \underbrace{\frac{dt'}{dt}}_{\frac{t}{\tau}} \\ \Rightarrow \tfrac{dV}{dt} &= \tfrac{1}{\tau} \quad \tfrac{dV}{dt'} \end{aligned}$$

ODE:

$$\begin{aligned} & \tfrac{c}{\tau}\tfrac{dV(t')}{dt'} + \tfrac{V(t')}{T} &= I(t') \\ \tau = RC \quad & \tfrac{1}{R}\tfrac{dV(t')}{dt'} + \tfrac{V(t')}{R} &= I(t') \\ \Leftrightarrow \quad & \end{aligned} \tag{N 1.23}$$

Step 2 voltage: let voltages be measured in units of Θ

$$\begin{aligned} & \upsilon = \tfrac{V}{\Theta} \qquad \text{(effectively the threshold has been set to 1)} \\ \Leftrightarrow \quad & V = \upsilon\Theta \\ \text{and} \quad & \tfrac{dV}{dt'} = \Theta\tfrac{d\upsilon}{dt'} \end{aligned}$$

N 1.23 $\Rightarrow$

$$\frac{1}{R}\Theta\frac{d\upsilon(t')}{dt'} + \frac{\Theta}{R}\upsilon(t') = I(t') \tag{N 1.24}$$

Step 3 current: let the current be in units of $\frac{\Theta}{R}$

$$i = \frac{I}{\frac{\Theta}{R}} \quad \Leftrightarrow \quad I = i\frac{\Theta}{R}$$

N 1.24 $\Rightarrow$

$$\begin{aligned} & \tfrac{\Theta}{R}\tfrac{d\upsilon(t)}{dt} + \tfrac{\Theta}{R}\upsilon(t') &= i\tfrac{\Theta}{R} \\ \Leftrightarrow \quad & \tfrac{d\upsilon(t')}{dt'} + \upsilon(t') &= i(t') \end{aligned}$$

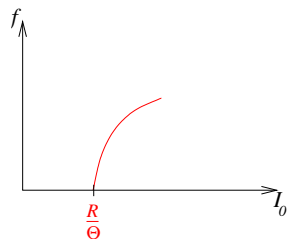


Figure N 1.13: The neuron starts to fire at $\frac{\Theta}{R}$

Now we name $t' : t$

$$\Rightarrow \frac{dv(t)}{dt} + v(t) \quad = \quad i(t) \tag{N 1.25}$$

threshold condition N 1.25

$$V(t) \geq \underbrace{1}_{\Theta} \quad \Rightarrow v(t^*) = 0 \tag{N 1.26}$$

Dimensionless equations have no more parameters! The dynamics of N 1.25, N 1.26 yields "typical results" which are very similar for different values of Θ, R, C. Finding suitable transformations is not easy.

N 1.4.3 A graphical method to determine the spike trains of an IaF neuron for an arbitrary current i(t) (Scharstein 1979)

Consider N 1.25, N 1.26

$$\begin{aligned} \frac{dV(t)}{dt} + v(t) \quad &= \quad i(t) \\ v(t) \geq 1 \quad &\rightarrow \quad v(t^*) = 0 \end{aligned}$$

The neuron fires at times t_k $(k = 1, 2, 3, ...)$; the membrane potential is set to zero at these times. Noe consider the neuron between the spikes at times t_k and t_{k+1}.

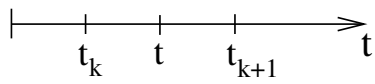
We had the general solution N 1.18 for $V(t_k) = 0$

$$V(t) = \frac{1}{C} \int_{t_k}^{t} e^{-\frac{1}{\tau}(t-\tilde{t})} I(\tilde{t}) d\tilde{t}$$

Now: $c = 1$, $\tau = 1 \Rightarrow$

$$V(t) = \int_{t_0}^{t} e^{-(t-\tilde{t})} i(\tilde{t}) d\tilde{t}$$

$t \leq t \leq t_{k+1}$now play ...



$$
\begin{aligned}
&= \int_0^t e^{-(t-\bar{t})} i(\tilde{t}) d\tilde{t} \quad - \int_0^{t_k} \underbrace{e^{-(t-\bar{t})} i(\tilde{t})}_{1 = e^{t_k - t_k}} d\tilde{t} \\
&= \int_0^t e^{-(t-\bar{t})} i(\tilde{t}) d\tilde{t} \quad - \int_0^{t_k} e^{-(t-t_k)} e^{-(t_k-\bar{t})} i(\tilde{t}) d\tilde{t} \\
&= \underbrace{\int_0^t e^{-(t-\bar{t})} i(\tilde{t}) d\tilde{t}}_{k(t)} \quad - e^{-(t-t_k)} \underbrace{\int_0^{t_k} e^{-(t_k-\bar{t})} i(\tilde{t}) d\tilde{t}}_{k(t_k)}
\end{aligned}
$$

$$
V(t) = u(t) - e^{-(t-t_k)} u(t_k) \qquad \text{(N 1.27)}
$$

$$
t_k \leq t \leq t_{k+1}
$$

$u(t)$: membrane potential at time t as if the threshold did not exist! The threshold is reached if $v(t) = 1$. This is the case for t_{k+1}. Insert this in N 1.27:

$$
\begin{aligned}
1 &= u(t_{k+1}) - e^{-(t_{k+1}-t_k)} u(t_u) \\
\Leftrightarrow \quad u(t_{k+1}) - 1 &= u(t) e^{-(t_{k+1}-t_k)}
\end{aligned} \qquad \text{(N 1.28)}
$$

In the graphical algorithm, we search for t_{k+1} once we have found t_k. In order to formulate the algorithm, we re-name $t_{k+1} := t$. Thus in case of a spike at time t, we have N 1.28

$$
u(t) - 1 = u(t_k) e^{-(t-t_k)} \qquad \text{(N 1.29)}
$$

Algorithm: graphical method to find the spike times. For given $i(t)$, compute the <u>subthreshold</u> response of the neuron <u>for all t</u>.

$$
u(t) = \int_0^t e^{-(\bar{t}-\bar{t}_k)} i(\tilde{t}) d\tilde{t} \quad \begin{array}{ll} \rightarrow & \text{analytical} \\ \searrow & \\ & \text{numerical (Euler)} \end{array}
$$

- Draw $u(t)$, $u(t) - 1$, where 1 is Θ
- After the k-th spike at time t_k draw the r.h.s. of N 1.29, $u(t_k) e^{-(t-t_k)}$
- The next spike (at time t_{k+1}) occurs when this curve intersects the function $u(t) - 1$ (r.b.s. of N 1.29)

Scharstein's method:

$$
\underbrace{u(t)}_{\substack{\text{subthreshold} \\ \text{response}}} - 1 = \underset{\substack{\downarrow \\ \text{spike}}}{u(t_k)} \quad e^{-(t-t_k)}
$$

Example: Oscillatory input

- phase coupling: spikes occur at the same phase (s) of the input
- bursting

Effect of increasing the current offset $I(t) = I_0 + I_1 \cos wt$

- spike frquencies are increased
- bursts are different: more spikes per burst $\Rightarrow$ ISI histograms change correspondingly

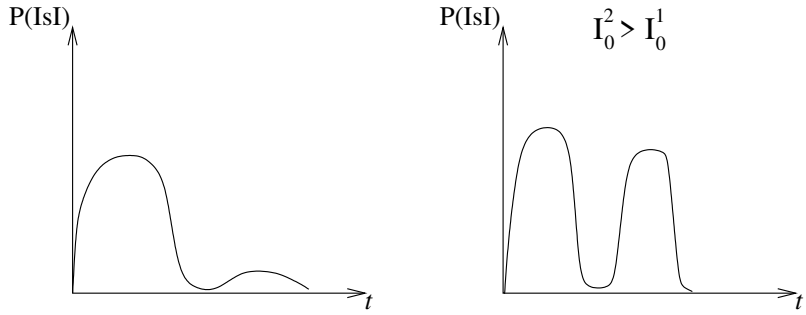


Figure N 1.14: IsI histograms

N 2 Neural populations: synchronization

We consider oscillators, systems which are periodical in time:

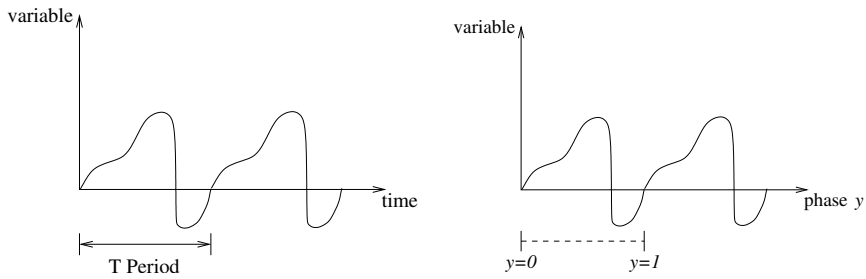


Figure N 2.1: periodical systems

It is frequently observed in nature that coupled oscillators synchronize, i.e. they oscillate with constant phase differences $\triangle y$. In many cases: $\triangle y = 0$

Example 1: pendulum clocks (C. Huygens, Hordogium Oscillatorium, 1673) - pendulum clocks synchronize with $\triangle y = 0$

Example 2: Fireflys in Asia

Example 3: synchronized clapping

- Transition from non-synchronous to synchronous clapping, accompanied by a period doubling
- subsequent enhancement of the clapping frequency leads to desynchronization (Neda et al., Nature 403 (2000), 849-850)

Example 4: <u>synchronous nerve cell activities</u>

- <u>binding problem</u>
- signal processing is distributed in the brain
- how are signals belonging to a single object bound
- suggestion (Wolf Singer, Reinhard Eckholm) cortical neurons which encode properties of the same object fire in synchrony: $\triangle\varphi = 0$
- synchronicity is statistical, single neurons fire irregularly

N 2.1 The model of Mirollo an Strogatz

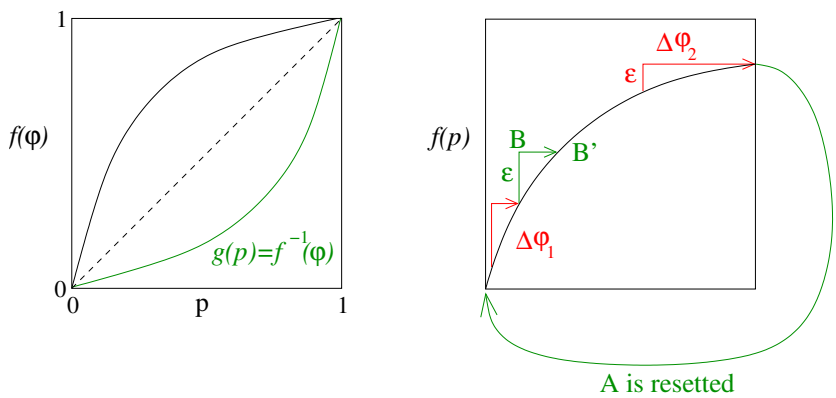


Figure N 2.2: Two oscillators

Oscillator A		Oscillator B
0		φ
	$\swarrow$	
$\varphi' = h(\varphi)$		0
	$\searrow$	
0		$h(\varphi') = h(h(\varphi))$

0 means: has fired (and is resetted)

Lemma 1: $h'(\varphi) < -1$

Lemma 2: $R'(\varphi) > 1$

<u>Domains of h and R</u>

$$h :]\delta, 1[\to \mathbb{R}$$

$$\varphi \mapsto h(y) \tag{N 2.1}$$

$$\delta = 1 - g(1 - \varepsilon)$$

$$h(\varphi) = g(\varepsilon + \delta(1 - \delta))$$

$$\rightarrow h(\varphi) = g(\varepsilon + \delta(1 - \varphi))$$

<u>$R(\varphi)$:</u>

$$R(\varphi) = h(h(\varphi))$$
$$h(\varphi) \in]\delta, 1[$$
$$\Rightarrow \varphi \in]h^{-1}(1), h^{-1}(\delta)[$$

h is strictly monotonic decreasing: Lemma 1

$$h^{-1}(1) = \delta$$
$$]\delta, h^{-1}(\delta)[$$
$$h(\delta) = 1$$

In summary:

$$R :]\delta, h^{-1}(\delta)[\rightarrow \mathbb{R}$$

$$\delta \mapsto R(\delta) \tag{N 2.2}$$

We show: R has a <u>unique fixed point</u> φ^*, the fixed point is <u>unstable</u> $\rightarrow$ we are done!

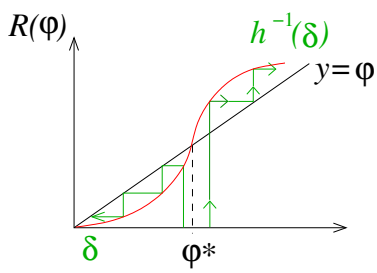


Figure N 2.3: fixed point at $\varphi*$: $R(\varphi*) = \varphi*$

We have to show:

1. The equation $R(y^*) = \varphi^*$ has a unique solution
2. $|R'(\varphi^*)| > 1$

If this situation is true, the system moves either towards δ or $h^{-1}(\delta)$ under iteration where synchronization occurs.

1. Fixed point equation

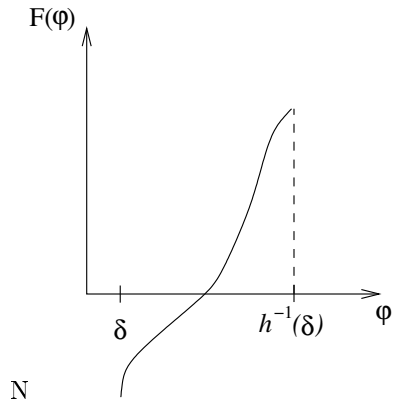
$$R(\varphi^*) = \varphi^*$$

$$R(\varphi) = h(h(\varphi)) \tag{N 2.3}$$

-search for a fixed point of h!

$$h(\varphi^*) = \varphi^*$$

Let $F(\varphi) = \varphi - h(\varphi)$, i.e. $F(\varphi^*) = 0$



N

Now:

$$F(\delta) = \delta - h(\delta) = \delta - 1 < 0 \tag{N 2.4}$$

$$h(\delta) = 1$$

$$F(h^{-1}(\delta)) = h^{-1}(\delta) - h(h^{-1}(\delta)) = h^{-1}(\delta) - \delta > 0$$

F is continuous $\Rightarrow$ there exists a φ^* in $]\delta, h^{-1}(\delta)[$ where $F(\delta^*) = 0$
The fixed point is unique, because

$$\begin{array}{rcccc} F'(\varphi) & = & 1 - \underbrace{h'(\varphi)}_{< -1} & > & 1 + 2 = 3 \\ & & & & \text{(Lemma 1)} \end{array} \tag{N 2.5}$$

Hence, R has a unique fixed point φ^*

2. $|R'(\varphi^*)| > 1$

   Lemma 2: $R'(\phi) > 1$ for all φ - the fixed point is unstable

Sumary: unless we start the system with a difference φ^*, it is driven towards $\triangle\varphi = 0$ or $\triangle\varphi = 1$: synchronicity for almost all initial conditions.

N identical oscillators: synaptic weights $\varepsilon > 0 \rightarrow$ the system synchronizes for almost all initial conditions

N 2.2 Extensions to the Mirollo-Strogatz model

Mirollo and Strogatz (1990) had very specific requirements:

- identical neurons
- global, identical coupling for all neurons
- no time delay

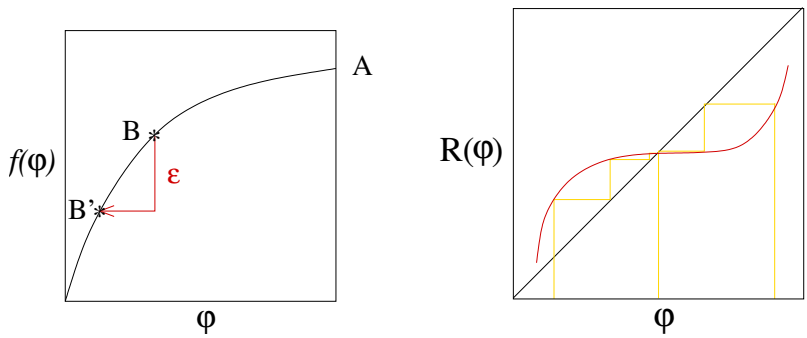
Subsequent models generalize the requisites and thereby extend the classes of networks for which the synchronization properties are known. Extensions are made with respect to

- inhibitory interactions
- non-identical oscillators (τ, I_0)
- variation of synaptic weight
- time delays

N 2.2.1 A few cases

1. <u>2 identical neurons with instantaneous inhibitory coupling</u>

   - synaptic coupling $\varepsilon < 0$
   - upon spike arrival neurons are shifted to the <u>left</u> on the phase



(a) stable fixed point, which is iterable from both sides

Figure N 2.4:

   Figure N 2.5 describes a stable fixed point φ correspondigly to an out-of-phase synchronization (Period T of neurons $\rightarrow$ neurons fire apart).

2. <u>2 non-identical neurons with non-instantaneous coupling</u>

3. <u>2 identical neurons with delay coupling</u> [U. Ernst, K. Pavel, T. Geisel, Phys. RER Lett. 74 (1993) 1570-1573]
   Delays occur everywhere in the nervous system:

- synaptic input
- dendritic tree
- axon

Behaviour changes quantitavely!

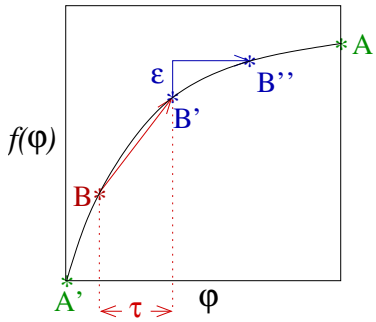


Figure N 2.5: This system is more complicated, because 1,2,3,... spikes can be on their way depending on the delay τ. Here: $\tau < 0.5, |\varepsilon| < 1$

- <u>Excitatory coupling</u>
  Return map $R(\varphi)$ has two stable fixed points at τ and $g(1-\varepsilon)-\tau$, synchronization with a phase lag τ. For larger couplings ε, different phase lags $< \tau$ may occur.

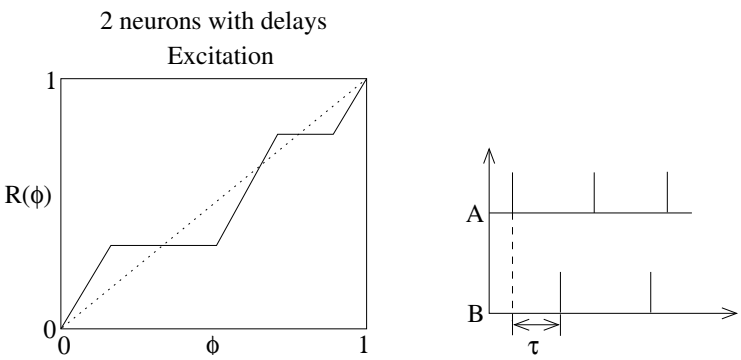


Figure N 2.6: out-of-phase synchronization

- <u>Inhibitory coupling</u>

  Return map $R(\varphi)$ has two stable fixed points at $\phi = 0$ and $\underbrace{\phi = 1 + \tau - g[\varepsilon + f(\phi + \tau)]}_{\frac{T}{2}}$.

  For $\varepsilon > f(\tau)$: different phase lags, depending an initial lag ϕ

4. <u>N identical neurons without delays</u>

- <u>excitatory coupling</u>: in-place sync. (Mirollo & Strogatz)

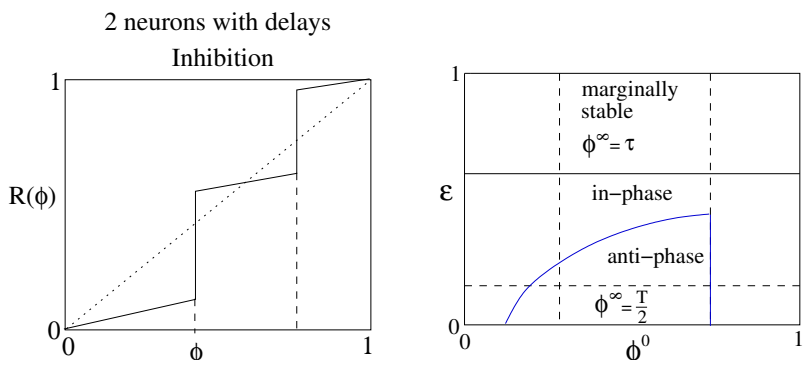


Figure N 2.7: In- or out-of-phase synchronization

- <u>inhibitory coupling</u>:

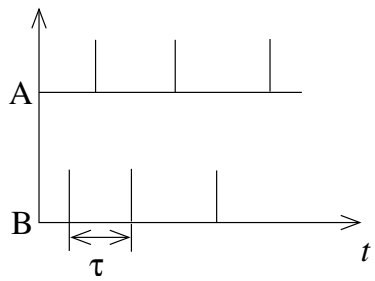


Figure N 2.8: 2 neurons: $\phi = \frac{t}{2}$

Neurons try to keep distances as large as possible on the ϕ axis.

5. <u>N identical neurons with delayed coupling</u> (Exercise 8_3) [K. Okuda, Physica D 63 (1993) 424-436; D. Golomb and J. Rinzel, Physica D 72 (1994) 259-282; Ernst et al. (1995)]

   - <u>Inhibitory coupling</u>
     Formation of multi-stable clusters: depending on the initial condition, synchronous clusters emerge which are stable. The number of clusters is statistical but depends on the delay τ : $\frac{1}{\tau}$
   - <u>Excitatory coupling</u>
     spontaneous emergence of synchronous clusters, these clusters are unstable and decay; formation of new clusters etc.
   - <u>More complex cases</u>
     - different neural properties
     - distribution of delays
     - excitation and inhibition
     - resistance dependent couplings

     $\rightarrow$ behaviour can be complex

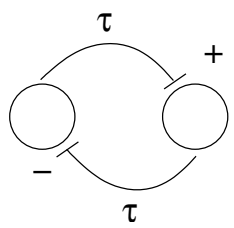


Figure N 2.9: two coupled neuron's

N 2.3 Synchronization in the nervous system

Some thoughts:

Massive synchronization of neuronal activity is found in the brain. best hit is given by the various EEG rhythms. In this case, however, currents perpendicular to the surface of the brain are recorded, no detection of high-frequency spikes.

Electrophysiology: synchronous - sometimes oscillatory activity - has been found (Eckhorn, Singer). Synchronization occurs within a cortical area, between areas and even inter-hemispheric phase delay is normally zero. Frequency of oscillations: ~ 40 Hz

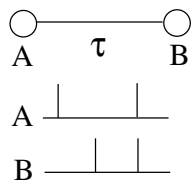


Figure N 2.10: synchronization

- suggestion by von der Malsburg, Eckhorn, Singer: synchronization (sometimes in combination with oscillation) may be a solution of the <u>binding problem</u>.

N 3 The synapse

In neural network theory the action of a synapse is simply modelled as a constant factor ω which is multiplied with the input signal α.

Out of the neuron: transfer function $f : y = f(h)$. y may be interpreted as the neural firing rate (<u>analog neuron</u>) within this framework, "<u>learning</u>" corresponds to a change in w, e.g.

$$w_i(t+1) = w_i(t) + \underbrace{\varepsilon}_{\text{learning rate}} x_i y$$

"Hebbian learning"

<u>But:</u> it is not really that simple!

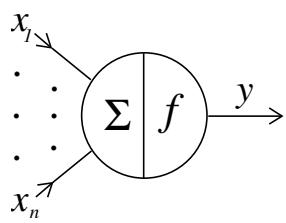


Figure N 3.1: Excitation of the neuron $x_1 w_1 + ... + x_n w_n = h$

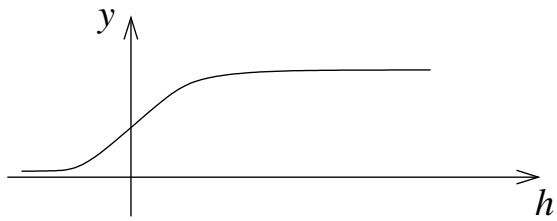


Figure N 3.2: e.g. a sigmoid function

- Synaptic inputs give rise to <u>p</u>ost<u>s</u>ynaptic <u>p</u>otentials (PSPs). These can be modelled as alpha functions:

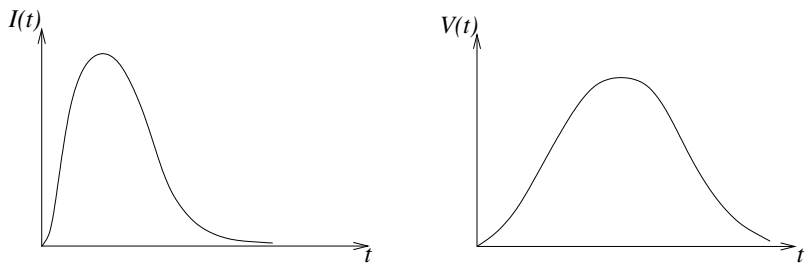


Figure N 3.3: PSPs

spike train:

spikes at times t :

$$\begin{aligned} I(t) &= \sum_i k(t-t_i)e^{-\alpha(t-t_i)} \\ I(t) &= kte^{-\alpha t} \end{aligned}$$

- the synaptic efficacy, measured as the amplitude of the postsynaptic potential or the area under the PSP, $\int_{t_0}^{\infty} v(t)dt$, depends on the <u>history</u> of the

spike input t_o at the synapse. Synaptic activity has to be described as a dynamical system (*dynamical synapses*).
Reference: M.V. Tsodyks, H. Markram, The neural code between neocortical pyramidal neurons depends on neurotransmitter release probability, Proc. Nat. Acad. Sci. USA (PNAS)
Successive spikes with short time intervals result in a succesively weaker response of the postsynaptic neuron. After a certain time ($\approx$ 1 s) the synapse has recovered (*depressive synapse*). Other synapses (*fascillitating synapses*) become stronger upon successive spike inputs.

- Model: a synaptic reservoir is assumed which can be depleted, e.g.
  - synaptic vesicles which are used up
  - postsynaptic receptors whose capacity is finite

  Elements of the reservoir can be in one of three states:

  $$\left.\begin{array}{lll} 1.\ \text{effective} & \rightarrow & \text{fraction } E \\ 2.\ \text{inactive} & \rightarrow & \text{fraction } I \\ 3.\ \text{recovered} & \rightarrow & \text{fraction } R \end{array}\right\} \quad E + R + I = 1$$

  A spike input results in a fraction K of the recovered elemts to become active ($R \rightarrow E$). The effective elements become rapidly inactive ($E \rightarrow I$, time constant τ_{inact}), inactive elements slowly recover ($I \rightarrow R$; time constant τ_{rec}).
  Differential equations:
  2 ODEs for $R(t)$, $E(t)$, plus the eq. $E(t) + R(t) + I(t) = 1$
  $\frac{dR}{dt} = \frac{1}{\tau_{rec}} I$ - slow recovery $I \rightarrow R$
  $\frac{dE}{dt} = -\frac{1}{\tau_{const}} E + UR\delta(t - t_{AP})$
  The excitatory postsynaptic current (EPSC) resulting from an action potential to E. The model is for average spike trains: no fluctuations.

- Further observations:
  - Consider a spike train with a firing frequency f. Beyond a certain limit frequency f_{lim} a stationary EPSP amplitude is found for which $\text{EPSP}_{\text{stat}} \approx \frac{E}{\delta \tau_{rec}}$, i.e. $\text{EPSP}_{\text{stat}} \sim \frac{1}{f}$
  - The limit frequency is given by $f_{lim} \approx \frac{1}{\tau_{rec} k}$. The larger k, the more resources are used per spike $\rightarrow$ depletion of the reservoir already for small input frequencies.

- Interpretation of K
  on average, U is the fraction of elements that become effective. For a single spike: neurotransmitter release is an all or non event. U is the probability of transmitter release!
  Hint: lowering of Ca^{2+} ions $\rightarrow$ probability of transmitter release is decreased $\rightarrow$ U is smaller in the model $\rightarrow$ limit frequency f_{lim} is increased.

- Hebbian learning
  It can be shown that hebbian learning affects the amplitude of the first EPSPs only but notthe stationary state. Interpretation of hebbian learning in the light of the model: hebbian learning corresponds to an increase

in K, i.e., in an increase in the probability of neurotransmitter release $\rightarrow$ synapses become more reliable.

There are other aspects of learning as well!

N 4 Hebbian learning

N 4.1 Introduction

Question: What are the physiological / anatomical / metabolical correlates of learning?

Gerneral idea: In the nervous system, there is an intimate relationship between the <u>structure</u> that can be observed and the <u>function</u> / <u>purpose</u> it serves.

Theory of Artificial Neural Networks (ANNs)

2 types of dynamics

$\swarrow$ $\searrow$

dynamics on a <u>fast</u> timeschedule: neural dynamics (summation of inputs, computation of output)	dynamics on a slow timescale: synaptic dynamics; changes in the synaptic weights learning

Types of learning in ANNs:

- supervised; an error signal is provided, e.g., backpropagation
- unsupervised; "self-organized", no error signal, e.g., *Hebbian learning, Kohonen map*
- reinforcement learning; yes-no signal is provided, e.g. *Neurogammon* (ANN trained to play Backgammon)

Where does the idea of synaptic plasticity come from?

N 4.2 The Hebbian postulate

Donald O. Hebb, psychologist McGill (Montreal) 1949: "The organization of behaviour"
$\rightarrow$ physiological basis of learning, memory, mental states
Hebb suggested a 2-stage mechanism for memory formation

- **short term memory**: "reverberating neural activity"
- **long term memory**: "structurally / metabolical changes, especially at the synapses

Connection between these mechanisms: long-term changes result from short-term neural activity
→ Hebbian learning

Important aspects of the postulated mechanism:

- time-dependent mechanism: the timing of pre- and postsynaptic activity matters
- local mechanism: changes result only from the neurons which are directly involved; no global error signal
- interactive mechanism: changes depend on the activity of both the presynaptic (A) and the postsynaptic neuron (B)
- type of interaction is not specified; is an occasional common firing sufficient?
- correlate of learning: Hebb and his successors concentrate on the synapse, but Hebb also considers other possibilities: neurobiotaxis, formation of synapses

Hebb only postulated this mechanism. More specific questions:

- Is there an activity-dependent plasticity in the nervous system?
- If yes, does it have to do with learning and memory
- Are there further phenomena which Hebb did not talk about?

N 4.3 LTP and early models of Hebbian learning

LTP (Long Term Potentiation)

- discovered by Bliss and Lomo (1973)
- Found in (rabbit) hippocampus (Schaeffer collateralus commissural input → CA1 pyramidal cells; mossy fibers → CA3 pyramidal cells). Subsequentially disovered in many subsystems /species
- Simultaneous pre- and postsynaptic activity increases the average PSP / the average PSC (Post Synaptic Current)
- Long-term effect (at least for hours)
- use-dependent depression (LTD)

Early learning rules

- time-discrete neural networks
- simple model neurons, e.g. *analog neuron.* Activation of neuron i :
  $h_i = w_{i1}y_1 + w_{i2}y_2 + ... + w_{iN}y_N = \sum$
  output of neuron i :
  $y_i = f(h_i)$, e.g. $f(h) = \frac{1}{1+e^{-h}}$ (Fermi function)
  y_i is interpreted as the firing rate

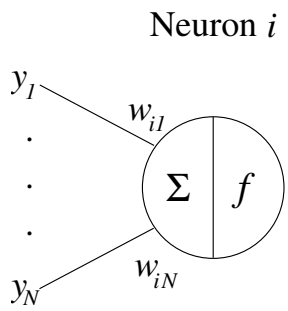


Figure N 4.1: analog neuron
w_{ix} is the synaptic weight
i : postsynaptic Neuron
y_x : presynaptic neuron

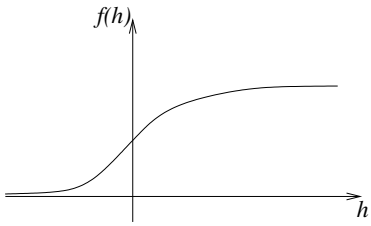
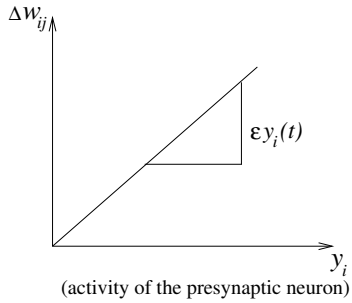


Figure N 4.2: *"squashing function"*; here: Fermi function: $f(h) = \frac{1}{1+e^{-h}}$

simplest Hebbian learning rule:
$w_{ij}(t+1) = w_{ij}(t) + \varepsilon y_i(t) y_j(t)$ ε is the learning rate, small$\Leftrightarrow$ $\underbrace{w_{ij}(t+1) - w_{ij}(t)}$ $=$ $\varepsilon y_i(t) y_j(t) \Delta w_{ij}(t+1)$



N 4.3.1 Problems with (N 4.1)

- w_{ij} can go to infinity while LTP saturates
- the learning rule produces <u>instabilities</u> in a network $w_{ij}(t)$ large $\rightarrow$ $y_i(t)$ is large, since the neuron is strongly activated $\rightarrow$ $w_{ij}(t+1)$ grows even faster. There is no balance.

How to avoid instabilities

1. <u>clipping</u>: synaptic weights are cut beyond a certain threshold

$$w_{ij}(t+1) \geq Q \Rightarrow \tilde{w}_{ij}(t+1) = \Theta$$

   Problem: all synaptic weights grow towards Θ

2. <u>Normalization</u>: application of

$$\Delta w_{ij}(t+1) = \varepsilon y_j(t) y_i(t)$$

   and then subsequently

$$\begin{aligned} w_{i,\,tot}(t+1) &= \sum_{j=1}^{N} w_{ij}(t+1) \leftarrow \text{all syn. weights of the postsyn. neuron} \\ \tilde{w}_{ij}(t+1) &= \frac{w_{ij}(t+1)}{w_{i,\,tot}(t+1)} \end{aligned}$$

Interpretation: The surface of the neuron which can be occupied by synapses is limited.

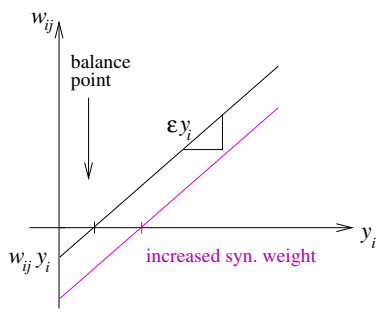
Problem: The modified learning rule is no longer local,

$$\begin{aligned} &\tilde{w}_{ij}(t+1) \quad \text{depends on} \\ &w_{ij}(t+1) \quad \text{for } j \neq k \text{ as well} \end{aligned}$$

Alternative learing rule

$$w_{ij}(t+1) = w_{ij}(t) + y_i\{\varepsilon y_j - w_{ij}(t)\} \tag{N 4.1}$$

$$\Rightarrow \Delta w_{ij(t+1)=y_i\{\varepsilon y_j - w_{ij}(t)\}}$$



There is a balance point for $y_i = \frac{w_{ij}}{\varepsilon}$: presynaptic input

$$\begin{aligned} y_j < \frac{w_{ij}}{\varepsilon} &\Rightarrow \text{synapse is weakened} \\ y_j > \frac{w_{ij}}{\varepsilon} &\Rightarrow \text{synapse is strengthened} \\ y_{j=\frac{w_{ij}}{\varepsilon}} &\Rightarrow \text{synapse remains unchanged} \end{aligned}$$

The balance point increases as the synapse gets stronger $\Rightarrow$ stronger input is needed to retain the status quo.
$\rightarrow$ theory of ANNs, Oja's learning rule, PCA etc.

N 4.4 LTP and learning

Is the phenomenon of LTP associated with learning? Yes!
Rioult-Pedotti et al (2000) demonstrate the occurence of LTP as a consequence of the learning of a motor task in rats.

N 4.5 Spike-timing-dependent plasticity experiments

Several discoveries where made since 1994. The important issues were:

- action potentials propagate back into the dendritic tree such that the synapses get information about the firing of the post-synaptic neuron (Stuart & Sakman, 1994)
- LTP and LTD occur within a short time window ($<$ 100ms) between pre- and postsynaptic activity. LTP is observed if presynaptic activity is followed by postsynaptic activity, LTD is observed in the inverse situation, if postsynaptic activity is followed by presynaptic activity (Markram et al., 1997)
- the time dependence of LTP and LTD can be measured exactly $\rightarrow$ *learning windows* (Zhang et al., 1998; Bi & Poo 1998), e.g.

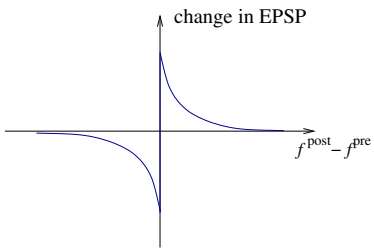


Figure N 4.3: change in EPSP

- polysynaptic connections with different delays lead to <u>structure formation</u>: neural activity results in both LTP and LTD at various synapses in the same neuron (Bi & Poo, 1999)
- LTP yields structural changes: emergence of new synaptic spines (Engert & Bonhoeffer, 1999)

N 4.6 Spike-timing-dependent plasticity: models

The time dependence of the learning rule allows the modelling of plastic changes in networks of spiking neurons,

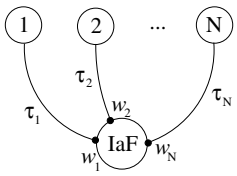
Example: adaptation of delays: Gerstner et al., Nature 383 (1996) 76-78; Eurich et al., Phy. Rev. Lett. 82 (1999) 1594-1597

- Gerstner's motivation: auditory object localization in the barn owl

- loacalization in azimuth: evaluation of the differences in the arrival time of the sound at both ears. Acuity: approximately 1.5 degree, "corresponding" to 1-2 μs of timing in the neurons
- model (proposal by Jeffress, 1948):
  - presynaptic neurons are phase-soupled to the sound signal
  - series of delay lines
  - postsynaptic neurons serve as coincidence detectors

  $\rightarrow$ temporal information is transformed into spatial information

- Identification of the corresponding neural structures in the midbrain of the barn owl (Konishi, Kundim, Cerr, Wagner, ...). E.g., delay lines run between the nervi magnocellulares and the nervi laminares
- Question: How is the high temporal precision obtained with neurons which operate on longer time scales than 1-2μs? (i.e., width of EPSPs 500...800 μs, membrane time constants $\geq 200\mu$s, maybe 1...2μs) and which also have variable spike times
- here: delay lines can be adapted through hebbian learning
- network:



- presynaptic neurons fire stochastically with

$$p(t) = \frac{\pi T}{\sqrt{2\pi}} \sum_{n=-\infty}^{\infty} e^{-\frac{(t-mT-\tau_i)^2}{2\sigma^2}}$$

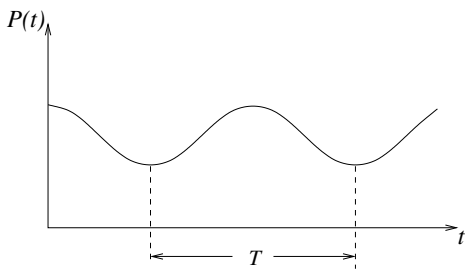


Figure N 4.4: T = $200\mu s$ ($f = 5kHz$), $\sigma = 40\mu s$

Neurons fire independently of each other, different delays τ_i lead to different spike arrival times at the postsynaptic IaF neuron.

- current injected into the postsynaptic cell upon the arrival of spike k from neuron j: $I_j^k(t) = w_j(t)\frac{1}{\tau_s}e^{-\frac{t-t_j^k}{\tau_s}}$, $t_s = 100\mu s$
- learning takes place according to a window function

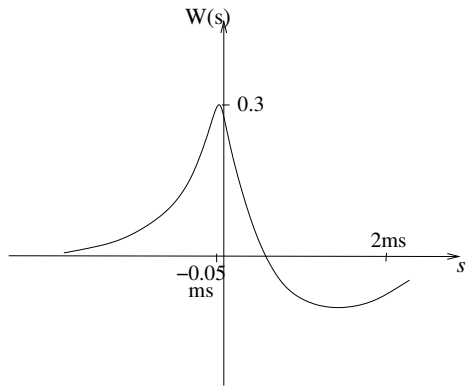


Figure N 4.5: $s = t^{pre} - t^{post} ms$

$$W(s) = \begin{cases} 0.3e^{\frac{s+0.005}{0.5}} & s < -0.05ms \\ 0.5e^{-\frac{s+0.005}{0.5}} - 0.2e^{-\frac{s+0.005}{5}} & s \geq -0.05ms \end{cases}$$

- learning rule:

$$\Delta w_j = \varepsilon \sum_k \left(\gamma + \sum_n W(t_j^k - t^n) \right)$$

  $\varepsilon = 0.002$, $\gamma = 0.1$
  k : spikes of jth presynaptic neuron
  n : spikes of the postsynaptic neuron
  Initially, $w_j = 1$ for all j

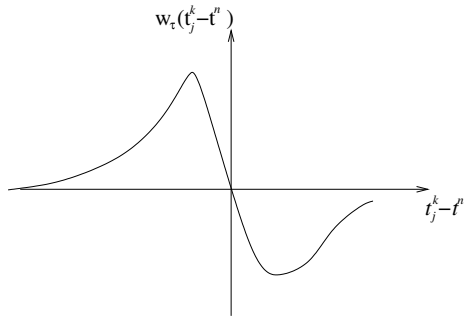
- result: most of the weights - and the corresponding neural connections - vanish. Only some of the presynaptic neurons are still sonnected to the postsynaptic neuron; their delays differ by mutliples of $T = 200\mu s$. Zhe postsynaptic neuron fires phase-coupled to the input with a precision of $25\mu s$. A higher acuity is obtained with a population of $\lesssim 100$ postsynaptic neurons

N 4.6.1 Delay shift instead of delay selection

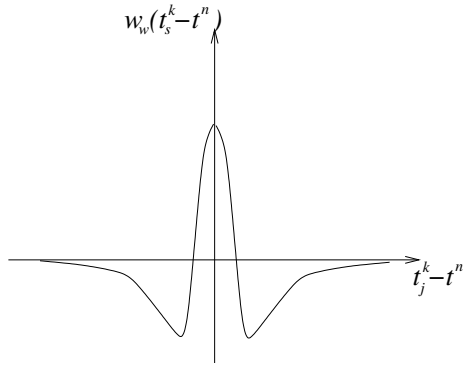
- delay selection is not economical, e.g. in the barn owl: many neurons / neural connections have to be produced most of which are finally destroyed
- is it possible that the delays themselves change (e.g., dendritic / axonal morphology; membrane properties)?
- Eurich et. al (1999): learning rule for delay shift $\Delta\tau = \gamma w_\tau(t_j^k - t^n)$, with a window function $w_\tau$different from Gerstner's

- mathematical methods:
  - simulation of a neural population
  - dynamical system for a whole population of neurons; equations for the density of neurons with delay τ and the total input current into the postsynaptic neuron

  $\rightarrow$ condition on the windows function: all delays become equal (corresponding to a stable fixed point) if the learning window is <u>antisymmetric</u>: e.g., $\rightarrow$ general framework for delay adaptation



  - <u>delay selection</u> á la Gerstner; works for symmetric window functions, e.g.,



  - <u>delay shift</u>, works for antisymmetric window functions

- empirically, delay shift has not been found yet. However, different shapes of window functions have been described for LTP / LTD (See Abbot & Nelson, suppl. to Nature Neuroscience, November 2000).

N 5 Neural Coding

N 5.1 Introduction

Nervous System

↙ ↘

Behaviour; dynamics	Function
What dows the system do?	What purpose does the system / a particular phenomenon have (chapter 5)
(chapters 1-4)	
typical approach of chemistry, physics	approach typical of biology but also of machines, e.g., computers

Here: The nervous system is considered to be a signal-processing system. We consider the issue of neural coding. [compare the approach that the brain is mainly concerned with constructing an internal world; constructivism]

Real or mental world	← correlations? →	Electrophysiological results (fMRI, PET, EEG,...)
sensory systems / motor systems mental states, e.g. attention	If yes, we say that aspects of the lefthandside are represented in the nervous system (working definition)	

Questions:

- Which stimuli / entities are represented in the brain?
- Where can we find reoresentations?
- How accurately are stimuli represented? (position of a prey; frequency of a tone; position of the own body; ...)
- How accurately
- Where / how accurately are motor actions represented?
- Which part(s) of the neural response carries the neural code?
  - firing rate
  - binary information: cell active / inactive
  - spike times of a neuron
  - population firing rate
  - spike times / synchronization
  - order of firing ("rank order code")
- What effects have attention, experience, learning on the neural coding?

- Current methods are applicable " close to the periphery": early sensory areas, motor ares

  → transparency (Fellermann & van Essen)

<u>Representational accuracy</u>

(sensory / motor systems)

↙ ↘

<u>direct computation of the resolution</u>	<u>reconstruction of stimuli / actions from neural activity</u>
(Hintin, Thang & Sejnowski, Abott, Eurich, ...)	(Georgopoulos, Bialek, Zhang, Nicodelis, ...)

N 5.2 Signal reconstruction

Comparison of several methods: K. Zhang et al., J. Neurophysiol. 79 (1998) 1017-1044

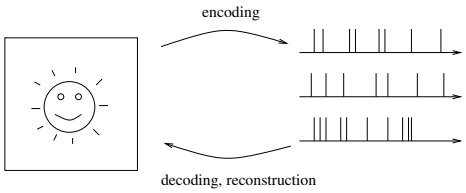


Figure N 5.1: encoding - decododing / reconsctruction

Examples:

1. Bialete et al., "Reading a neural code", Science 252 (1991) 1854-1857. See also "Spikes - Exploring a neural code", MIT Press: recondtruction of the velocity of a stimulus from the firing of a particular neuron (H1) of the blowfly
   - linear reconstruction
2. Georgopoulos et al., Neuronal population coding of movement direction, Science 233 (1986) 1416-1419
   - reconstruction of the direction of an arm movement from the firing of motor cortical neurons in rhesus monkey
   - single neurons are very unspecific
   - single neurons are stochastic
   - "population vector"
3. Wessburg et al. (2000)
   Reconstruction of arm trajectories from the neural activity in premotor cortex, primary motor cortex and posterior parietal cortex of monkeys

- linear reconstruction
- neural network

4. Stanley et al. (1999)
   Reconstruction of videos from the firing of a population of LGN neurons in the anaesthetized cat
   - linear reconstruction
5. Zhang et al. (1998)
   Reconstruction of the trajectory of a cat from the activity of hippocampal place cells
   - Bayesian reconstruction

N 5.2.1 Bayesian reconstruction

Simple introduction: Oram et al., Trends in Neuroscience 21 (1998) 259-265

- Stimulus is parametrized, variable x, e.g., spatial position: $x \in \mathbb{R}, \mathbb{R}^3$; frequency $x \in \mathbb{R}^+$, orientation $x \in S^1$ (circle). More generally, $x \in \begin{pmatrix} x_1 \\ \vdots \\ x_D \end{pmatrix}$, D properties of a stimulus

Simple neuron

- Presentation of the stimulus x_1, counting of the spikes which occur within a time interval τ after stimulus onset $\Rightarrow$ n_1, n_2, n_3 ... spikes / rates $r_1 = \frac{n_1}{\tau}$, $r_2 = \frac{n_2}{\tau}$, $r_3 = \frac{n_3}{\tau}$
- computation of a <u>distribution</u> of spike sounts, interpreted as the conditional probability $P(n|x_1)$