7. BIOLOOGILISTE PROTSESSIDE MODELLEERIMINE

Enamiku bioloogiliste protsesside modelleerimiseks tuleb kasutada lihtsustusi, taandades protsesse
füüsikaliste
keemiliste jt
protsesside argumenteeritud teele

omapära:

- bioloogiline süsteem on seostatud ümbritseva keskkonnaga energiavahetuse kaudu, mis lubab struktuuride teket kaugel tasakaalust;
- hulk keemilisi reaktsioone ja ülekandemehhanisme, lineariseerimine tihti võimatu; faktorid molekulaarse iseloomuga;
- tugevalt mitte-tasakaalustatud süsteemid nii energia kui massiülekande seisukohalt

Probleemid:

1.	Inimene kui biol. olend	rütmid biomehaanika füsioloogia . . .
2.	Bioloogilised süsteemid	olelusvõitlus haigused . . .
3.	Bioloogilise maailma dünaamika kasv	. . .
4.	Info levi bioloogilistes süsteemides	närvivõrgud . . .

. . .
G.Vollmer, 1991

The limits of biology

Bioloogia omapära:

- bioloogia küsimuste spekter laiem kui füüsikal;
- bioloogia seadused vähem tuntud;
- matemaatika ja aksiomaatika vähem kasutused;
- enamus bioloogia seadusi lubab erandeid;
- kõikidele faktidele pole rahuldavaid seletusi;
- ennustamine raske ja tihti võimatu; teooriaid saab kontrollida, kuid tihti raske tõestada, et nad on väärad;
- bioloogilised alusuuringud võivad tulevikus olla kulukamad kui näiteks tuumauuringud;
- rohkem kui teistes valdkondades kerkivad esile moraali ja eetika küsimused;
- küsimus meie tunnetuse võimalikest piiridest.

7.1. Näited ja mudelid

- struktuuride hierarhia (vt. musklid)
- inimene kui punktmasside süsteem
  vibratsiooniprobleemide lahendamised
- spordimehaanika
- lind, rohutirts – mõjuvad jõud
- hobune
- fraktaalsed struktuurid
- loomade mustrid
- kalade optimaalne kuju

7.2. Närviimpulsi levi

- närvikiu ehitus
- tavamudelid
- evolutsioonivõrrandid
- läve tähtsus impulsi genereerimisel
- näide erutusprotsessi modelleerimisest
- kooseksisteerivad atraktorid

7.3. Südame vasaku vatsakese pingeolukord

- üldised mudelid
- südamelihase struktuur
- kontraktsioonimehhanism
- kontraktsiooni modelleerimine
- arvutatud pingeseisundid

7.4. Kokkuvõte

- bioloogiliste süsteemide/struktuuride omapära
- raskused
- kirjandus

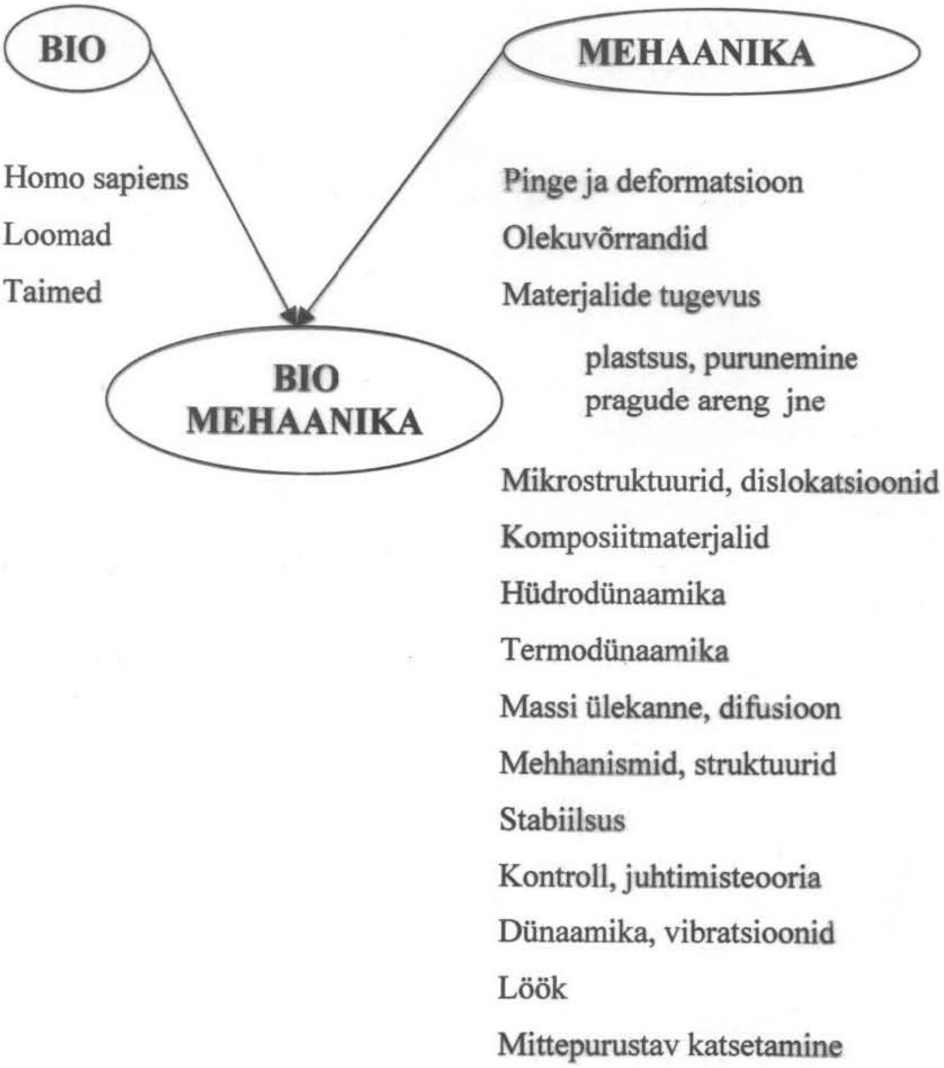
1. Sissejuhatus

bio + mehaanika = biomehaanika
= mehaanikaprobleemid bioloogilistes objektides, s.o. elusas looduses

mehaanika → Galileo Galilei 1638
Discorsi et Dimonstrazioni Matematiche, intorno à due nuoue Scienze Attenenti alla <u>Mecanica</u> & Movimenti Locali
tänapäeval → teadus liikumisest (paigalolek on erijuhtum)

bioloogia → Gottfried Reinhold Treviranus, 1802
bioloogia on teadus, mis käsitleb elusorganisme (loomad, taimed);
vrdl. natural history

Elada tähendab liikuda



EESMÄRGID:

- aru saada funktsioonidest;
- ennustada muutusi (võimalik ohte);
- projekteerida tehisstruktuure bioobjektide (osade) asendamiseks;
- leida analoogiaid bioloogiast tehisstruktuuride või materjalide loomiseks.

Biomehaanika probleemid

elusolendi kui terviku liikumine

maismaal	→	käimine, jooksmine, hüppamine
vees	→	ujumine
õhus	→	lendamine

organite liikumine

vedelike liikumine kehas

pinged kehas, kehaosades

väliskoormuse mõju elusolendile

mehaanika patoloogiaga olendil

bioloogilised muutused kasvul ja vananemisel

- pinged, mõju liikumisele

elusolendi kui mehaanikalise objekti olekuvõrrandid

- luud, pehmed koed, vedelikud

Uusi probleeme

Voolamine läbi fraktaalse struktuuri

solitonid (üksiklained) pikkades molekulides (DNA)

kaootilised võnkumised (südamerütmid)

vibratsioonide biomehaanika

rakuenergeetika ja lihaste kontraktsioon

RAKENDUSED

rakubioloogia → molekulide käitumine, membraanid

üldkirurgia → kudede, luude paranemine
rehabilitatsioon

kardioloogia → tehissüda (klapid), tehisveresooned
vereringvool (ateroskleroos, …)

ortopeedia → proteesid (jäsemed, nahk, …)
abivahendid

traumad → löögidünaamika

sport → liigutuste kinemaatika,
spordivahendid, jõuseadmed

tehnoloogia → vibratsioonitehnika

kajalokatsioon

ehituskonstruktsioonid
- koorikud, mastid

laevaehitus
- materjalid

hüdrodünaamika
- voolamine torudes

mõõtmistehnika

ruumide disain
- liikumise kinemaatika

reoloogia

anisotroopsed materjalid

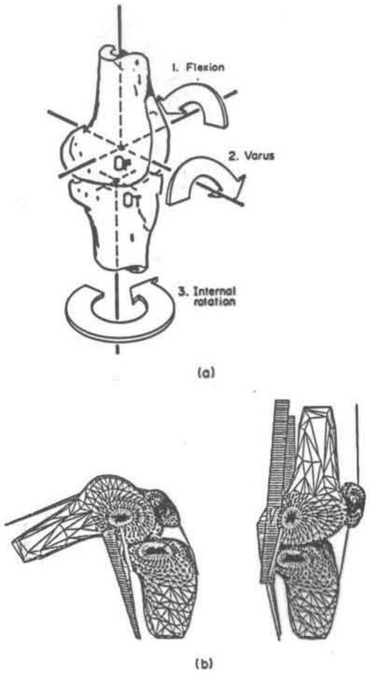


Figure 2
(a) An Eulerian system for describing three-dimensional joint motion using rotations about axes in the femur and tibia; and (b) computer model showing the rotations and displacements that occur in the normal knee during flexion: the tibia rotates internally, while the femur displaces posteriorly

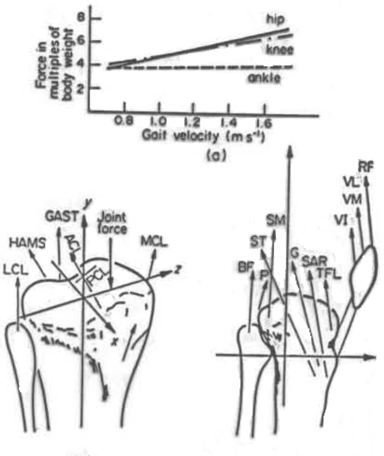


Figure 3
(a) Forces in lower extremity joints as a function of walking speed (Rohrle *et al.* 1984), (b) model for calculating knee forces used by Morrison (Paul 1976) and (c) a more recent model incorporating all of the muscles and using optimization techniques (Mikosz *et al.* 1988)

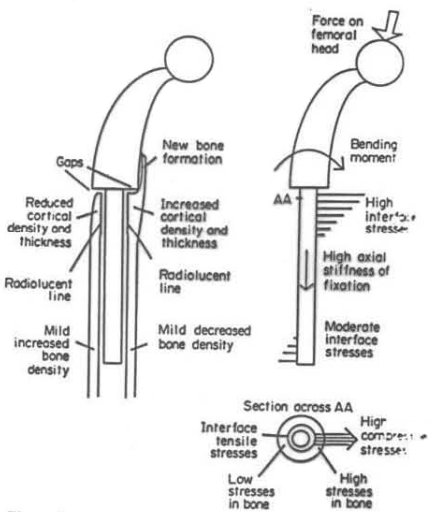


Figure 4
Bone remodelling and interface changes related to forces and stresses for a proximal femoral replacement

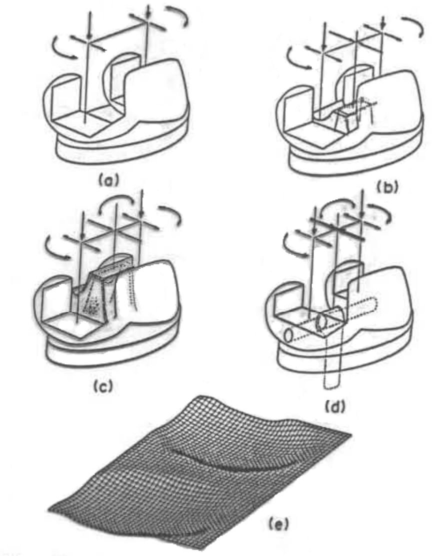
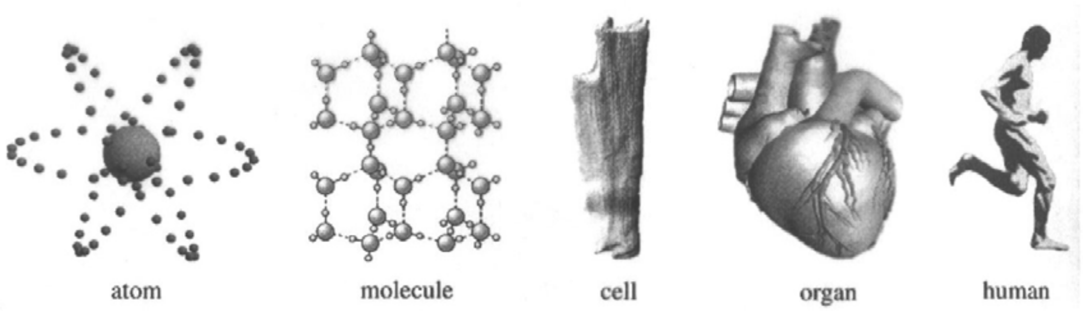
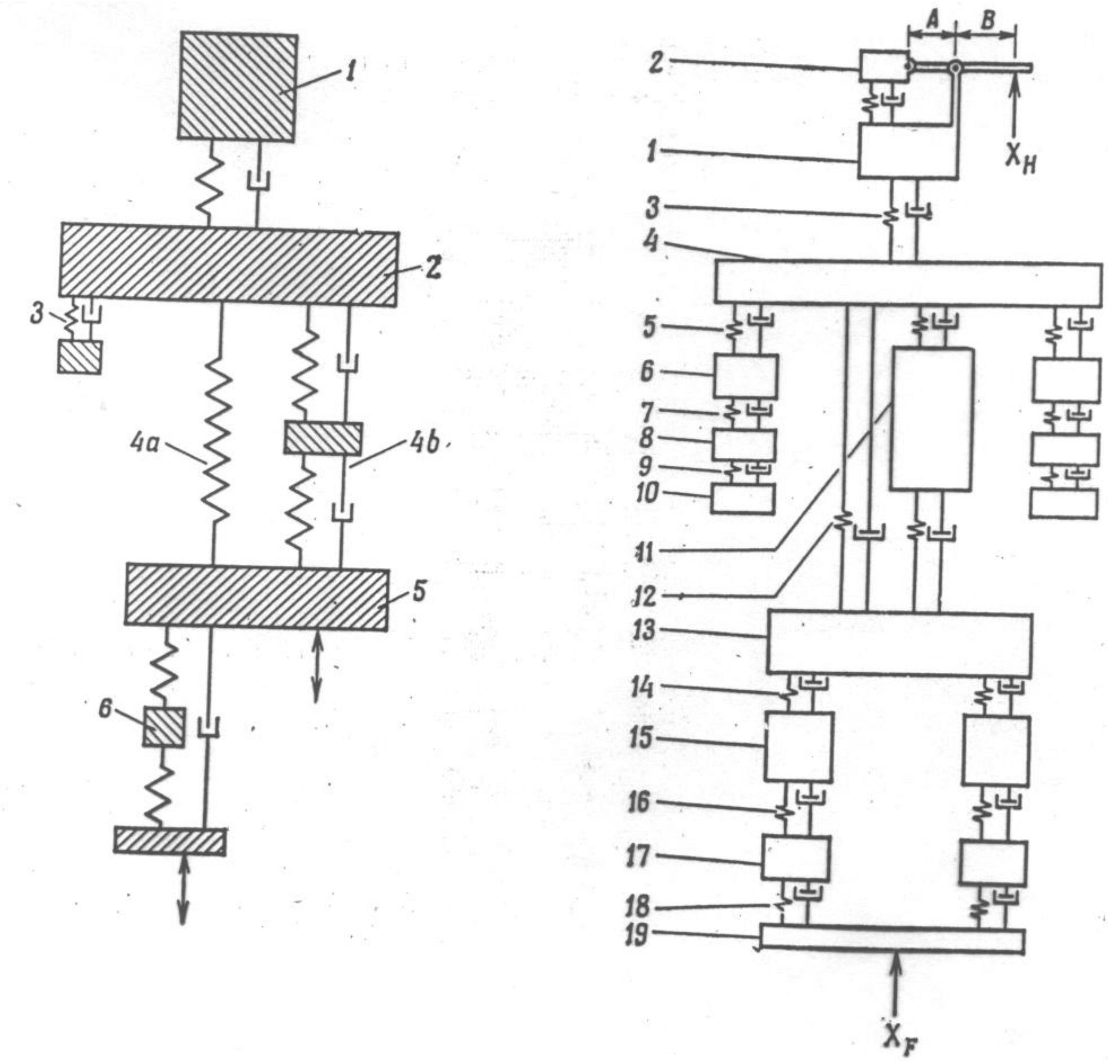


Figure 6
Four basic types of total knee replacement, all incorporating condylar replacement surfaces: (a) unlinked, (b) unlinked with anterior–posterior intercondylar stability, (c) unlinked with anterior–posterior and varus–valgus stability, (d) linked with internal–external rotational laxity and (e) a computer-generated laxity surface for the tibial component

Mudelid – tugevusõpetus

7.1 Näited ja mudelid





Mudelid masspunktide liikumise süsteem

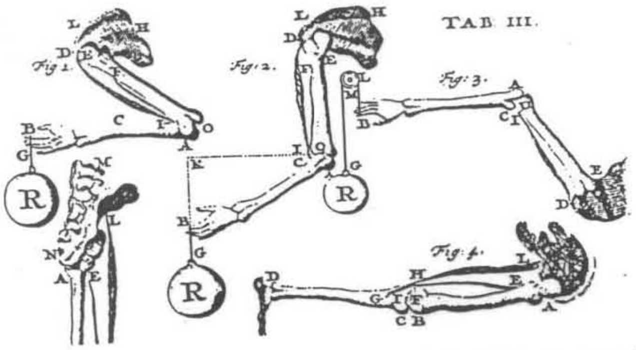


FIGURE 1.4:1 A leaf from Giovanni Alfonso Borelli's book, *On the Movement of Animals*, published in 1680/1681, illustrating his research on biomechanics. Borelli (1608–1679) was professor of mathematics at Pisa. This book was translated recently by Paul Maquet, and published in 1989 by Springer-Verlag.

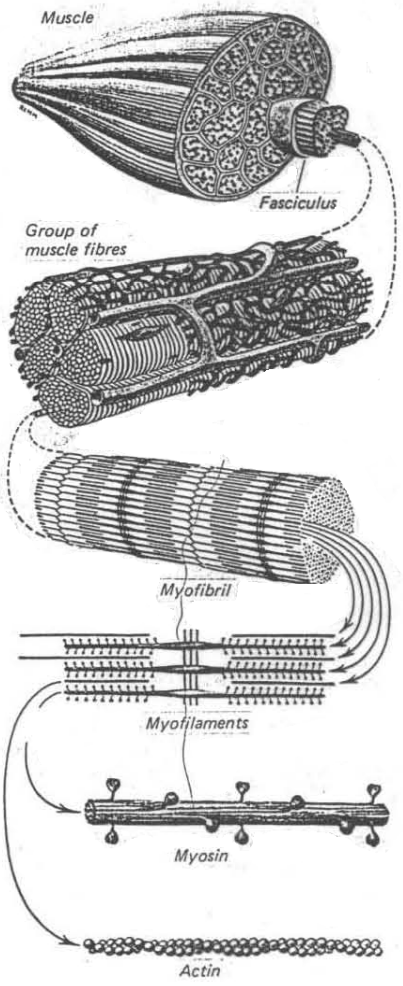


Figure 9.3:1 The organizational hierarchy of skeletal muscle. From *Gray's Anatomy*, 35th British edn. (1973), edited by Warwick and Williams, by permission.

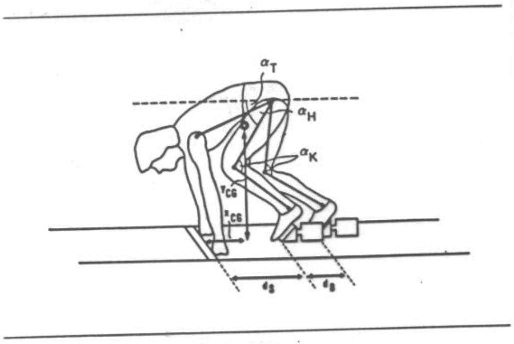


Abb. 47 Körperwinkel beim Sprintstart

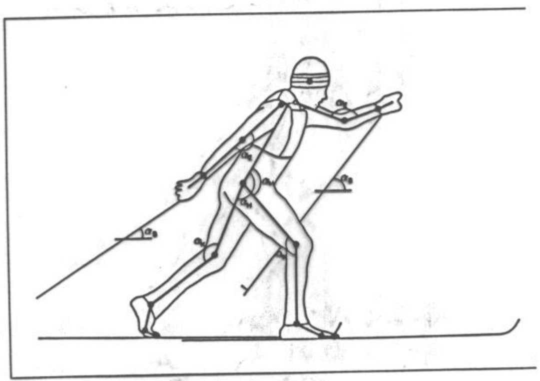


Abb. 48 Körperwinkel beim Skilanglauf

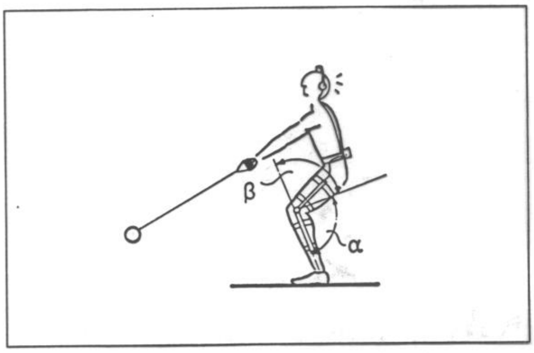
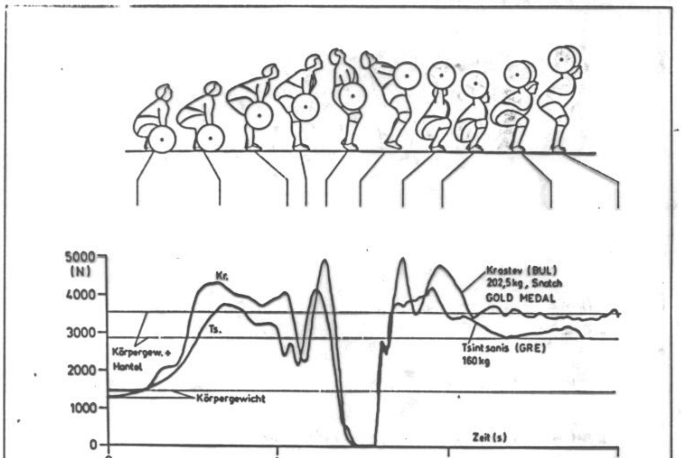


Abb. 71 Anwendung des Goniometers beim Hammerwurf



Mudel – liikumisvõrrandid

M. Ekevad and B. Lundberg

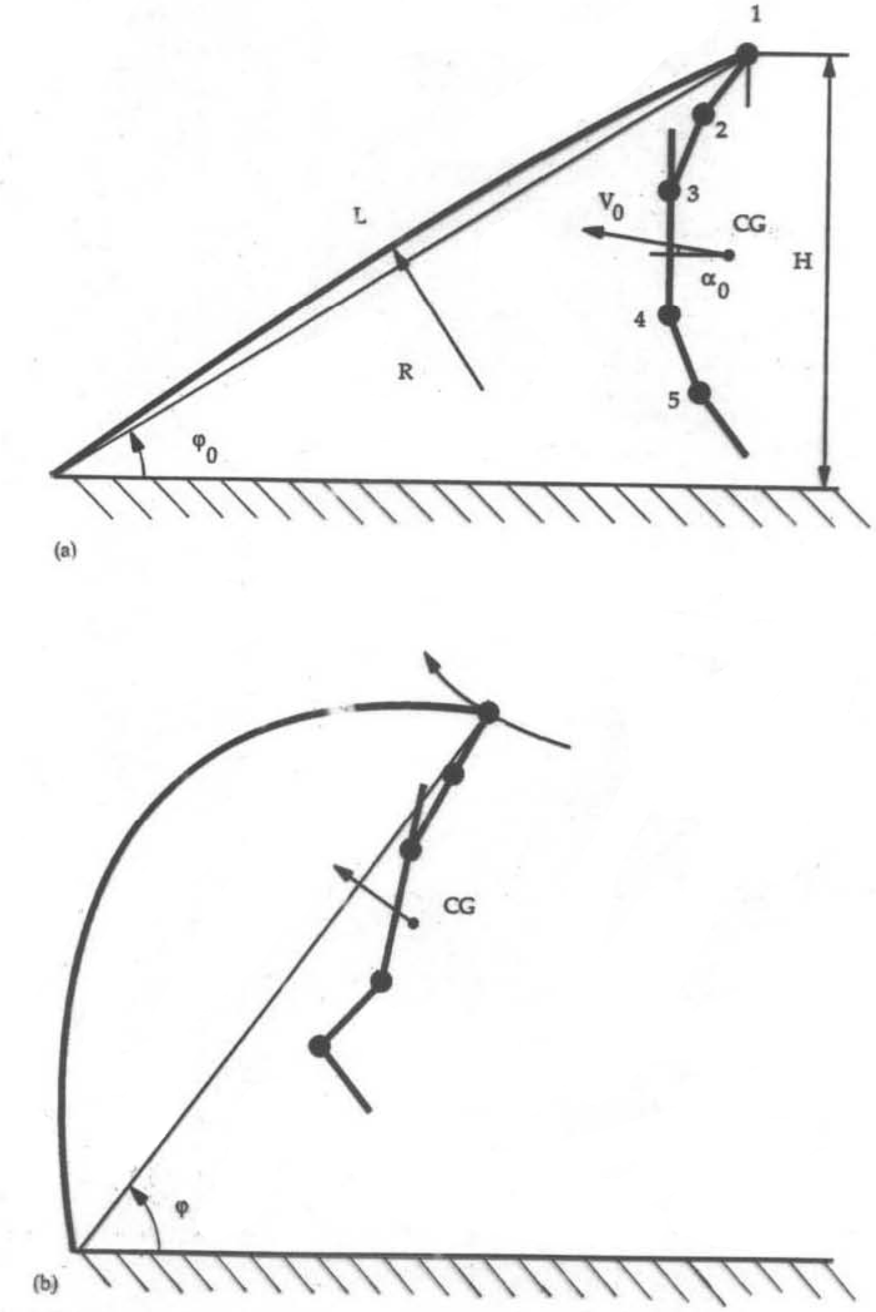
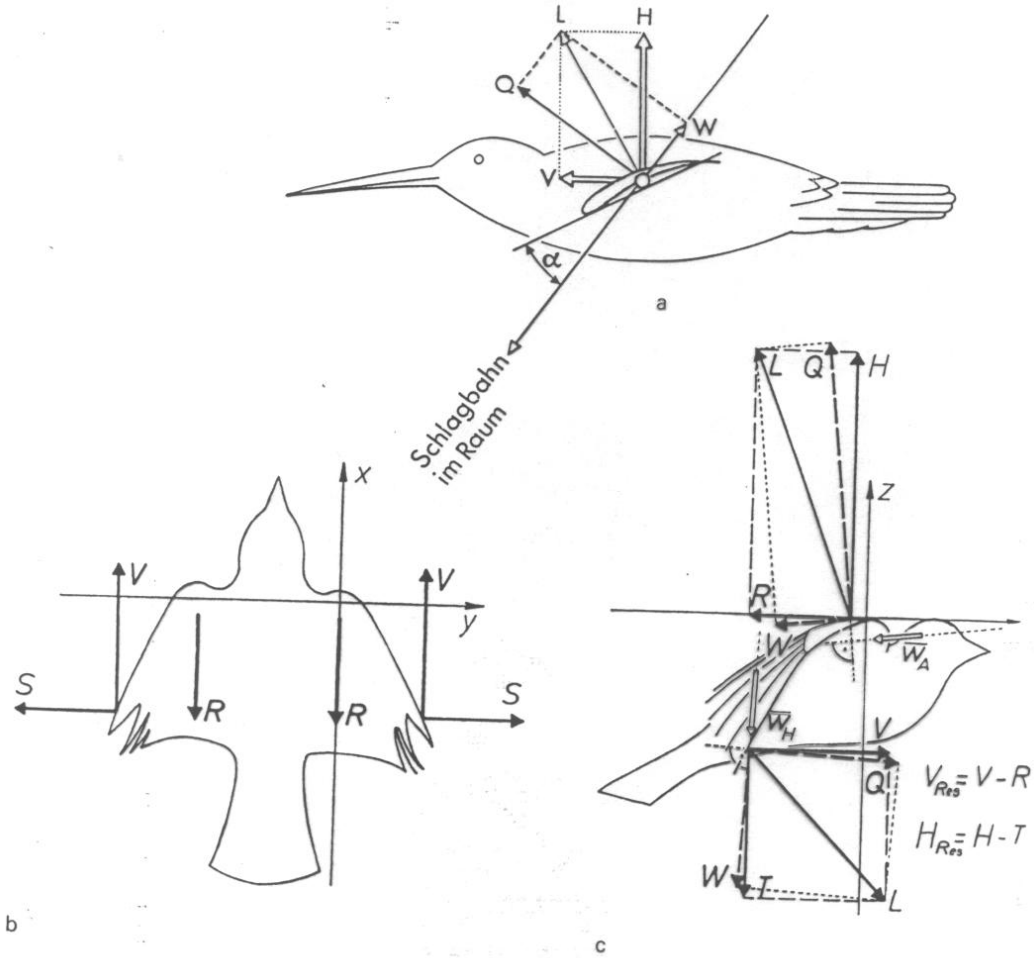
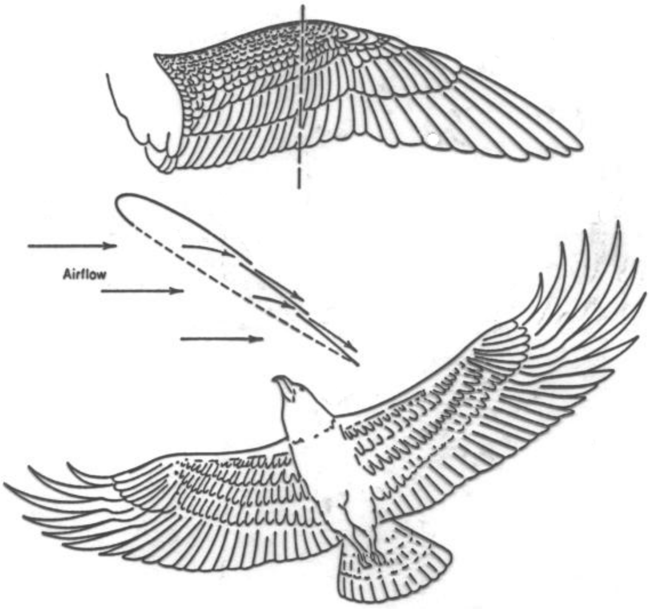


Fig. 6. (a) Pole and vaulter in initial configuration when the last foot of the vaulter leaves the ground. The leg shown is in an intermediate position between the two real legs. CG denotes the centre of gravity of the vaulter and R is the initial constant radius of curvature of the pole. (b) Pole and vaulter at time t.

Mudel – vt. artikkel



Mudel – aeromehaanika



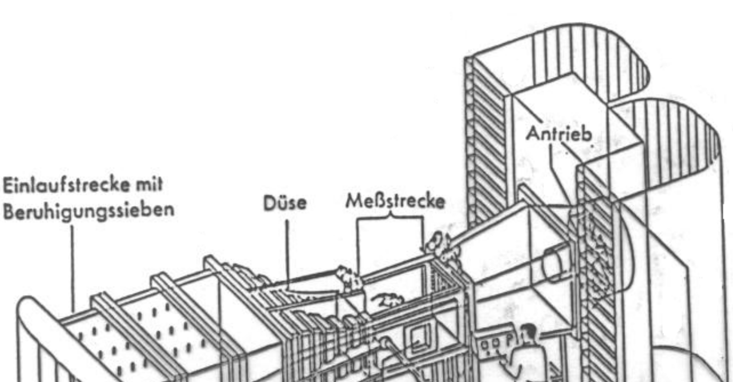


Abb. 1A. Großer Windkanal der Arbeitsgruppe NACHTIGALL an der Universität des Saarlandes

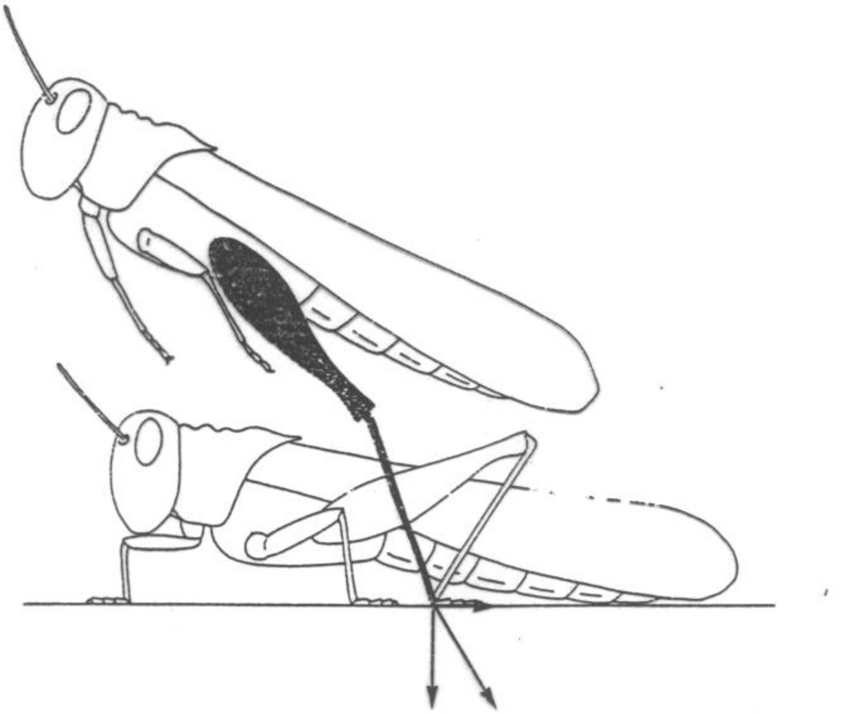


Fig. 84. Diagram of a locust jumping, showing the thrust exerted by the hind leg and its vertical and horizontal components.

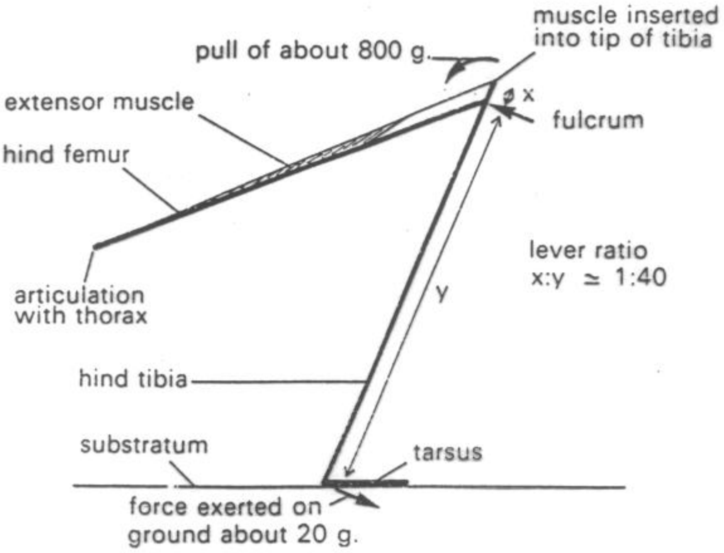


Fig. 85. Diagram to show the lever effect of the hind tibia of a locust with the tip of the femur acting as a fulcrum.

Mudel – liikumisvõrrand

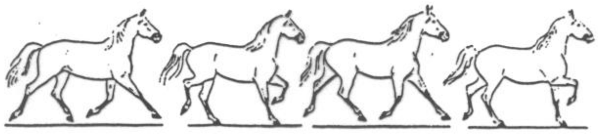


Figure 8.4 The trot of a horse

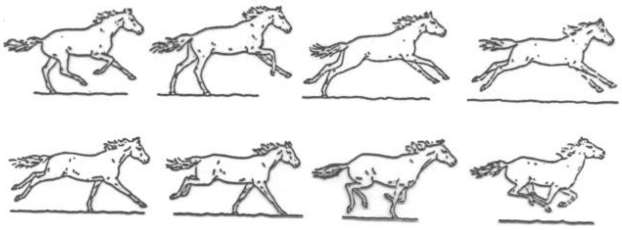
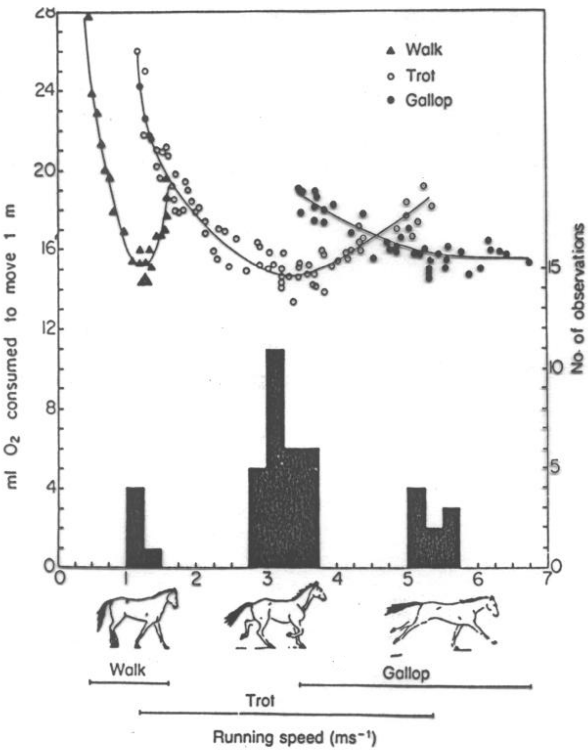
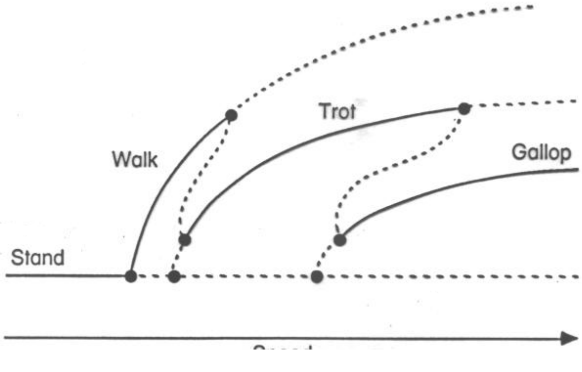
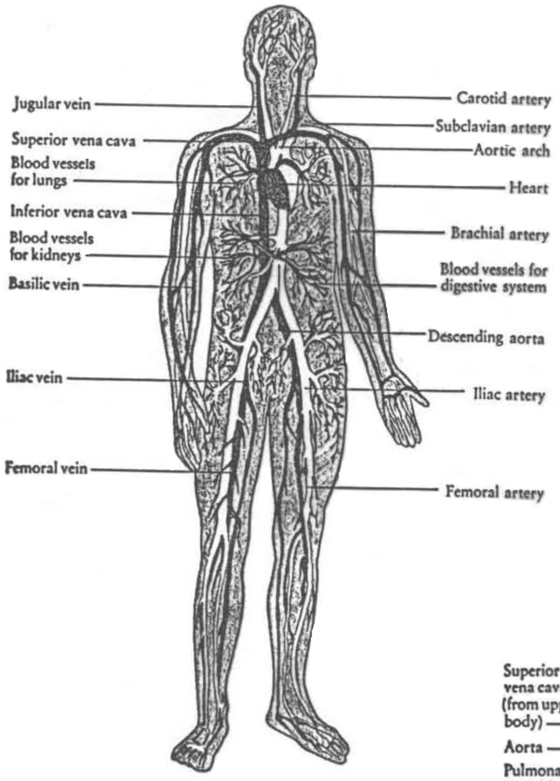


Figure 8.6 The rotary gallop of a horse

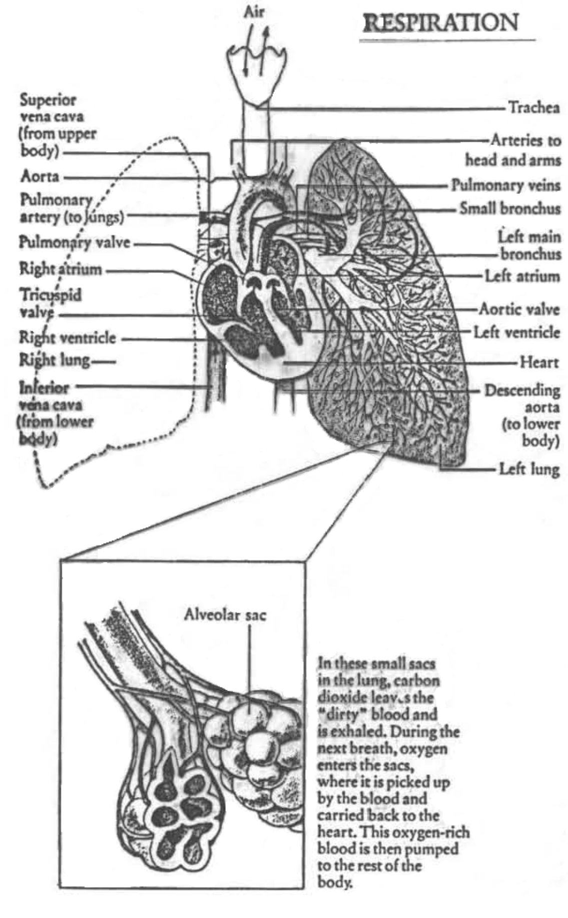




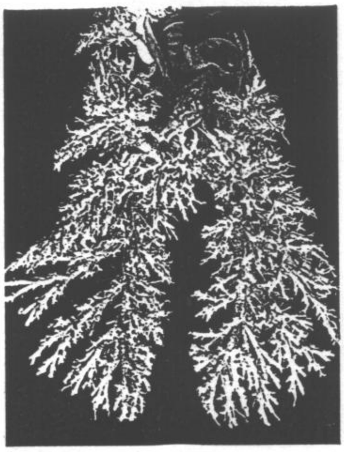
THE CIRCULATORY SYSTEM



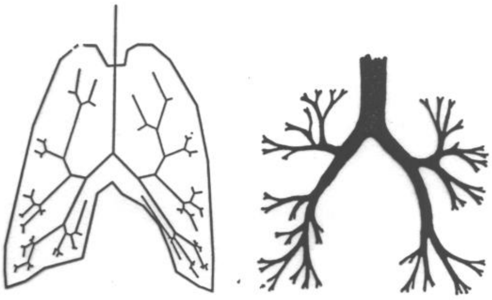
RESPIRATION



In these small sacs in the lung, carbon dioxide leaves the "dirty" blood and is exhaled. During the next breath, oxygen enters the sacs, where it is picked up by the blood and carried back to the heart. This oxygen-rich blood is then pumped to the rest of the body.



Freipräpariert enthüllen die Bronchien eines Menschen ihre baumähnliche, fraktale Struktur: die großen Verzweigungen ähneln den kleinen – und umgekehrt



A computer simulation of a fractal lung is depicted in which the boundary condition influence the morphogenesis. The boundary was derived from a chest radiograph. The model data are in good agreement with actual structural data (from Nelson and Manchester, 1988 with permission).

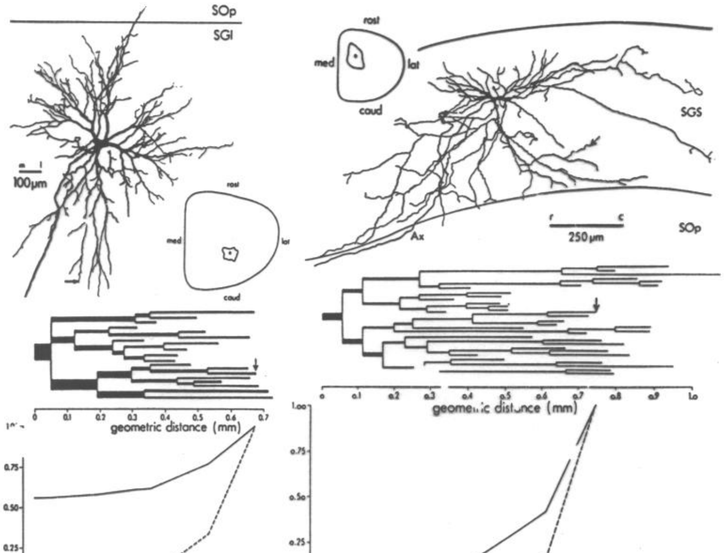
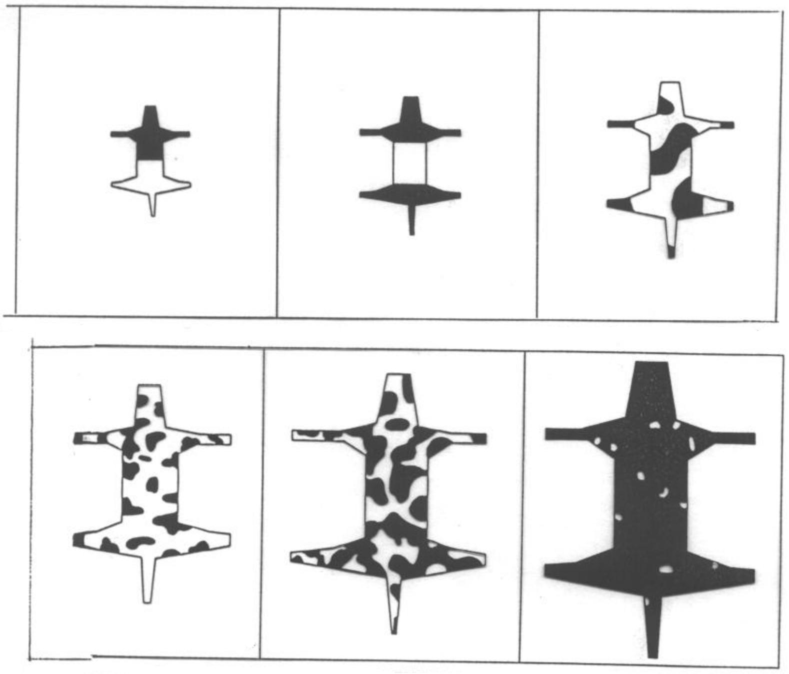
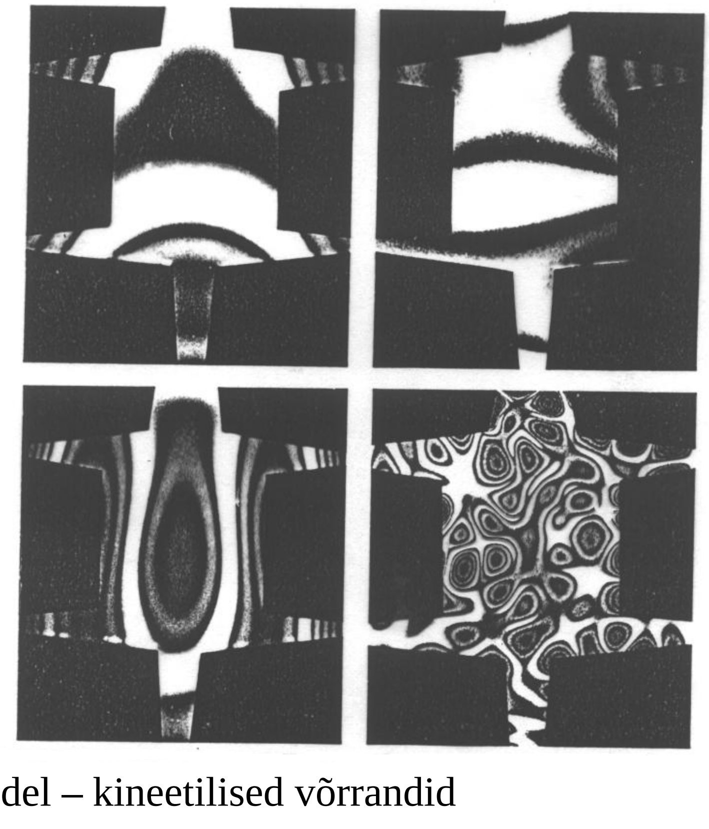


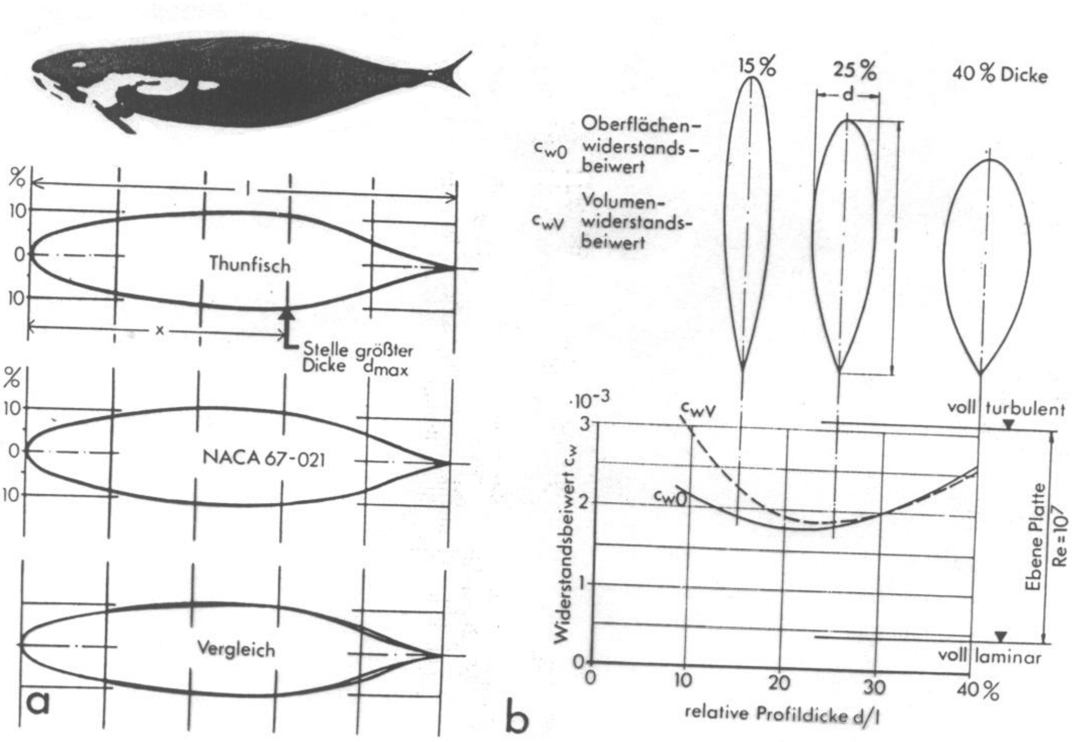
Fig. 1. Dendritic arborization and transfer properties of a TRSN (left) as compared with a SLN (right). The distinct structural patterns (above) are mirrored by the corresponding transfer ratios which has been calculated for a tonic synapse located on a dendritic termination (arrow). Whereas voltage transfer (dashed line) is negligible in both neurones, current transfer (continuous line) is considerably higher, but significantly different in TRSN (56%) and SLN (7%).

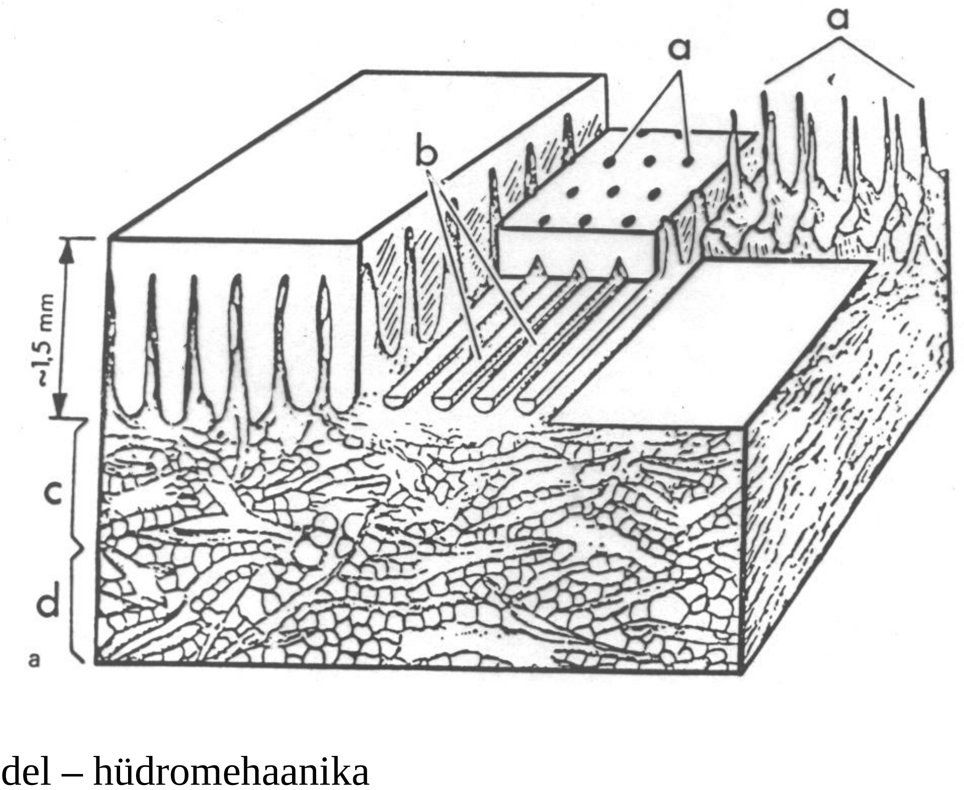
Mudel – fraktaalsed struktuurid





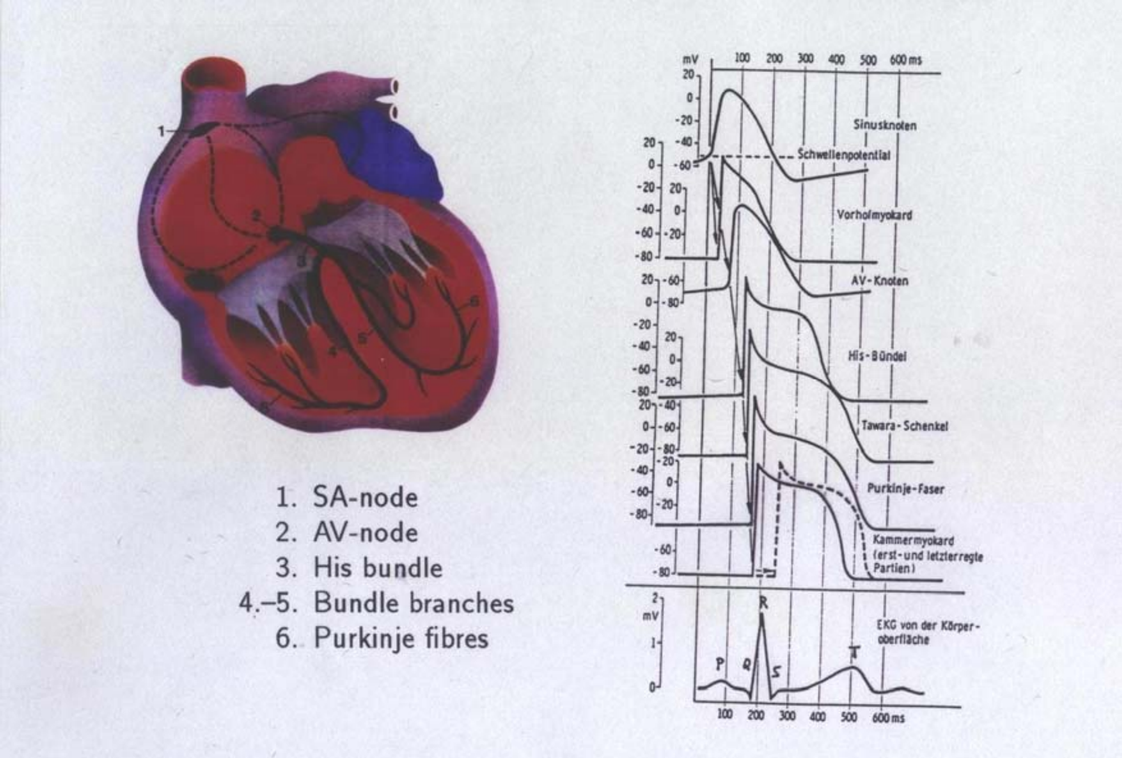
Mudel – kineetilised võrrandid

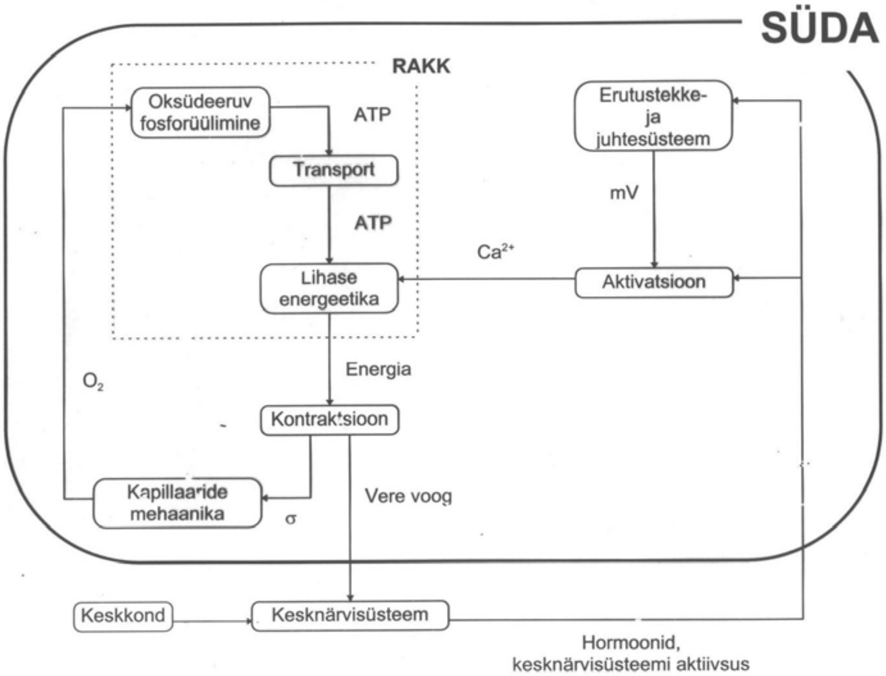




Mudel – hüdromehaanika

7.1. Südame erutusmehhanism





1. Normally beating heart

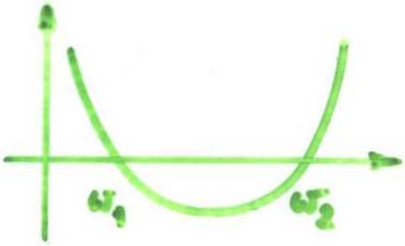
2. Mobitz2 — second order A-V block with constant PQ-time

3. Wenckebach — second order AV block with progressively increasing PQ-time

Derivation of the NPE:
Engelbrecht J. *An Introduction to Asymmetric Solitary Waves.* Longman. London & Harlow, 1991.

Nerve pulse equation:

$$\ddot{w} + \varepsilon_w (w - w_1)(w - w_2)\dot{w} + w = 0, \;\; w_1 w_2 > 0.$$



Van der Pol equation:

$$\ddot{u} + \varepsilon_u (u^2 - 1)\dot{u} + u = 0.$$

Our case:

$$\ddot{w} + \varepsilon (w - w_1)(w - w_2)\dot{w} + w = I \sum_{k=-\infty}^{\infty} \delta\,(t - kT)\,,$$

where

$$\varepsilon = 3.265, \;\; w_1 = 0.5, \;\; w_2 = 1.9, \;\; T = \frac{2\pi}{\omega}.$$

Driven nerve pulse equation

$$w'' + f(w)w' + kw = F$$

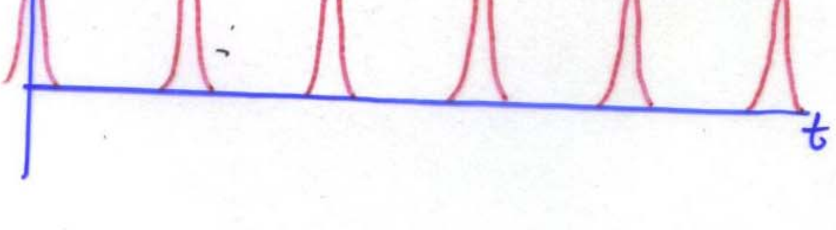
$$F = I\sum_{n=0}^{\infty}\delta(t - nT)$$

$$F = Iu(\omega t) + C$$

$$F = I\sin Bt$$

$$f(w) = q(w - w_1)(w - w_2)$$

$$3)\ w'' + f(w)\omega' + kw = A\sum_{n=0}^{\infty}\delta(t - nT)$$



$$T, \quad \omega = \frac{2\pi}{T}$$

NPE driven by Dirac delta spikes:

$$\ddot{w} + \varepsilon(w - w_1)(w - w_2)\dot{w} + w = I \sum_{k=-\infty}^{\infty} \delta\left(t - \frac{2k\pi}{\omega}\right).$$

R.h.s. given as a Fourier series:

$$I \sum_{k=-\infty}^{\infty} \delta\left(t - \frac{2k\pi}{\omega}\right) = I_0 + 2I_0 \sum_{n=1}^{\infty} \cos n\omega t,$$

where

$$I_0 = \frac{I\omega}{2\pi}$$

The NPE after a transformation and truncation of r.h.s.

$$\ddot{v} + \varepsilon(v - v_1)(v - v_2)\dot{v} + v = 2I_0 \cos \omega t,$$

where

$$v = w - I_0,\ v_1 = w_1 - I_0,\ v_2 = w_2 - I_0.$$

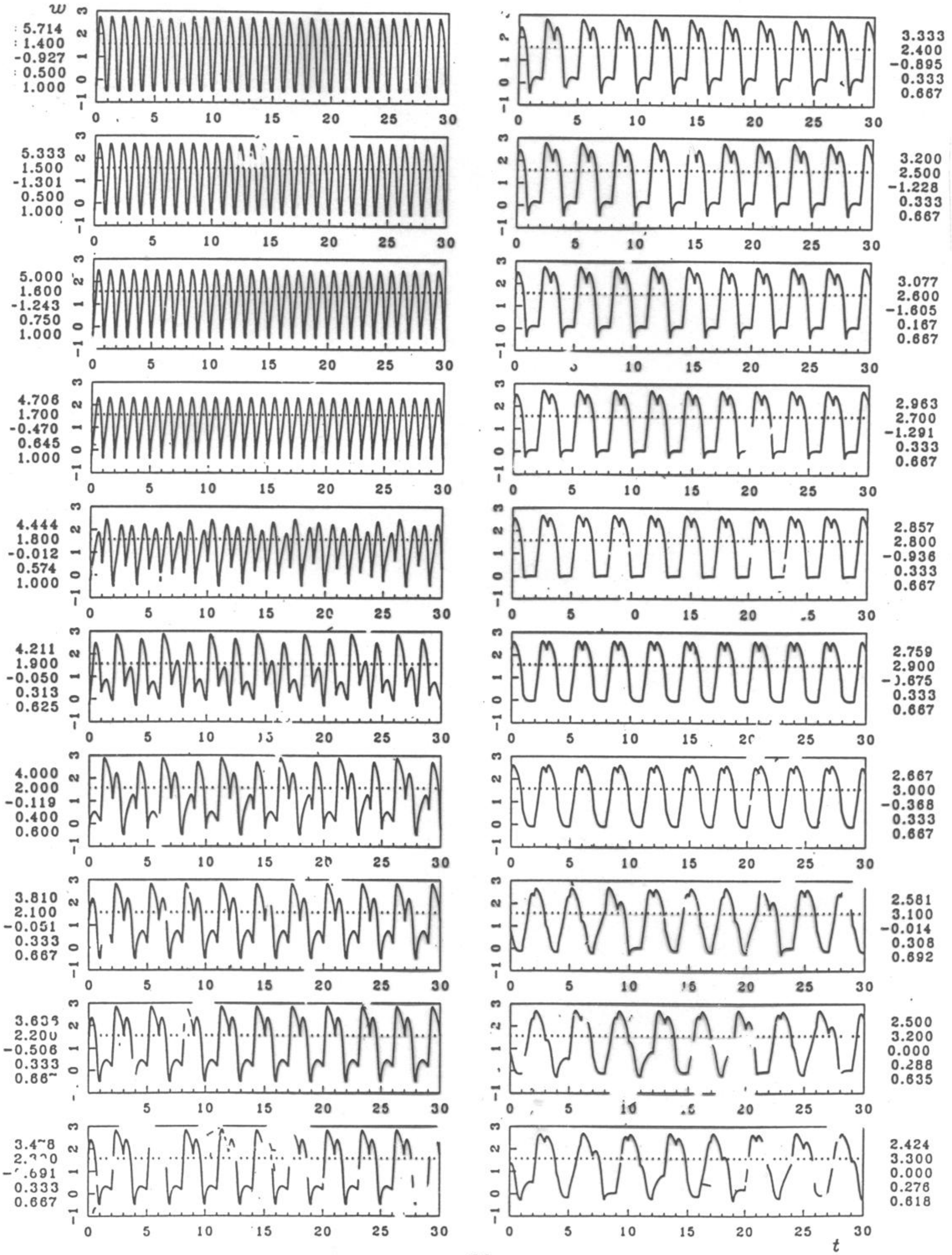
For constant ω and increasing I we expect

(a) $I_0 = w_1$, Neimark-Sacker;

(b) $I_0 = \dfrac{w_1 + w_2}{2}$, symmetric van der Pol equation — no inversion-symmetric solutions of even period (inversion-symmetry: $F(\ddot{v}, \dot{v}, v, t) = -F(-\ddot{v}, -\dot{v}, -v, t + T/2)$);

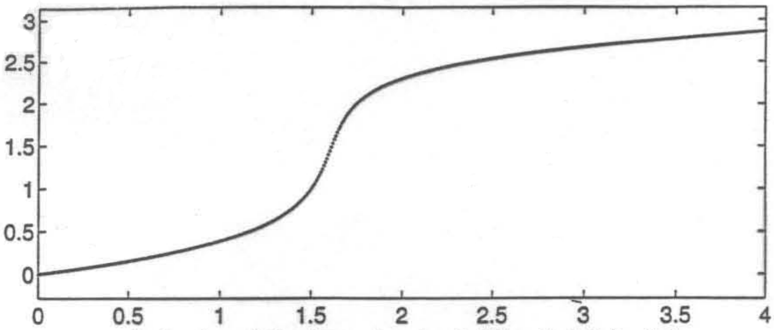
(c) $I_0 = w_2$, inverse Neimark-Sacker.

$I\ \omega = 8.00$


w
5.714
1.400
-0.927
0.500
1.000
5.333
1.500
-1.301
0.500
1.000
5.000
1.600
-1.243
0.750
1.000
4.706
1.700
-0.470
0.645
1.000
4.444
1.800
-0.012
0.574
1.000
4.211
1.900
-0.050
0.313
0.625
4.000
2.000
-0.119
0.400
0.600
3.810
2.100
-0.051
0.333
0.667
3.636
2.200
-0.506
0.333
0.667
3.478
2.300
-1.691
0.333
0.667
3.333
2.400
-0.895
0.333
0.667
3.200
2.500
-1.228
0.333
0.667
3.077
2.600
-1.605
0.167
0.667
2.963
2.700
-1.291
0.333
0.667
2.857
2.800
-0.936
0.333
0.667
2.759
2.900
-0.675
0.333
0.667
2.667
3.000
-0.368
0.333
0.667
2.581
3.100
-0.014
0.308
0.692
2.500
3.200
0.000
0.288
0.635
2.424
3.300
0.000
0.276
0.618
-1 0 1 2 3
0 5 10 15 20 25 30
t

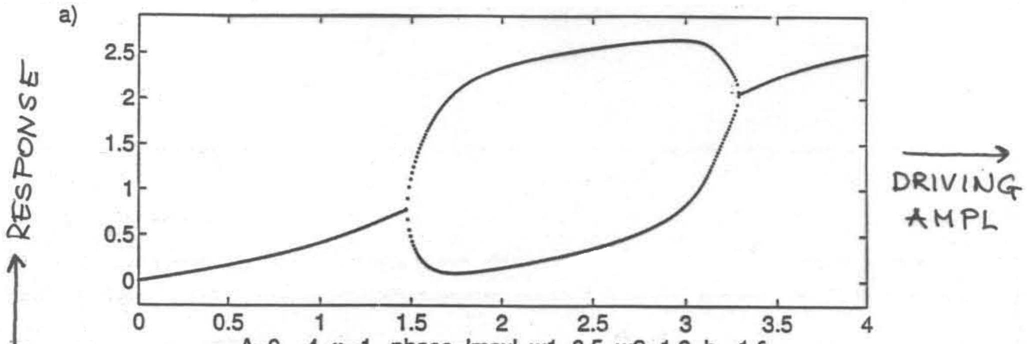
Poincare section w''+F(h)(w-w1)(w-w2)w'+w=A*delta(ωt)

a)



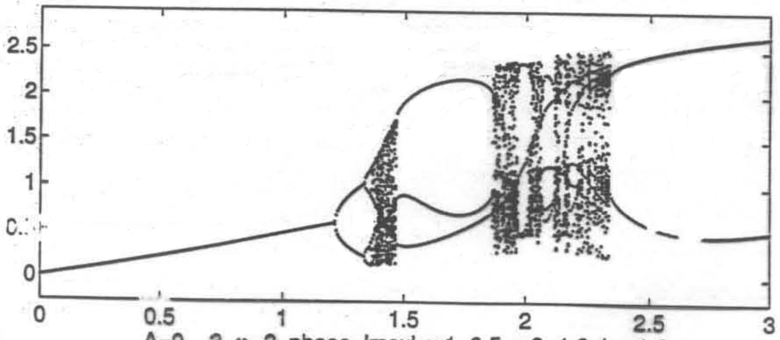
A=0 .. 4, ω=0.2, phase='max', w1=0.5, w2=1.9, h=-1.6

a)



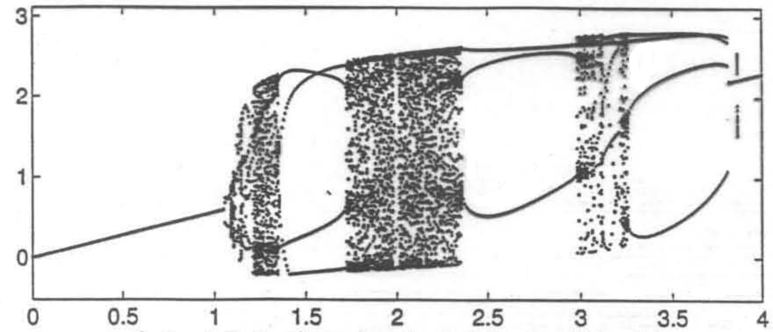
A=0 .. 4, ω=1, phase='max', w1=0.5, w2=1.9, h=-1.6

a)

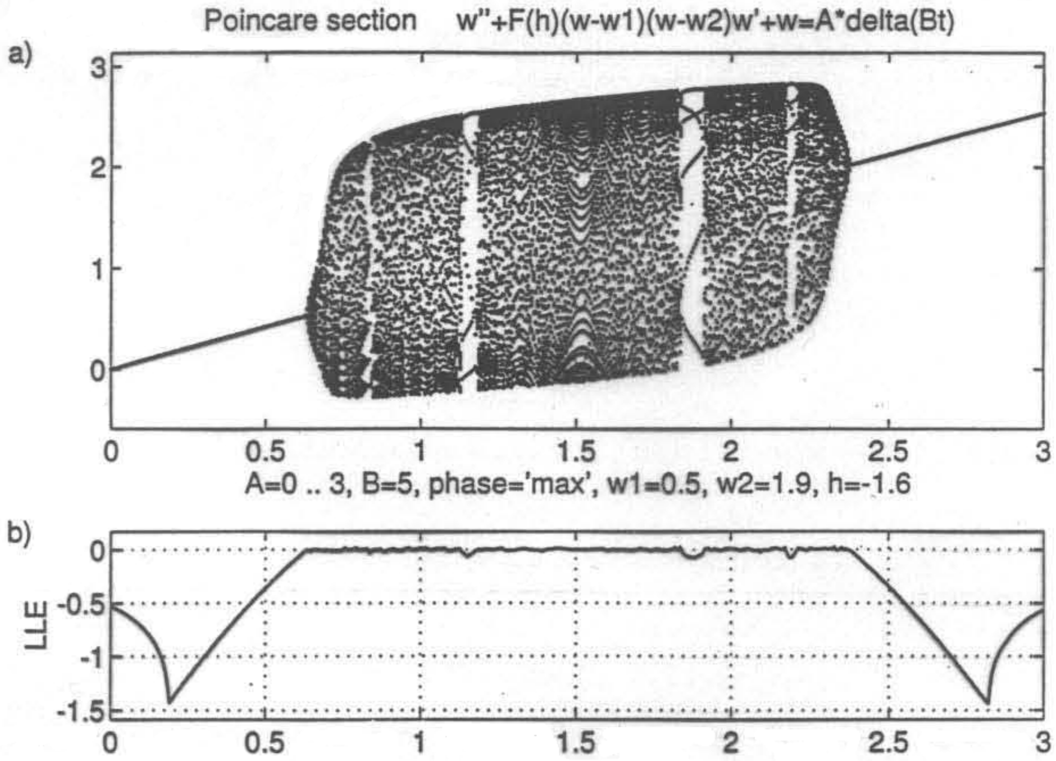


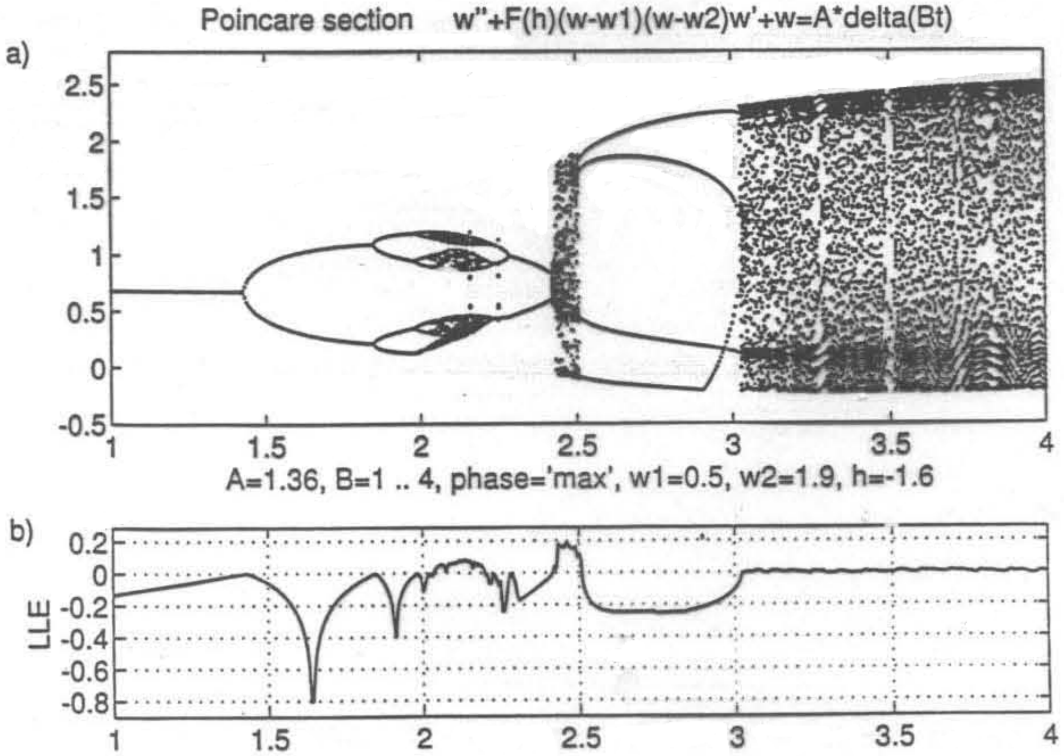
A=0 .. 3, ω=2, phase='max', w1=0.5, w2=1.9, h=-1.6

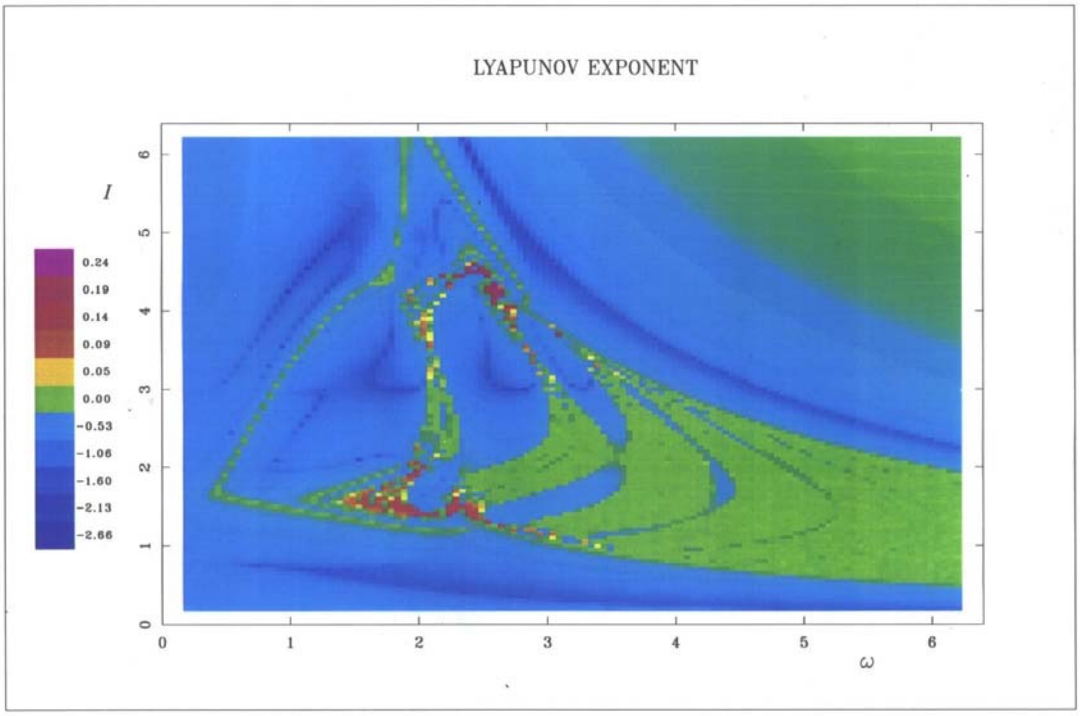
a)

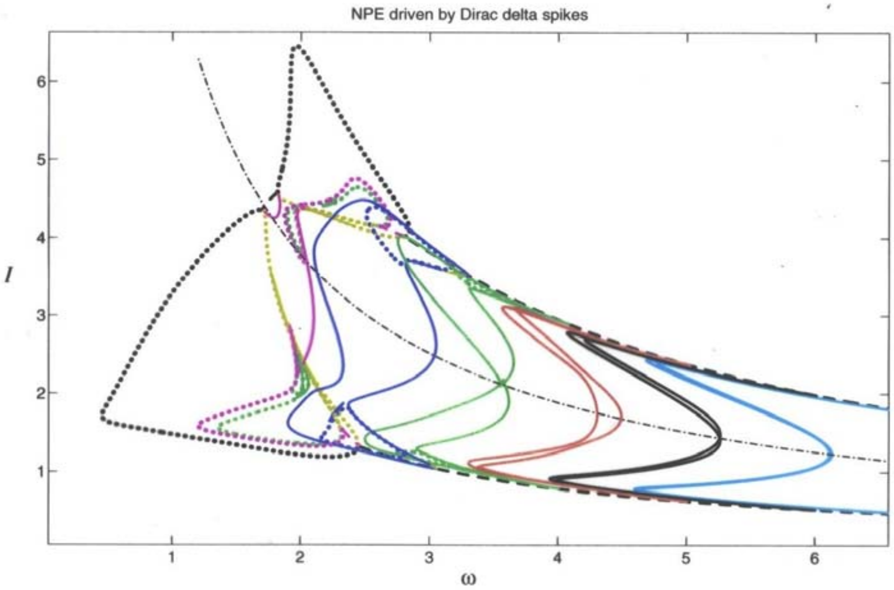


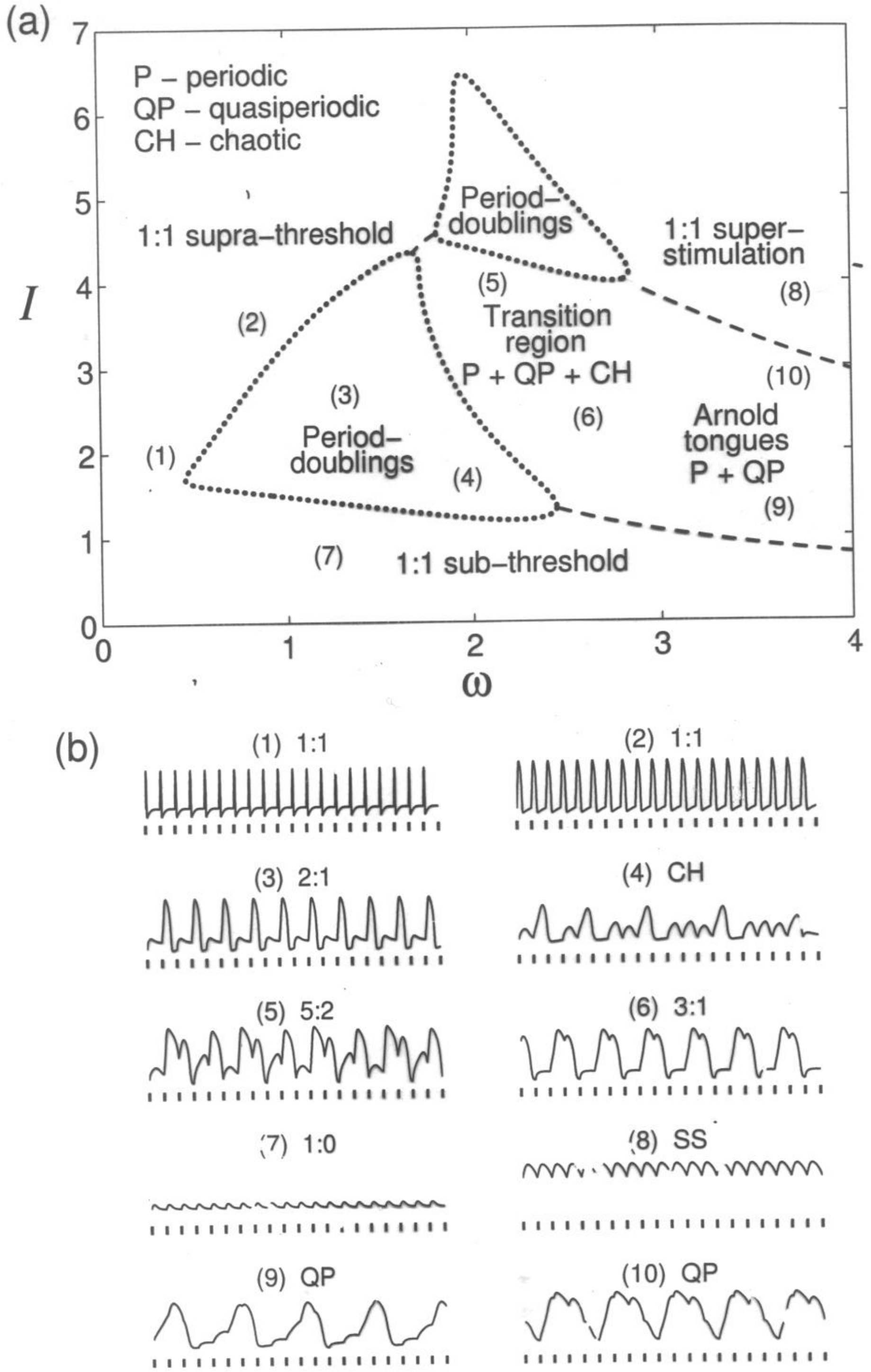
A=0 .. 4, B=3, phase='max', w1=0.5, w2=1.9, h=-1.6

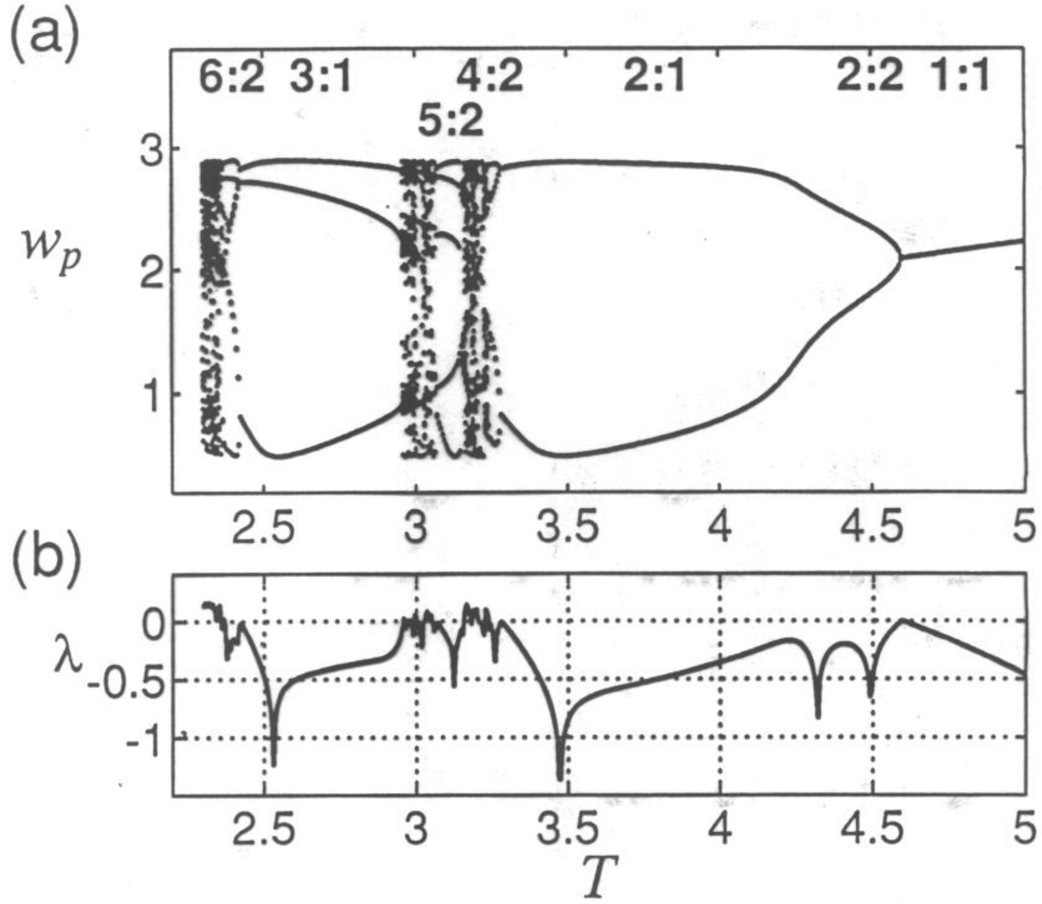

Poincare section w''+F(h)(w-w1)(w-w2)w'+w=A*delta(Bt)
a)
3
2
1
0
0
0.5
1
1.5
2
2.5
3
A=0 .. 3, B=5, phase='max', w1=0.5, w2=1.9, h=-1.6
b)
LLE
0
-0.5
-1
-1.5
0
0.5
1
1.5
2
2.5
3


Poincare section w''+F(h)(w-w1)(w-w2)w'+w=A*delta(Bt)
a)
2.5
2
1.5
1
0.5
0
-0.5
1
1.5
2
2.5
3
3.5
4
A=1.36, B=1 .. 4, phase='max', w1=0.5, w2=1.9, h=-1.6
b)
LLE
0.2
0
-0.2
-0.4
-0.6
-0.8
1
1.5
2
2.5
3
3.5
4

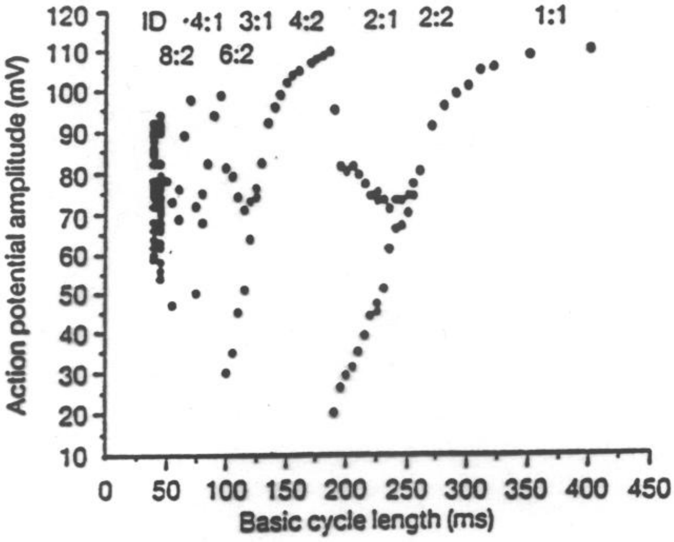

LYAPUNOV EXPONENT
I
ω
0
1
2
3
4
5
6
0.24
0.19
0.14
0.09
0.05
0.00
-0.53
-1.06
-1.60
-2.13
-2.66


NPE driven by Dirac delta spikes
I
ω
1
2
3
4
5
6

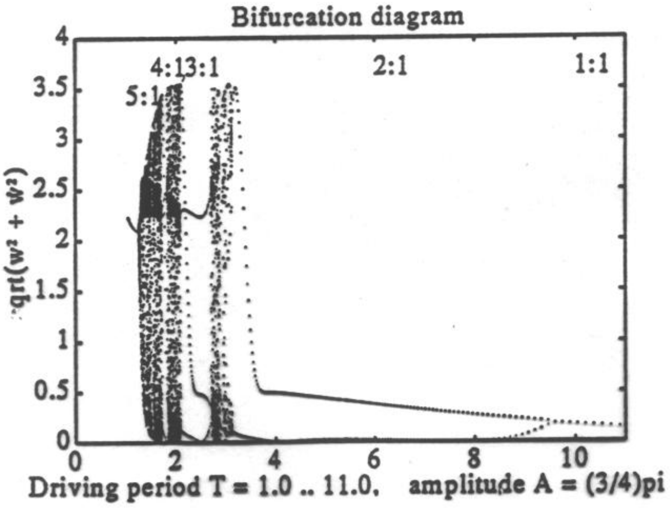

(a)
P – periodic
QP – quasiperiodic
CH – chaotic
1:1 supra–threshold
Period–doublings
1:1 super–stimulation
(5)
Transition region
P + QP + CH
(2)
(3)
(6)
(8)
(10)
Arnold tongues
P + QP
(1)
Period–doublings
(4)
(9)
(7)
1:1 sub–threshold
I
ω
0
1
2
3
4
5
6
7
(b)
(1) 1:1
(2) 1:1
(3) 2:1
(4) CH
(5) 5:2
(6) 3:1
(7) 1:0
(8) SS
(9) QP
(10) QP



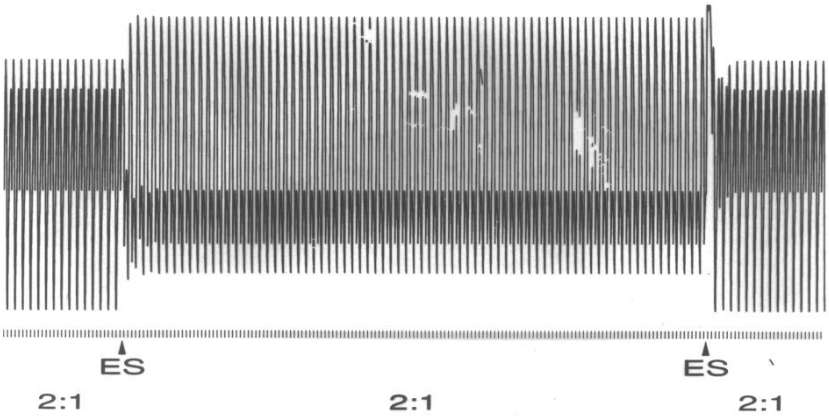
$A \sum \delta(t - nT), \quad A = 4.0 \quad (25\text{x threshold})$



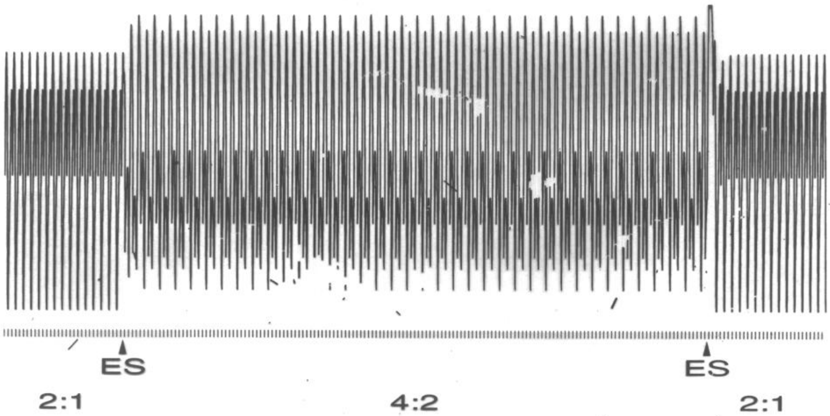
Experimental action potential from a driven sheep cardiac Purkinje fibre.



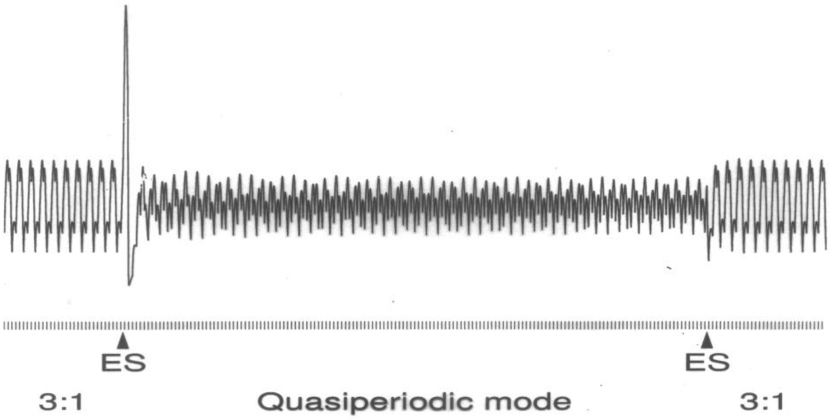
Action potential calculated from the driven nerve pulse equation.



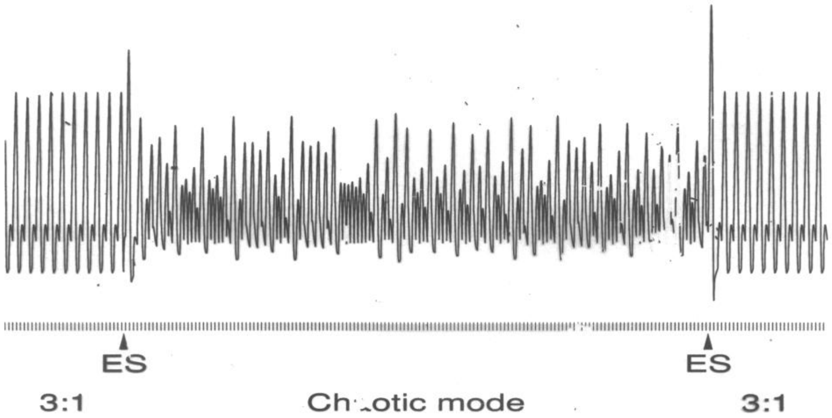
Saddle-node ⟵ Bistability ⟶ Saddle-node



Saddle-node ⟵ Bistability ⟶ Saddle-node



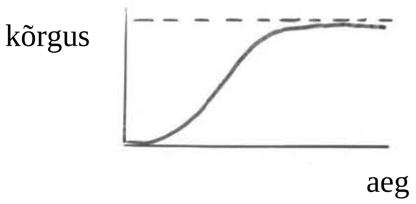
Saddle-node ← Bistability → Quasiperiodic blue sky catastrophe

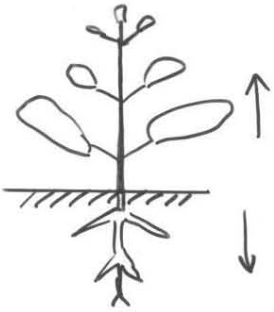


Saddle-node ← Bistability → Chaotic blue sky catastrophe

Näide 3. Taimed

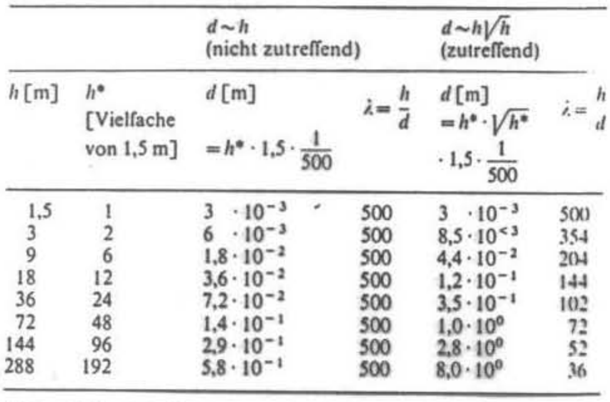
Taimede kasv





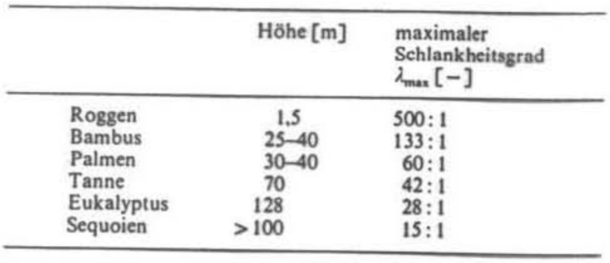
Mõjuvad faktorid

sisemised	välised
geenid	keskkond
hormoonid	vesi
	temperatuur
	valgus
	toit ained



		$d \sim h$ (nicht zutreffend)		$d \sim h\sqrt{h}$ (zutreffend)	
h [m]	h^* [Vielfache von 1,5 m]	d [m] $= h^* \cdot 1{,}5 \cdot \frac{1}{500}$	$\lambda = \frac{h}{d}$	d [m] $= h^* \cdot \sqrt{h^*} \cdot 1{,}5 \cdot \frac{1}{500}$	$\lambda = \frac{h}{d}$
1,5	1	$3 \cdot 10^{-3}$	500	$3 \cdot 10^{-3}$	500
3	2	$6 \cdot 10^{-3}$	500	$8{,}5 \cdot 10^{<3}$	354
9	6	$1{,}8 \cdot 10^{-2}$	500	$4{,}4 \cdot 10^{-2}$	204
18	12	$3{,}6 \cdot 10^{-2}$	500	$1{,}2 \cdot 10^{-1}$	144
36	24	$7{,}2 \cdot 10^{-2}$	500	$3{,}5 \cdot 10^{-1}$	102
72	48	$1{,}4 \cdot 10^{-1}$	500	$1{,}0 \cdot 10^{0}$	72
144	96	$2{,}9 \cdot 10^{-1}$	500	$2{,}8 \cdot 10^{0}$	52
288	192	$5{,}8 \cdot 10^{-1}$	500	$8{,}0 \cdot 10^{0}$	36

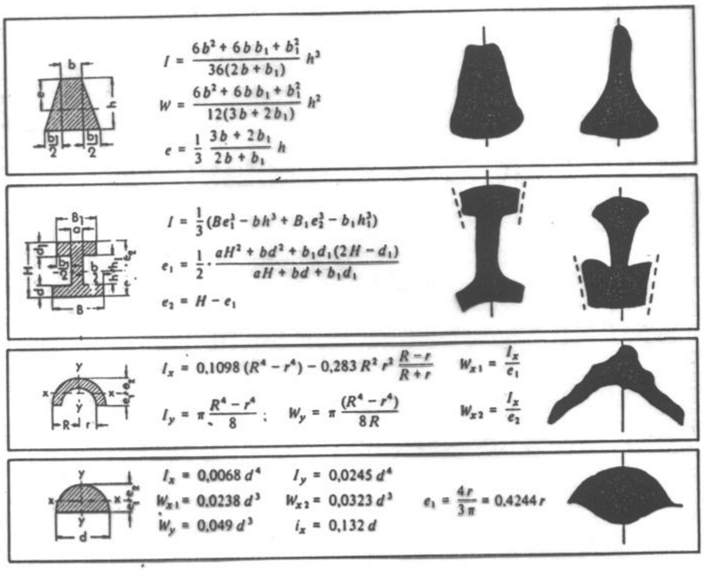
Abb. 14.13a. **Beispielrechnung für höhenabhängige Änderung der Schlankheitsgrade**



	Höhe [m]	maximaler Schlankheitsgrad λ_{max} [−]
Roggen	1,5	500 : 1
Bambus	25–40	133 : 1
Palmen	30–40	60 : 1
Tanne	70	42 : 1
Eukalyptus	128	28 : 1
Sequoien	> 100	15 : 1

Abb. 14.13b. **Höhen und Schlankheitsgrade von Gräsern und Bäumen**

Abb. 14.13a und b. **Erläuterungen im Text. (Nach Nachtigall)**



$$I = \frac{6b^2 + 6bb_1 + b_1^2}{36(2b + b_1)} h^3$$

$$W = \frac{6b^2 + 6bb_1 + b_1^2}{12(3b + 2b_1)} h^2$$

$$e = \frac{1}{3} \frac{3b + 2b_1}{2b + b_1} h$$

$$I = \frac{1}{3}(Be_1^3 - bh^3 + B_1e_2^3 - b_1h_1^3)$$

$$e_1 = \frac{1}{2} \cdot \frac{aH^2 + bd^2 + b_1d_1(2H - d_1)}{aH + bd + b_1d_1}$$

$$e_2 = H - e_1$$

$$I_x = 0{,}1098\,(R^4 - r^4) - 0{,}283\,R^2 r^2 \frac{R - r}{R + r} \qquad W_{x1} = \frac{I_x}{e_1}$$

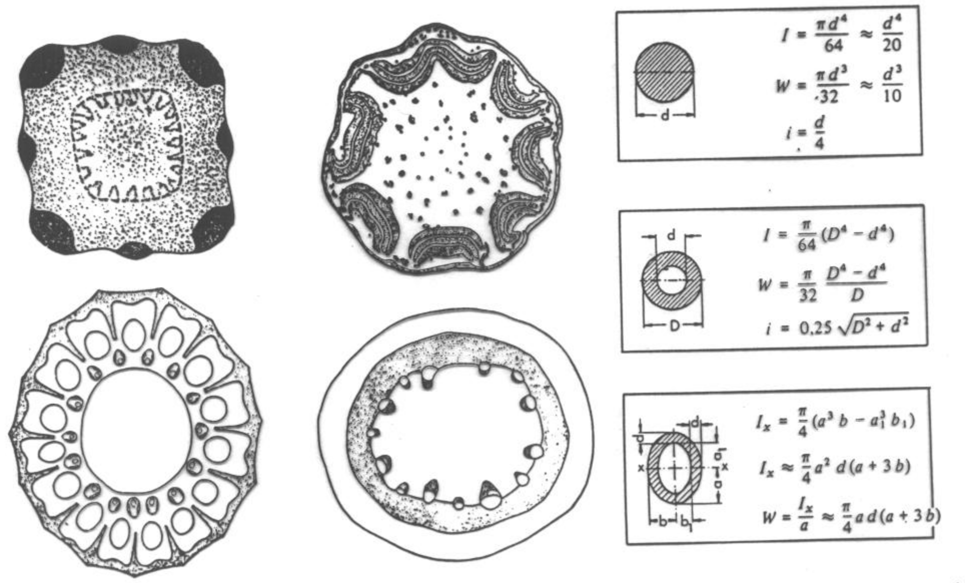
$$I_y = \pi \frac{R^4 - r^4}{8}; \quad W_y = \pi \frac{(R^4 - r^4)}{8R} \qquad W_{x2} = \frac{I_x}{e_2}$$

$$I_x = 0{,}0068\,d^4 \qquad I_y = 0{,}0245\,d^4$$

$$W_{x1} = 0{,}0238\,d^3 \qquad W_{x2} = 0{,}0323\,d^3 \qquad e_1 = \frac{4r}{3\pi} = 0{,}4244\,r$$

$$W_y = 0{,}049\,d^3 \qquad i_x = 0{,}132\,d$$

Abb. 14.17. Technische Trägerquerschnitte, ihr axiales Flächenträgheitsmoment I, Widerstandsmoment W und mittlerer Biegeabstand e, sowie den technischen Trägern ähnliche botanische Trägerquerschnitte (Skerenchymzüge). Von oben nach unten und von links nach rechts: *Osmunda spec., Kopresia carcina, Juncus spec., Molinia coerulea, Pinus spec., Sambucus spec.* (Nach verschiedenen Autoren zusammengestellt; Formeln nach Böge)



$$I = \frac{\pi d^4}{64} \approx \frac{d^4}{20}$$

$$W = \frac{\pi d^3}{32} \approx \frac{d^3}{10}$$

$$i = \frac{d}{4}$$

$$I = \frac{\pi}{64}(D^4 - d^4)$$

$$W = \frac{\pi}{32} \frac{D^4 - d^4}{D}$$

$$i = 0{,}25\sqrt{D^2 + d^2}$$

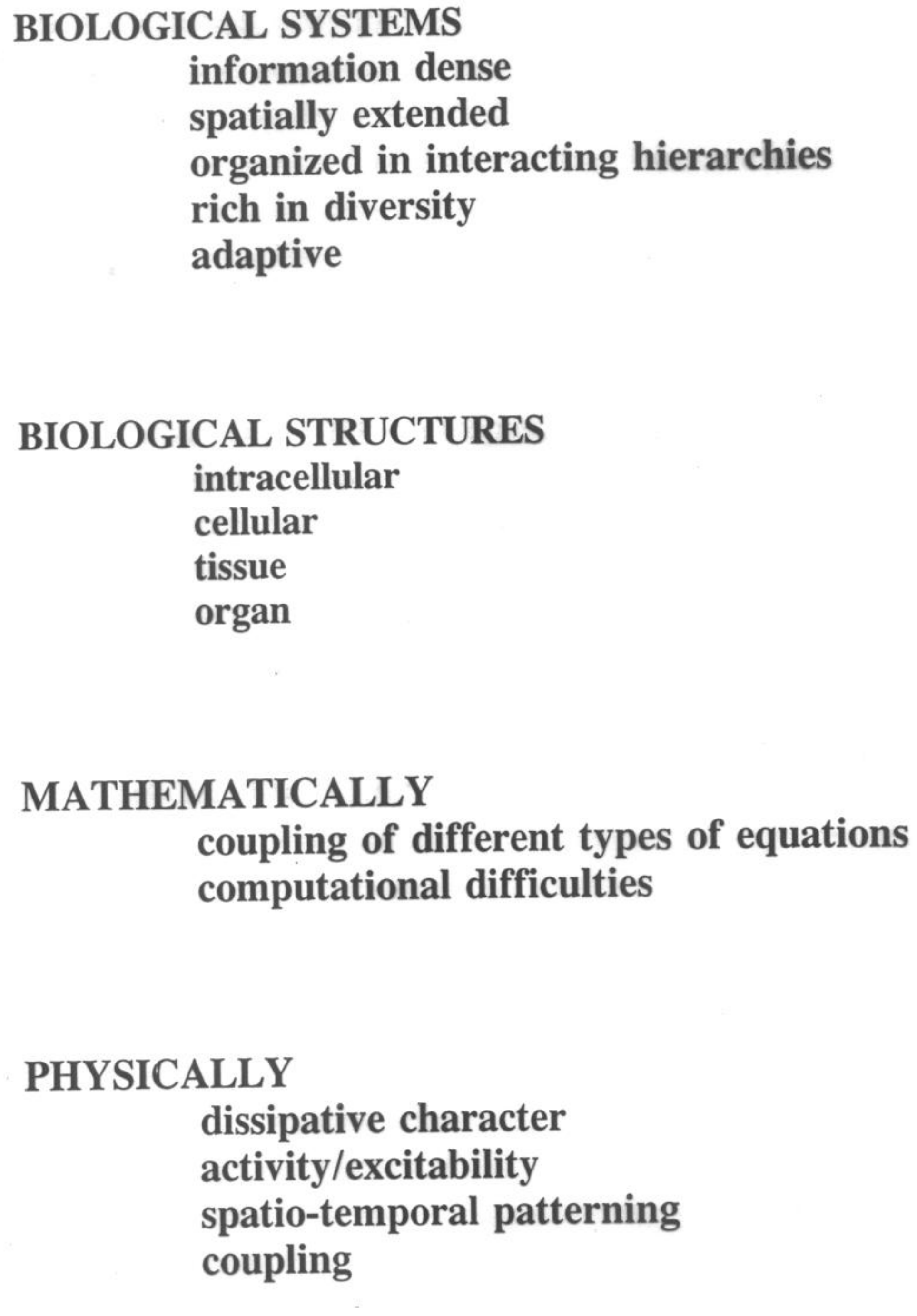
$$I_x = \frac{\pi}{4}(a^3 b - a_1^3 b_1)$$

$$I_x \approx \frac{\pi}{4} a^2 d(a + 3b)$$

$$W = \frac{I_x}{a} \approx \frac{\pi}{4} a d(a + 3b)$$

Abb. 14.18. Querschnitte durch pflanzliche Stengel und Sprosse sowie analoge Querschnitte durch technische Körper hohen polaren Flächenträgheitsmoments. Von oben nach unten und links nach rechts: *Sambucus spec.* (Holunder), *Cyathea usambarensis* (ein tropischer Baumfarn), *Equisetum telmateja* (ein Schachtelhalm), *Armeria elongata* (eine Grasnelke). (Nach verschiedenen Autoren zusammengestellt; Formeln nach Böge)

7.2. Kokkuvõte



BIOLOGICAL SYSTEMS
- information dense
- spatially extended
- organized in interacting hierarchies
- rich in diversity
- adaptive

BIOLOGICAL STRUCTURES
- intracellular
- cellular
- tissue
- organ

MATHEMATICALLY
- coupling of different types of equations
- computational difficulties

PHYSICALLY
- dissipative character
- activity/excitability
- spatio-temporal patterning
- coupling

RECOMMENDED READING

1. P. Kohl, D. Noble, R.L. Winslow, P.J. Hunter, Computational modelling of biological systems: tools and visions. Proc. Royal Soc. London, 2000, A 358, 579-610.

2. P.J. Kolston, Finite-element modelling: a new tool for the biologist. Proc. Royal Soc. London, 2000, A 358, 611-631.

3. J.D. Humphrey, Continuum biomechanics of soft biological tissues. Proc. Royal Soc. London, 2003, A 459, 3-46.