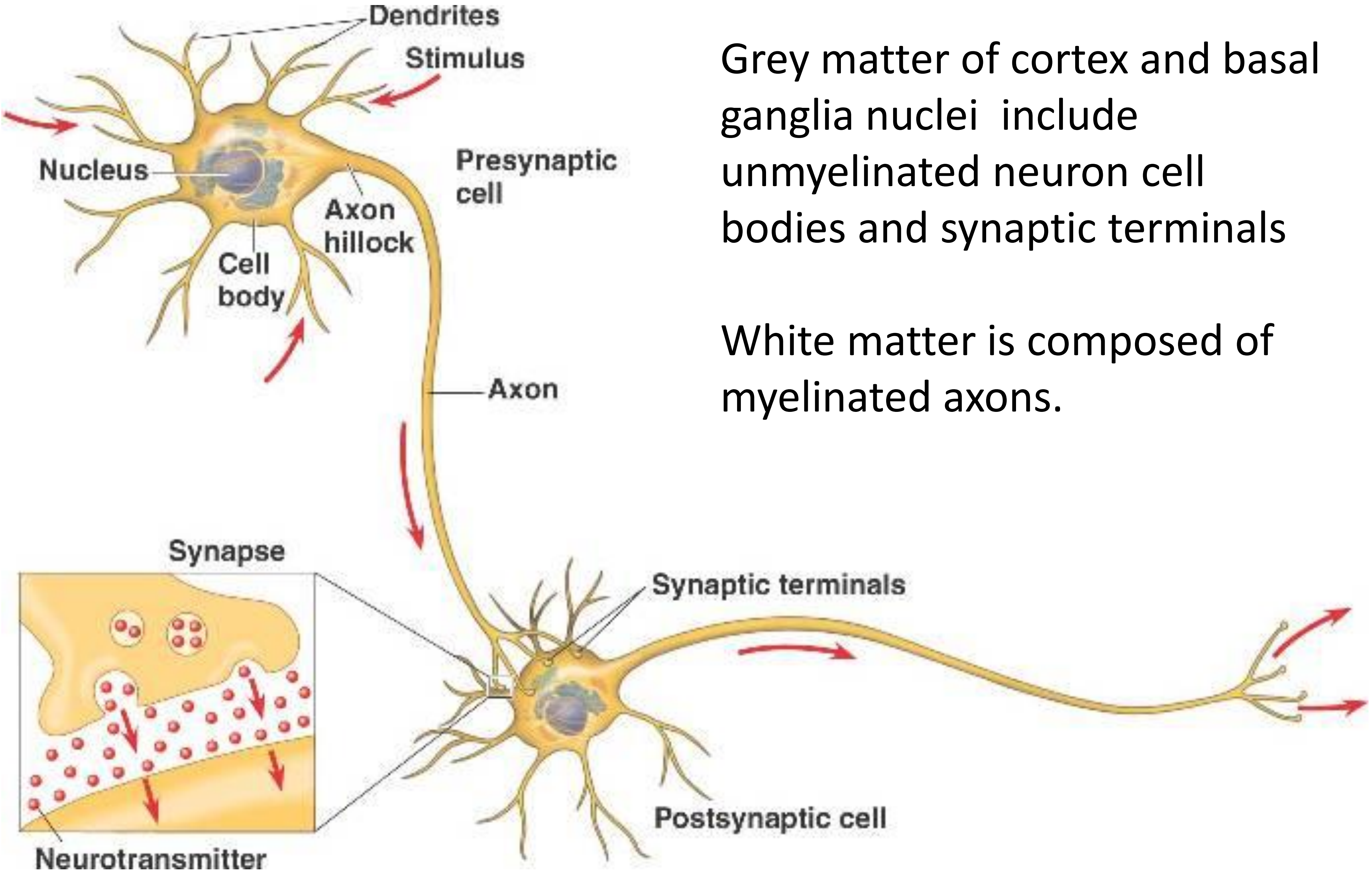
International Course on Functional Stereotactic Neurosurgery, Beijing, May 2015

Basic Electrophysiology of Neurons
Recording and stimulation technology
Recording and stimulation in the operating room

Dr Bernard PIDOUX, MD, PhD

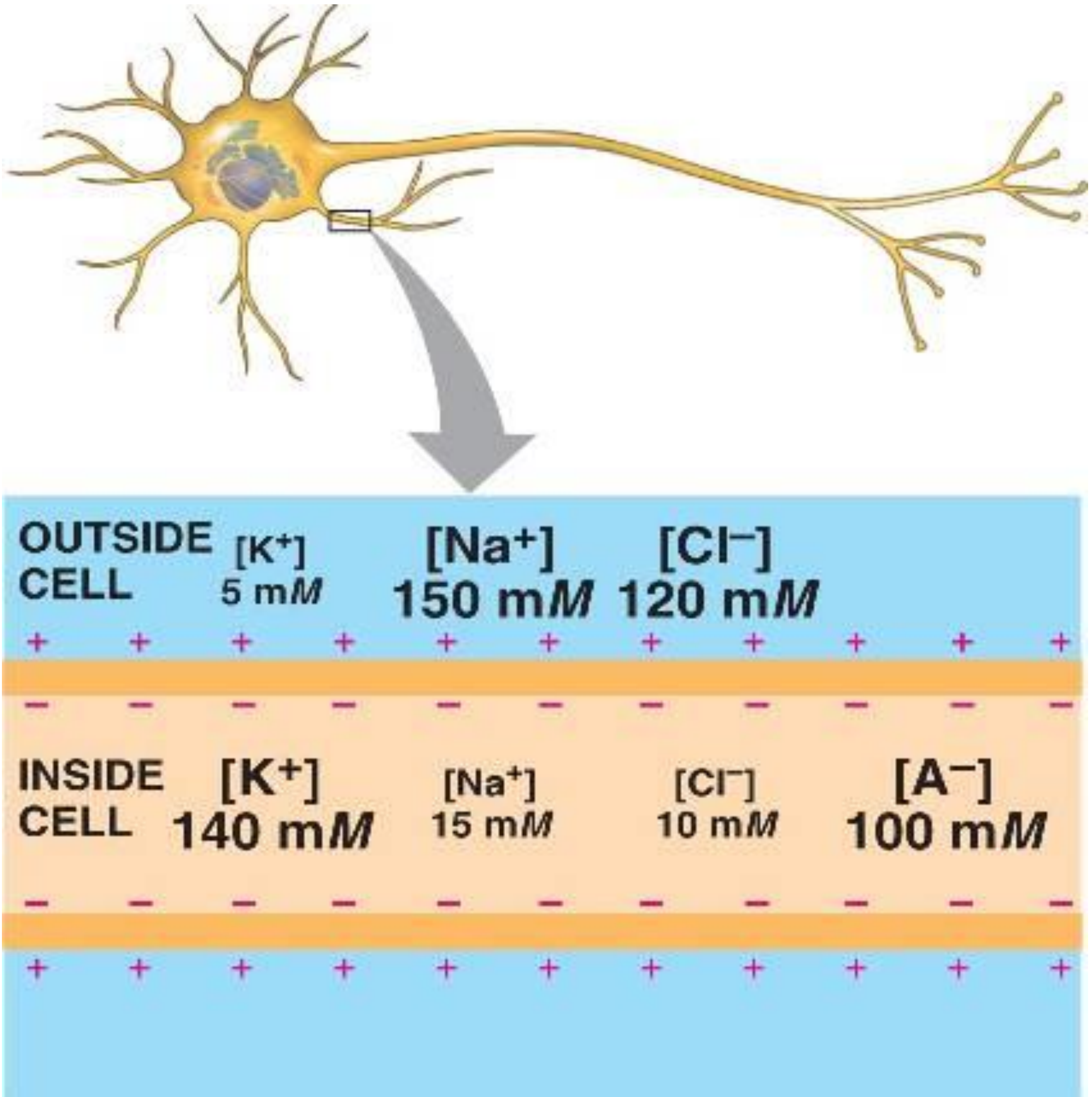
Université Pierre et Marie Curie, Paris 6

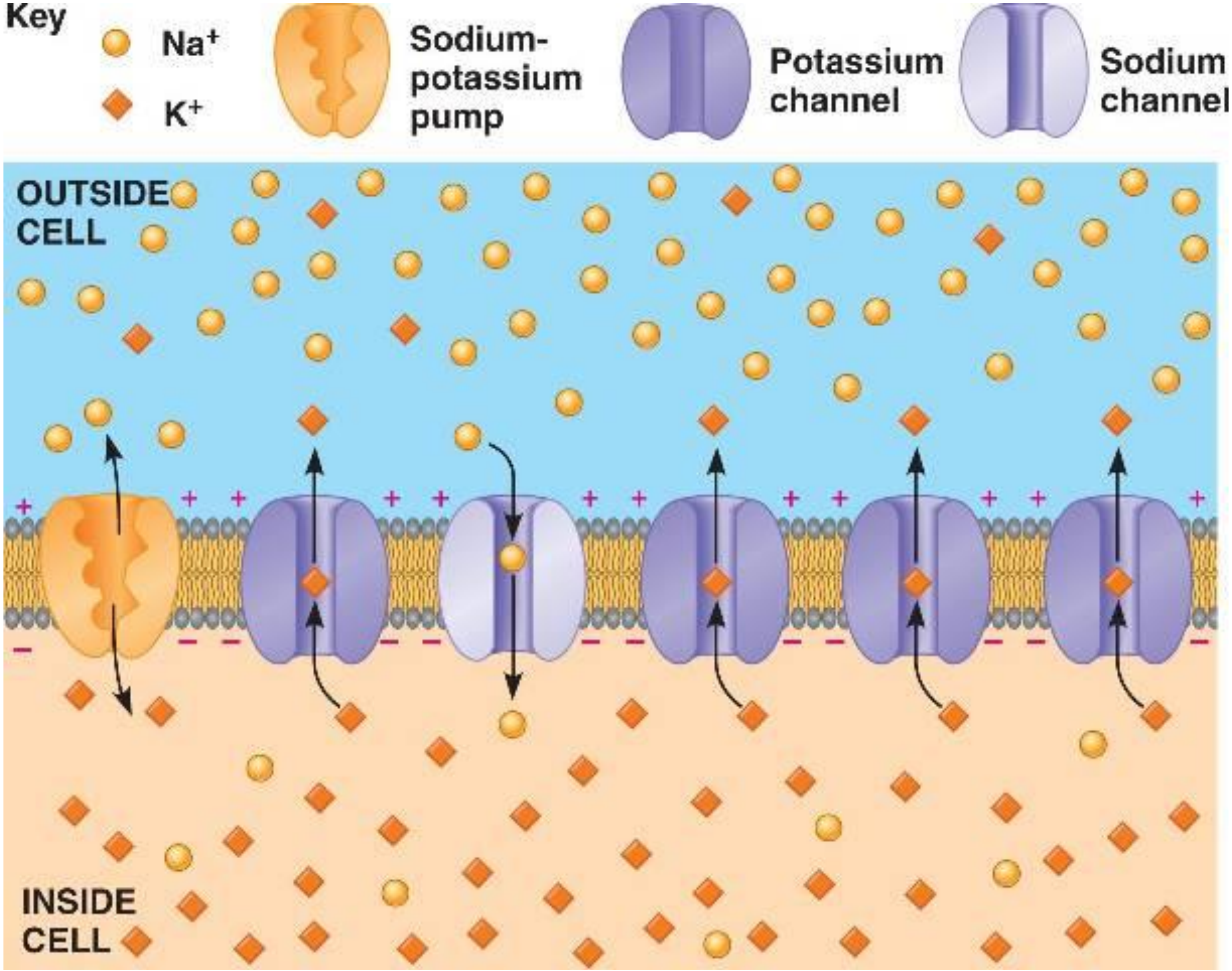
Hôpital Pitié-Salpêtrière, Paris, France



Grey matter of cortex and basal ganglia nuclei include unmyelinated neuron cell bodies and synaptic terminals

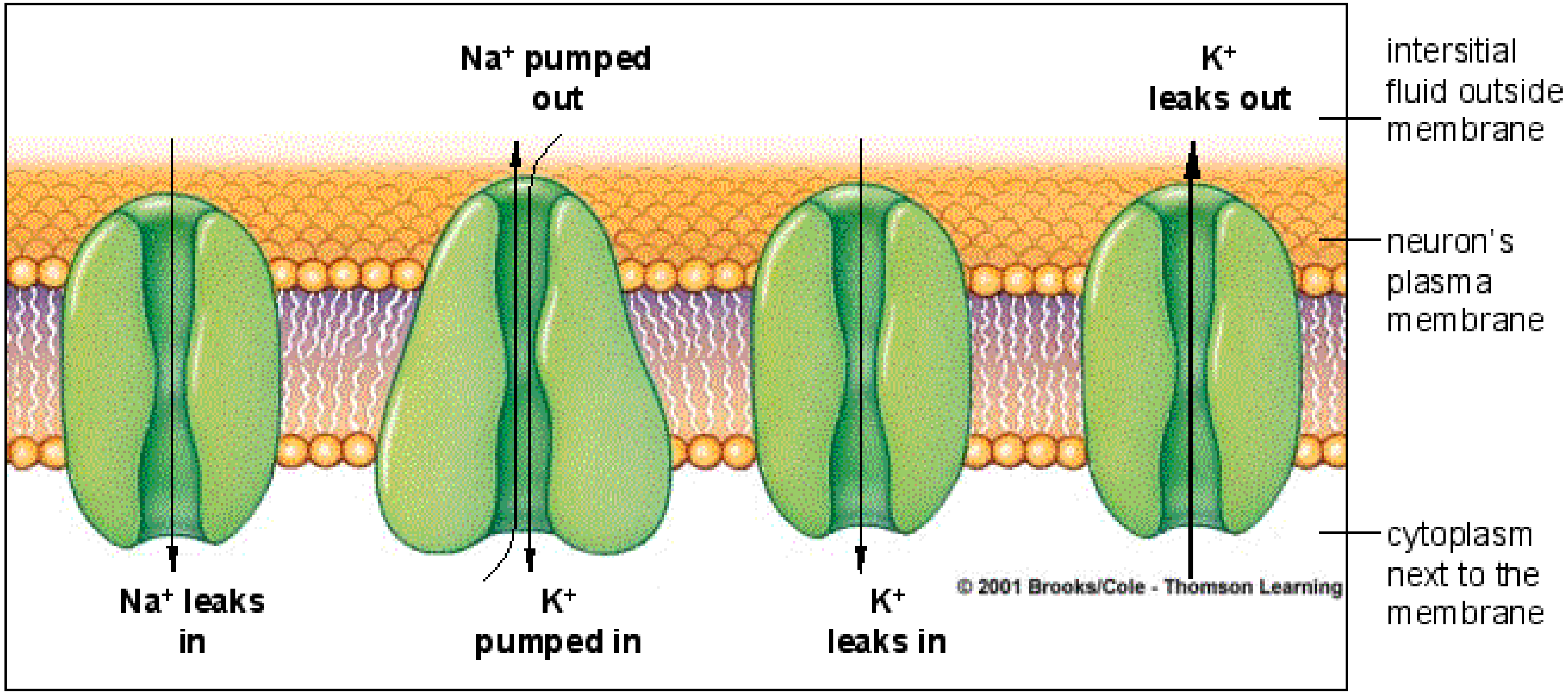
White matter is composed of myelinated axons.

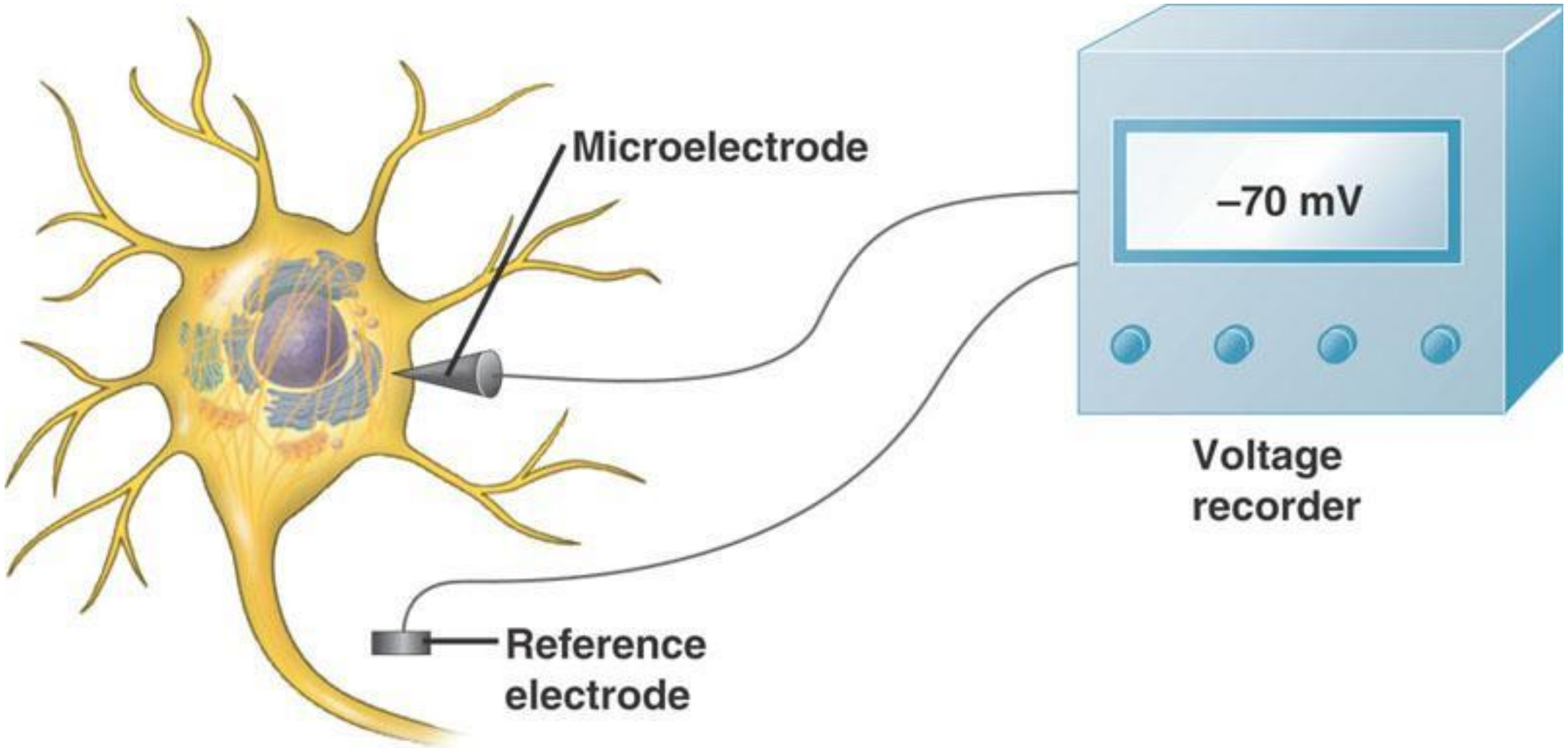

OUTSIDE CELL
[K+] 5 mM
[Na+] 150 mM
[Cl−] 120 mM
INSIDE CELL
[K+] 140 mM
[Na+] 15 mM
[Cl−] 10 mM
[A−] 100 mM


Key
Na+
K+
Sodium-potassium pump
Potassium channel
Sodium channel
OUTSIDE CELL
INSIDE CELL

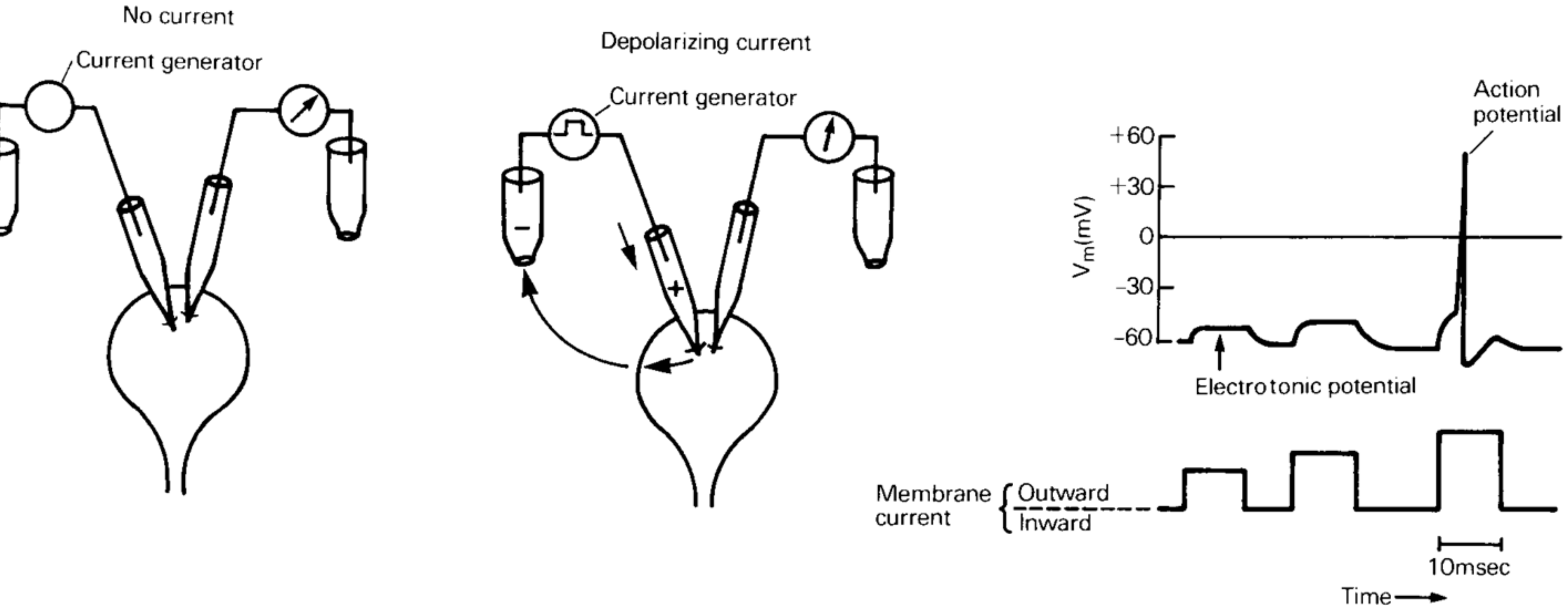
Maintaining Resting Potential

K^+ and Na^+ can't diffuse across bilayer



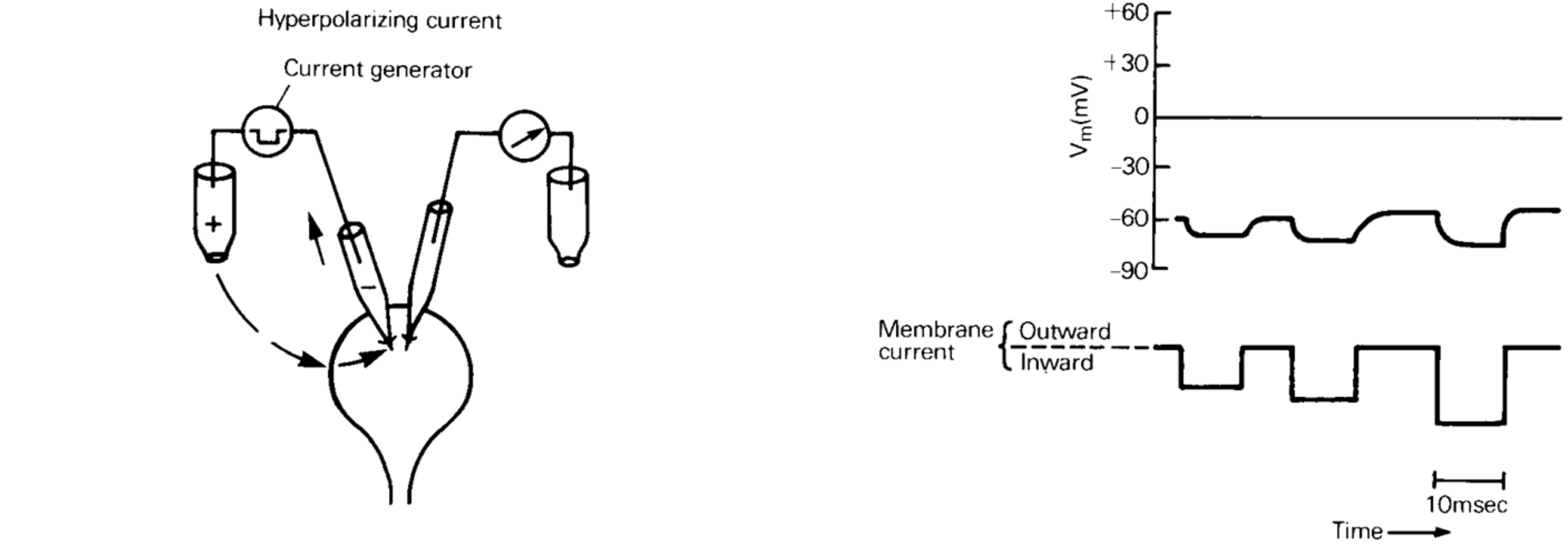

Microelectrode
–70 mV
Voltage recorder
Reference electrode

B

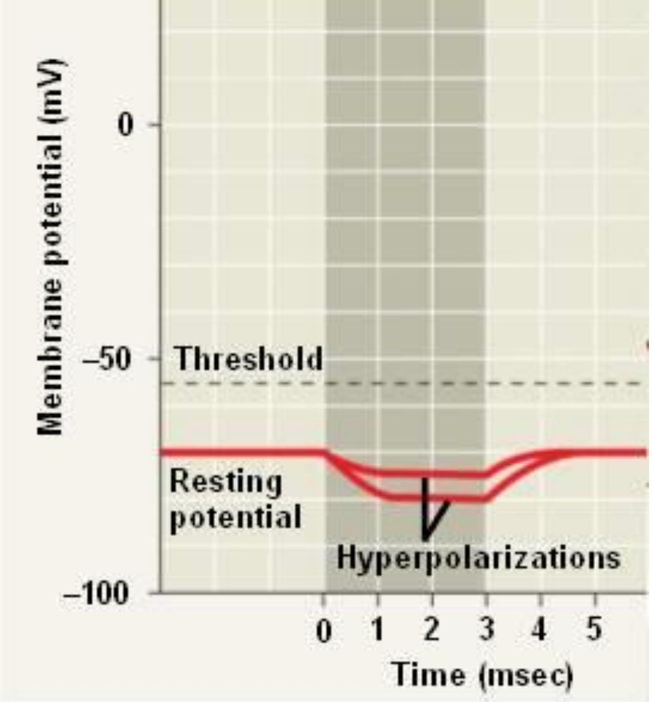


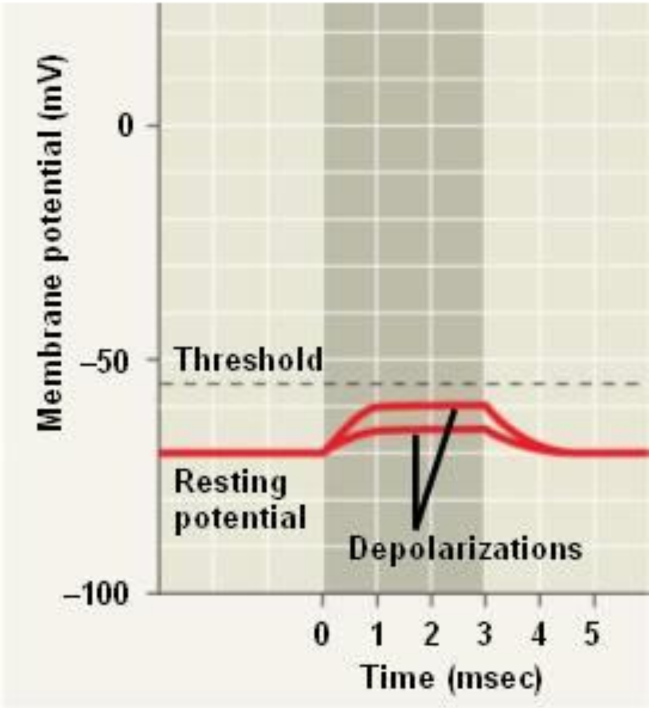
No current
Current generator
Depolarizing current
Current generator
Action
potential
+60
+30
0
-30
-60
V_m(mV)
Electrotonic potential
Membrane
current
Outward
Inward
10msec
Time

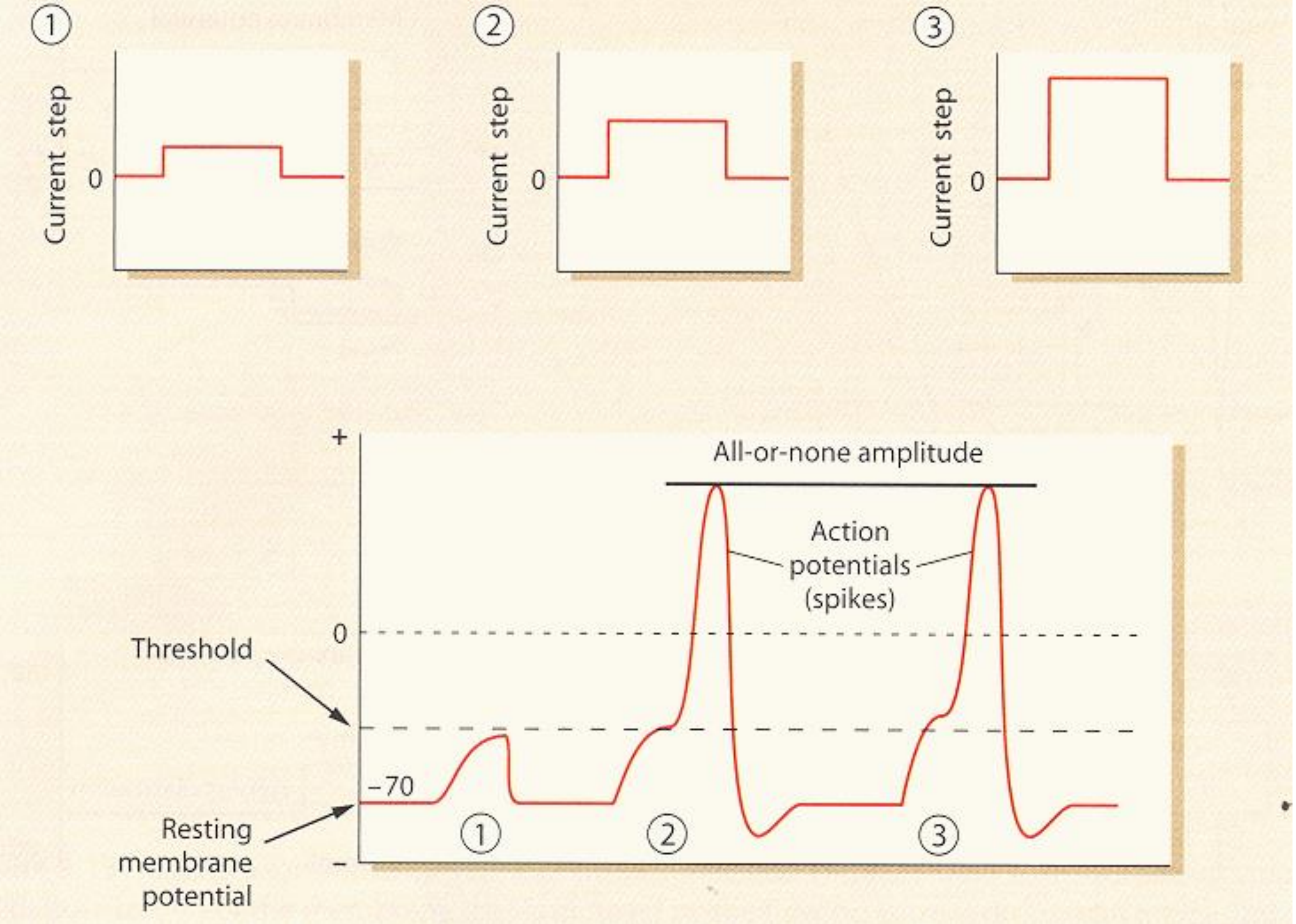
C



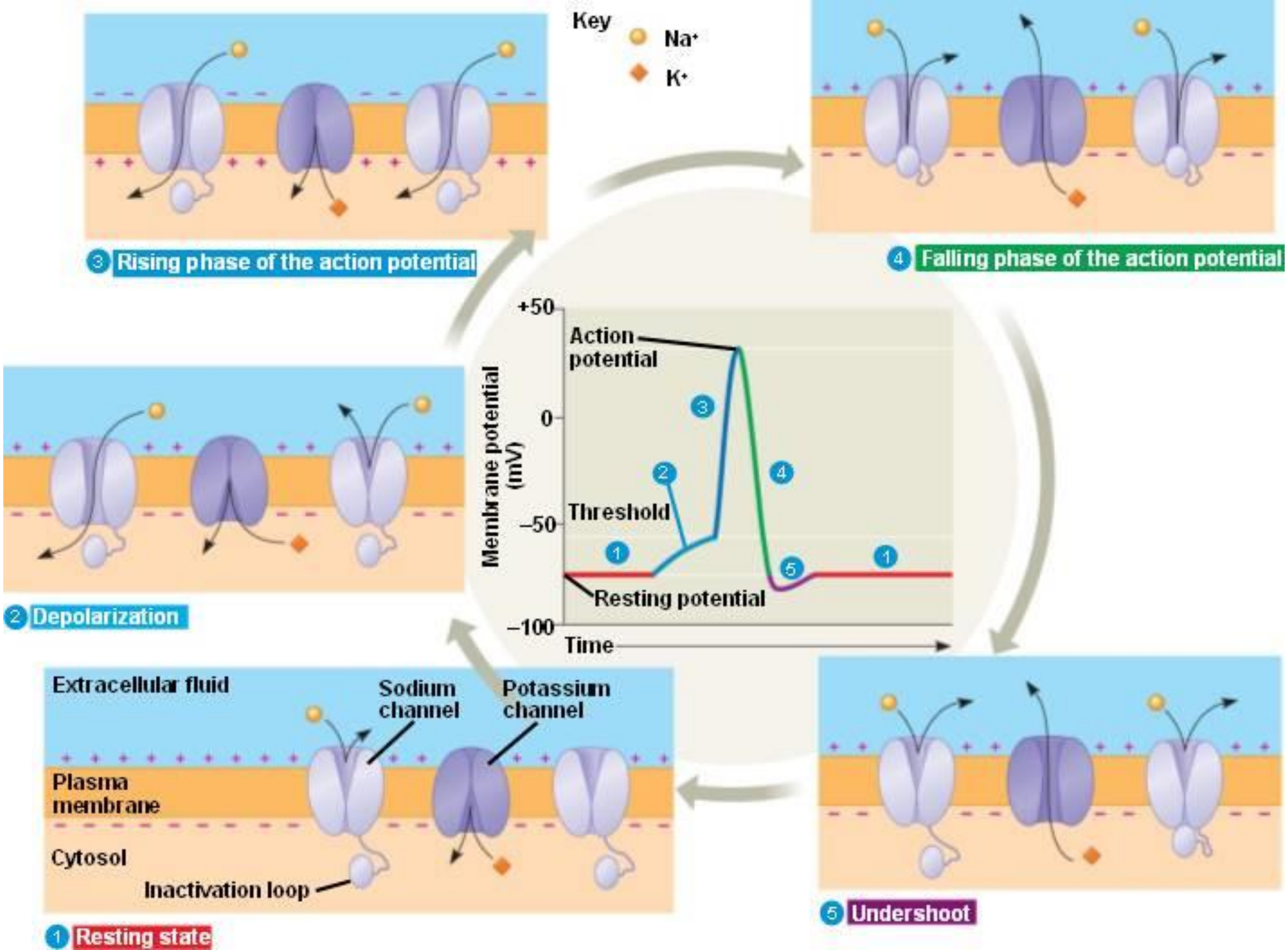
Hyperpolarizing current
Current generator
+60
+30
0
-30
-60
-90
V_m(mV)
Membrane
current
Outward
Inward
10msec
Time


Membrane potential (mV)
0
–50
–100
Threshold
Resting potential
Hyperpolarizations
0 1 2 3 4 5
Time (msec)

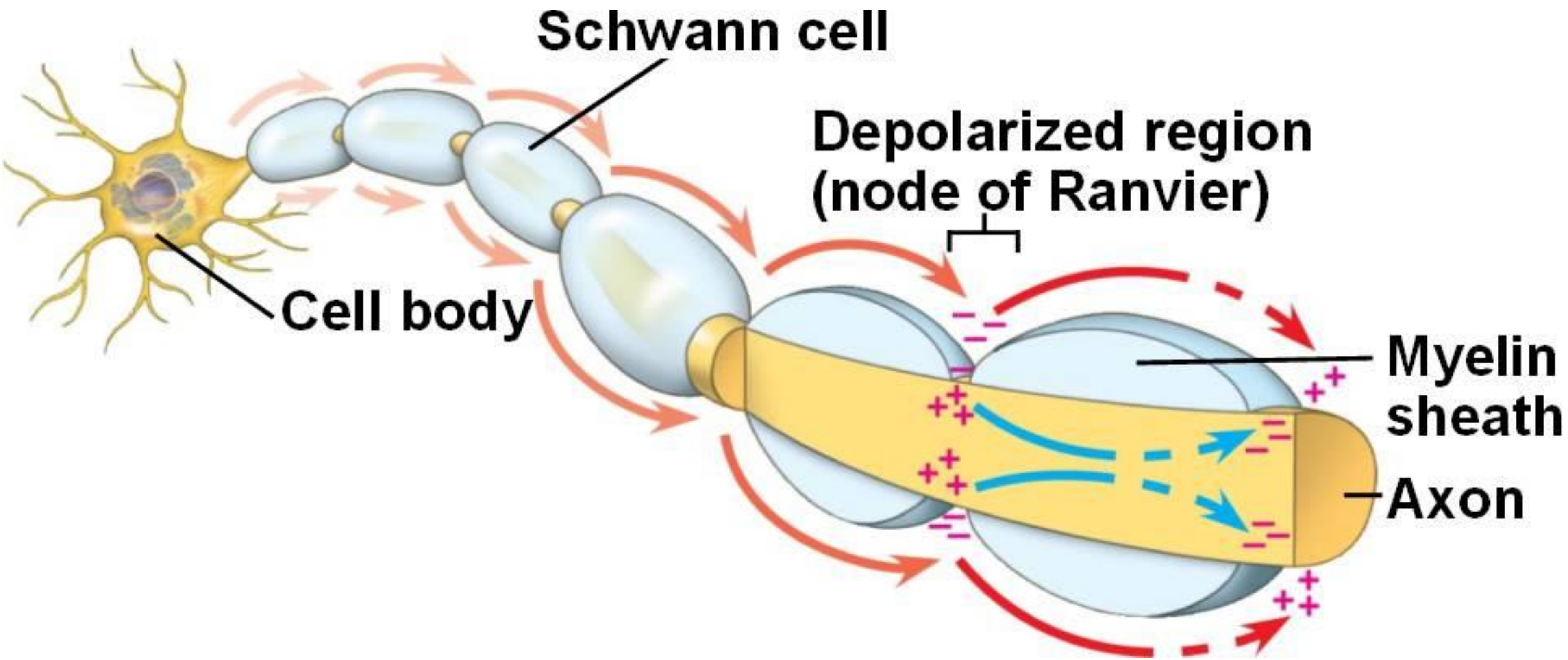

Membrane potential (mV)
0
–50
–100
Threshold
Resting potential
Depolarizations
0 1 2 3 4 5
Time (msec)

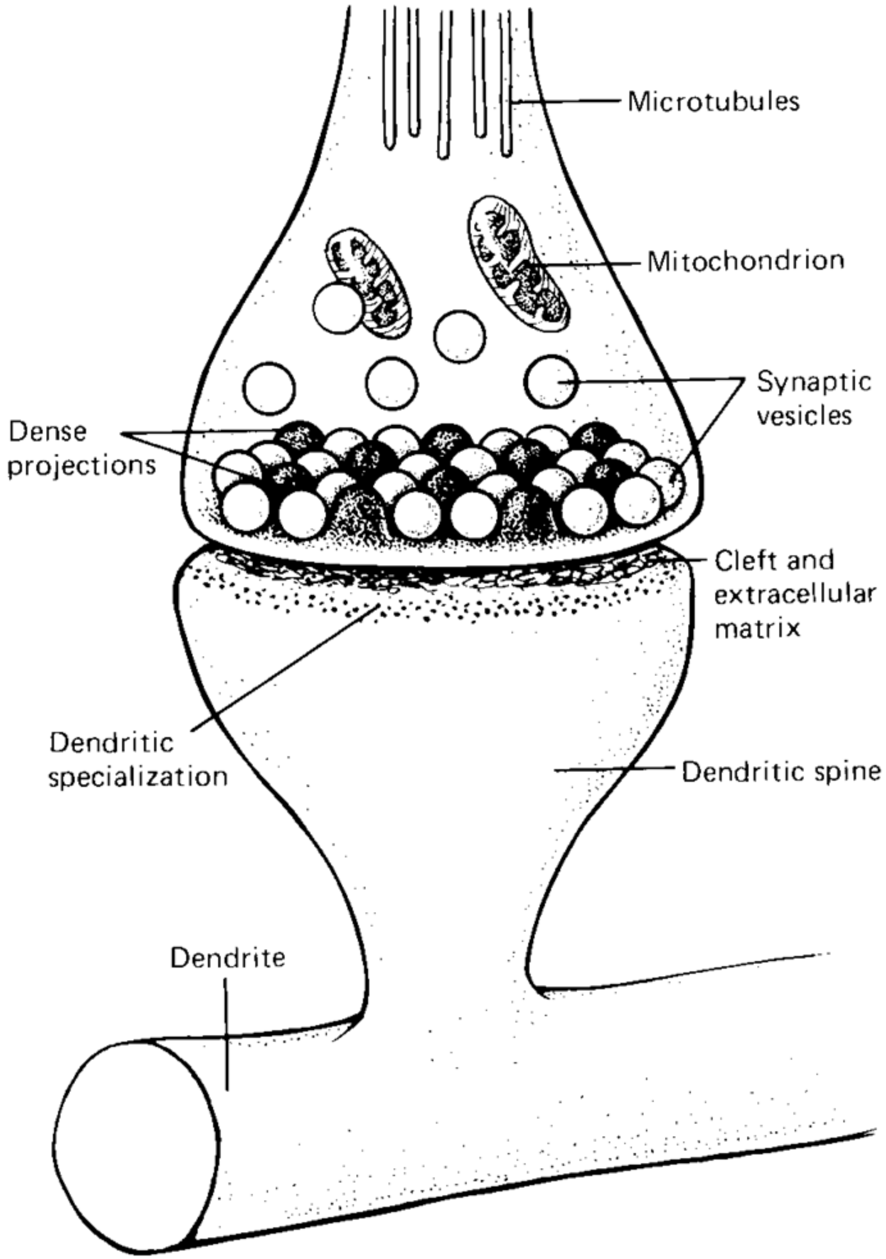


1
Current step
0
2
Current step
0
3
Current step
0
+
All-or-none amplitude
Action
potentials
(spikes)
0
Threshold
−70
Resting
membrane
potential
1
2
3
−

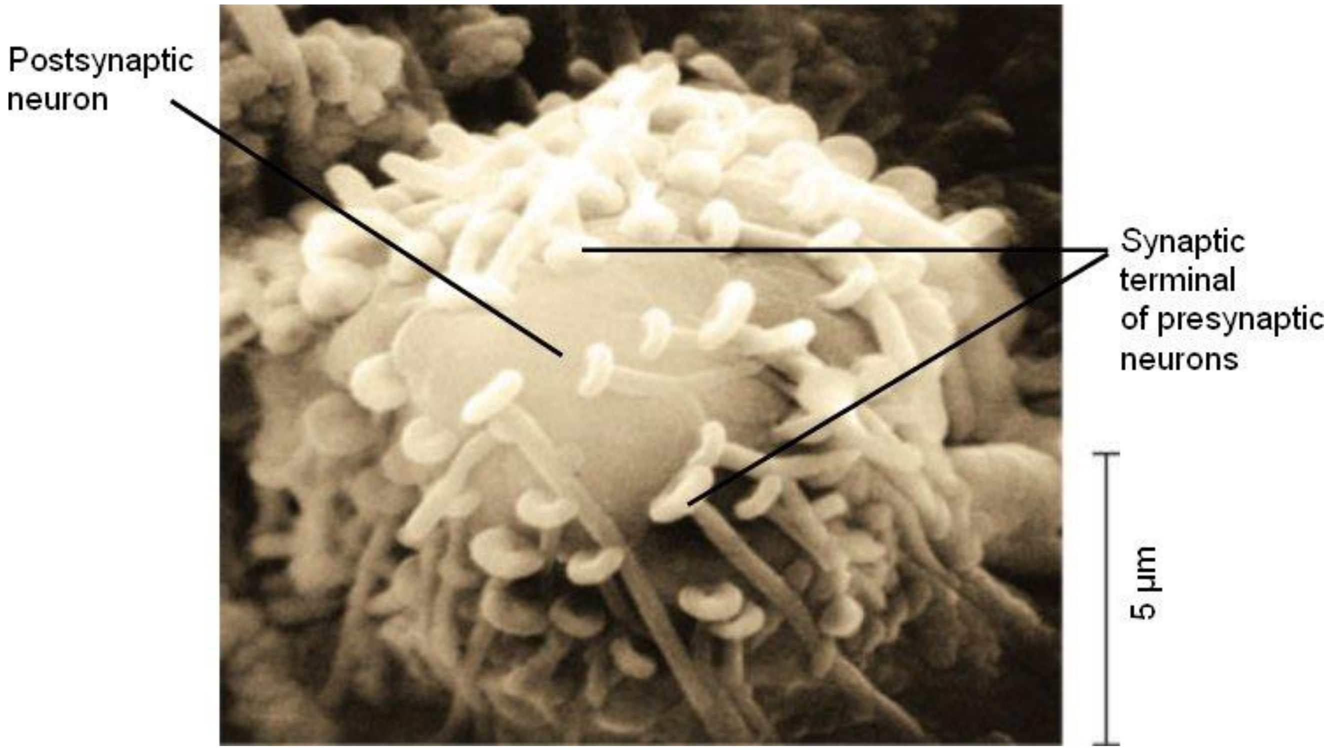


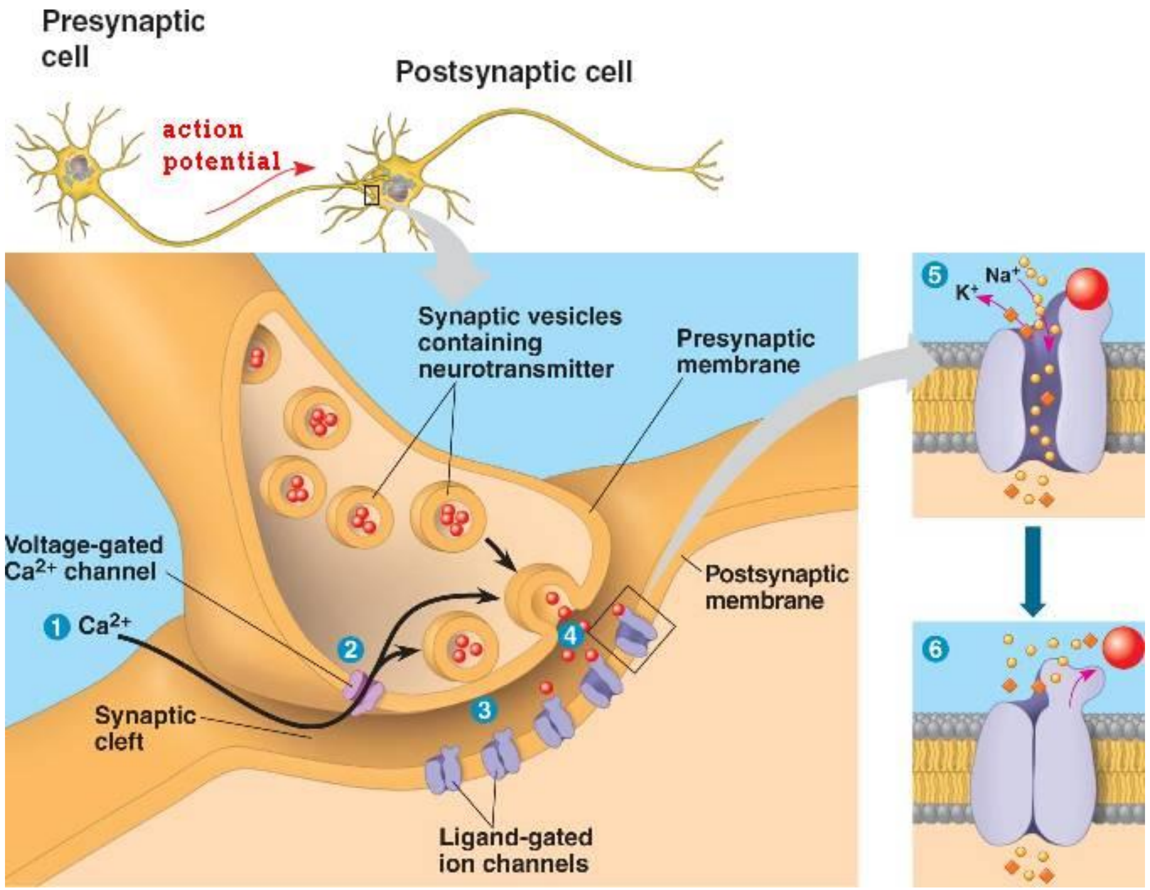
Key
Na+
K+
3 Rising phase of the action potential
4 Falling phase of the action potential
+50
0
−50
−100
Membrane potential (mV)
Action potential
Threshold
Resting potential
Time
2 Depolarization
Extracellular fluid
Sodium channel
Potassium channel
Plasma membrane
Cytosol
Inactivation loop
1 Resting state
5 Undershoot

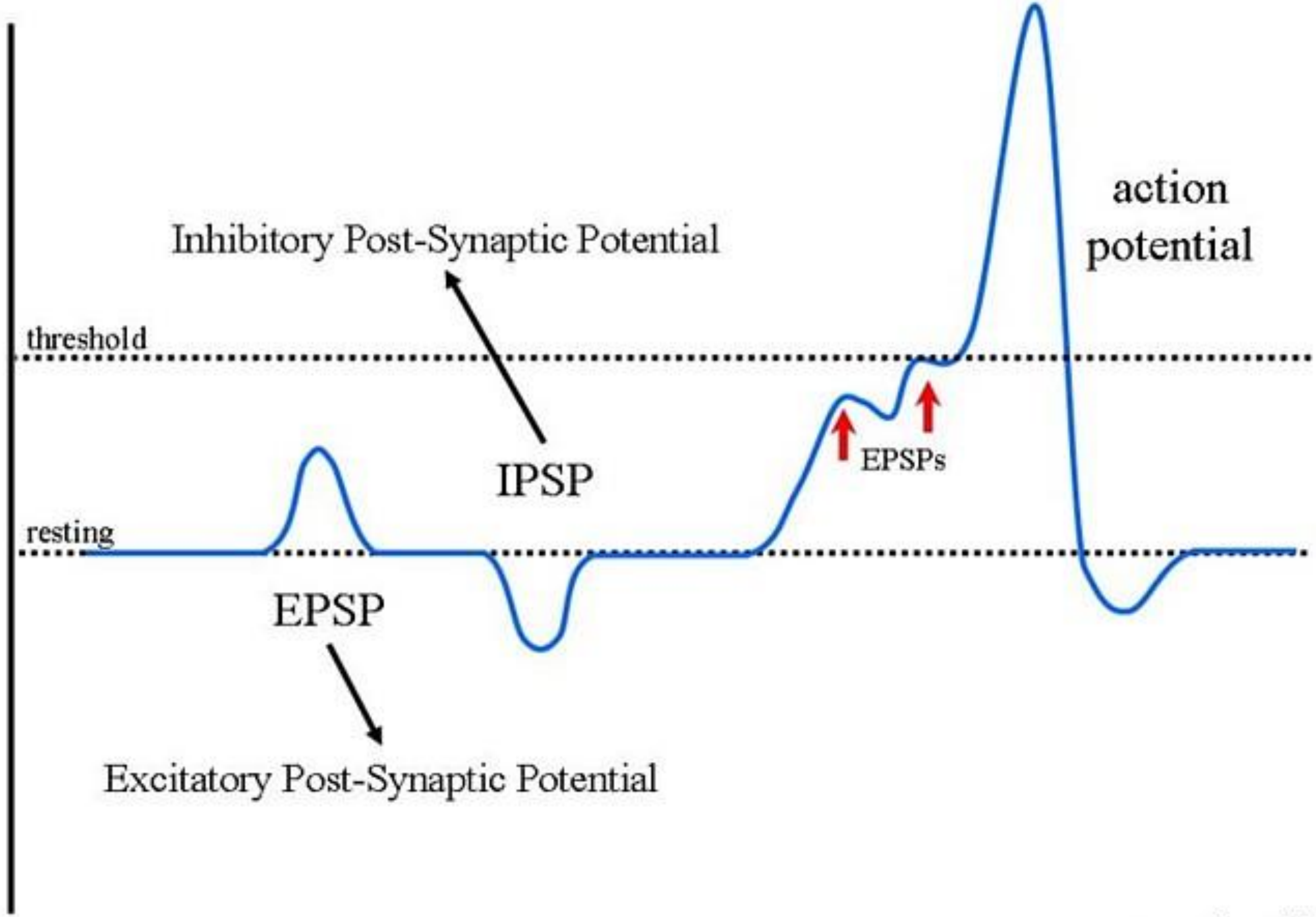

Schwann cell
Depolarized region
(node of Ranvier)
Cell body
Myelin
sheath
Axon


Microtubules
Mitochondrion
Synaptic
vesicles
Dense
projections
Cleft and
extracellular
matrix
Dendritic
specialization
Dendritic spine
Dendrite

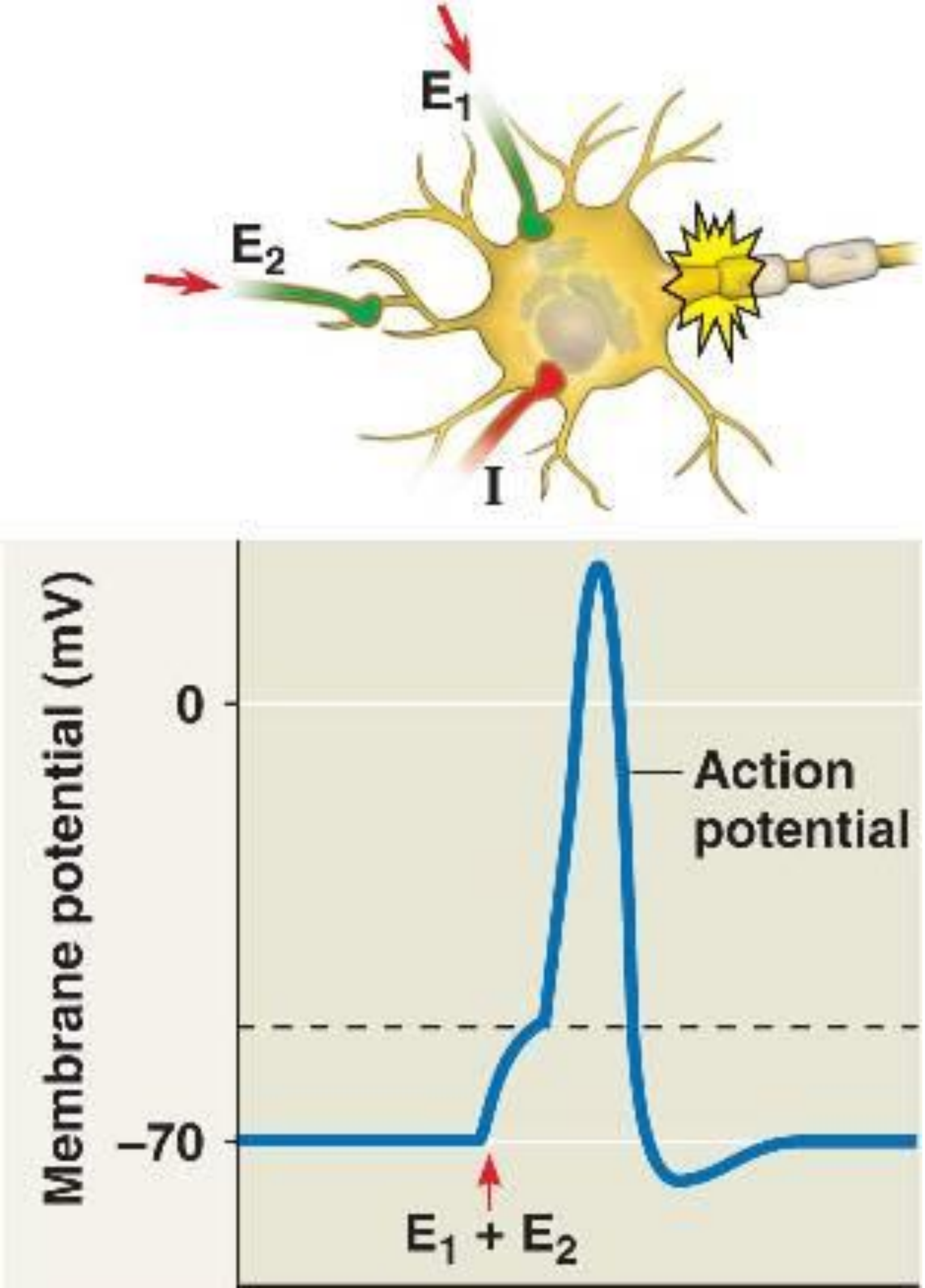
Synaptic transmission





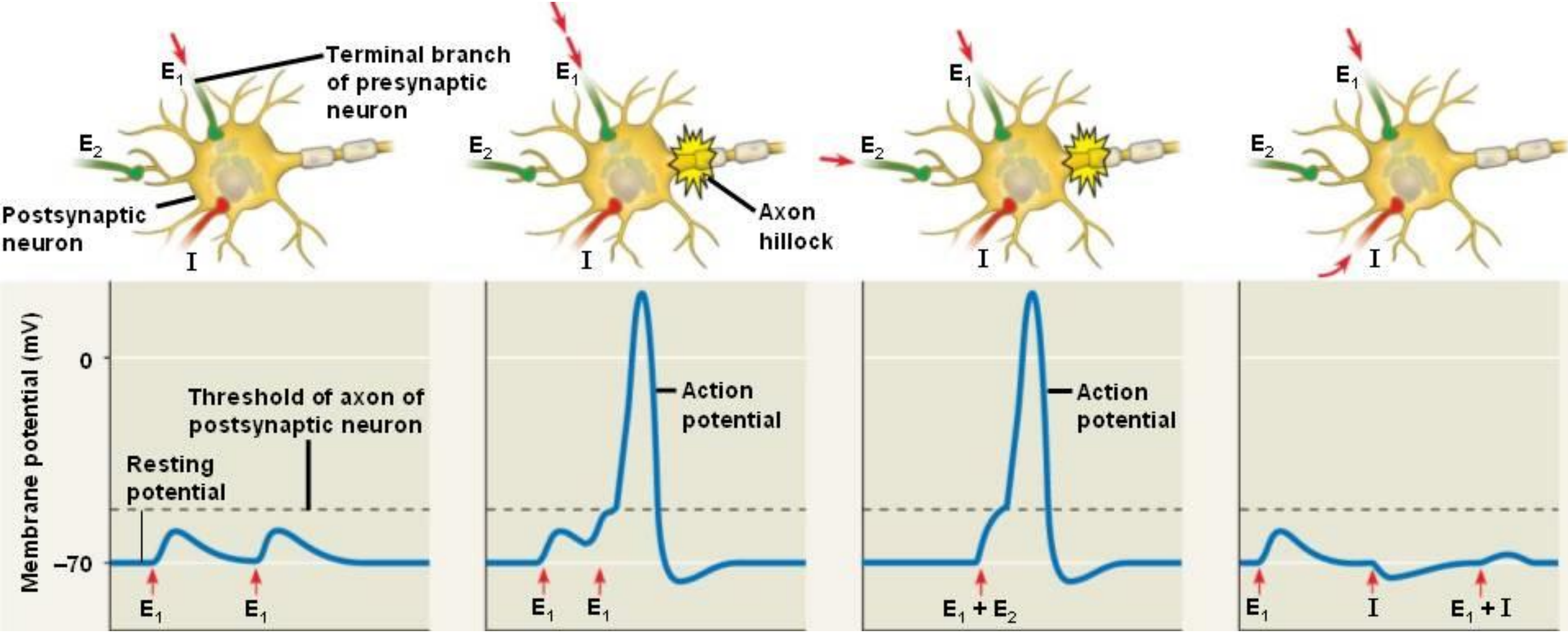

action
potential
Inhibitory Post-Synaptic Potential
threshold
EPSPs
IPSP
resting
EPSP
Excitatory Post-Synaptic Potential

see fig. 48.12



E_1
E_2
I
Membrane potential (mV)
0
–70
Action potential
$E_1 + E_2$

Temporal and spatial Post Synaptic Potentials arithmetic summations

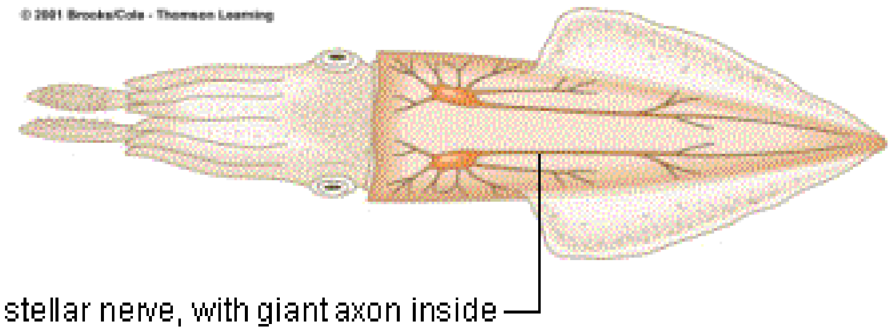


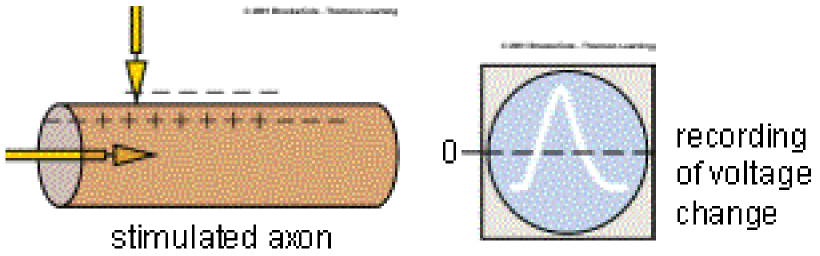
How to record neurons action potentials ?

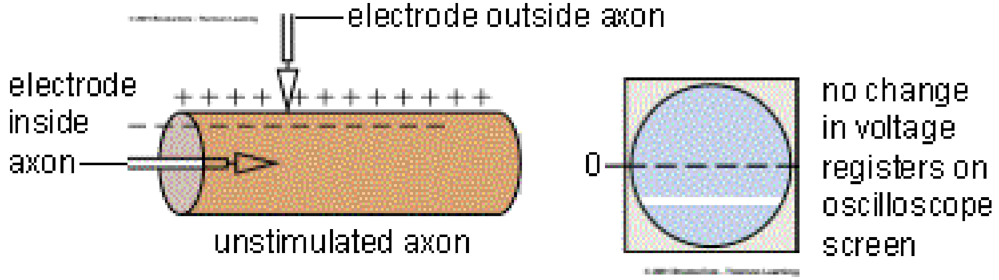
In the laboratory :
- Intracellular recording
- Glass microelectrodes

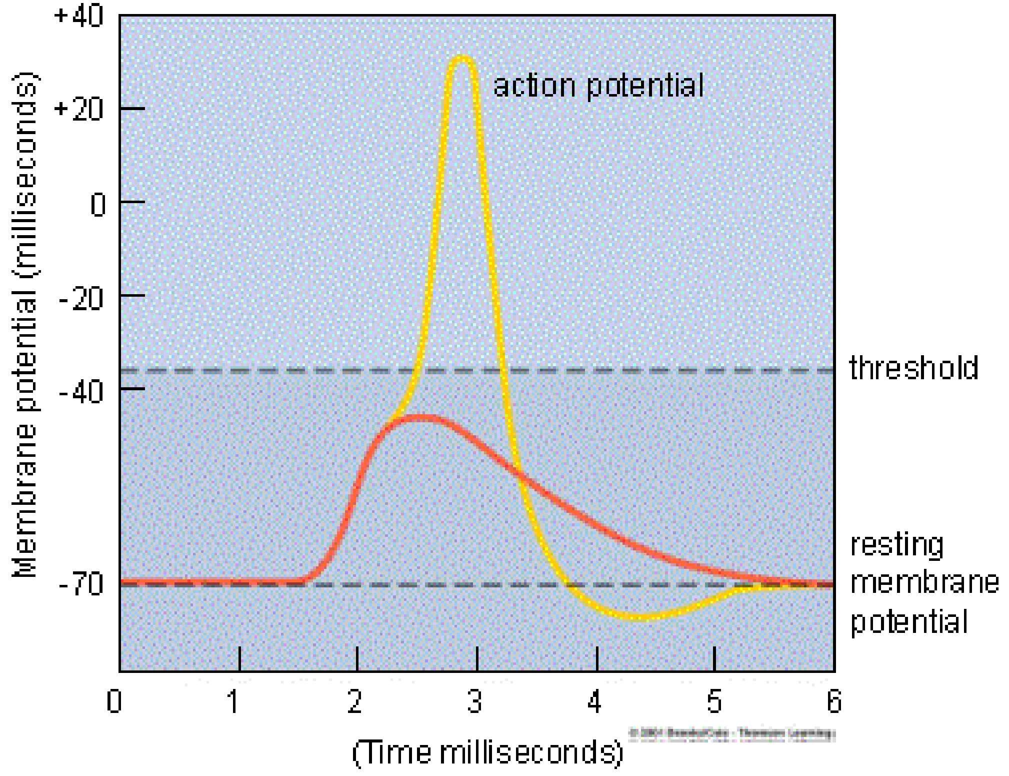
On human subjects :
- Extracellular recording
- metallic macro or semi microelectrodes (tungsten)

Recording of Action Potential







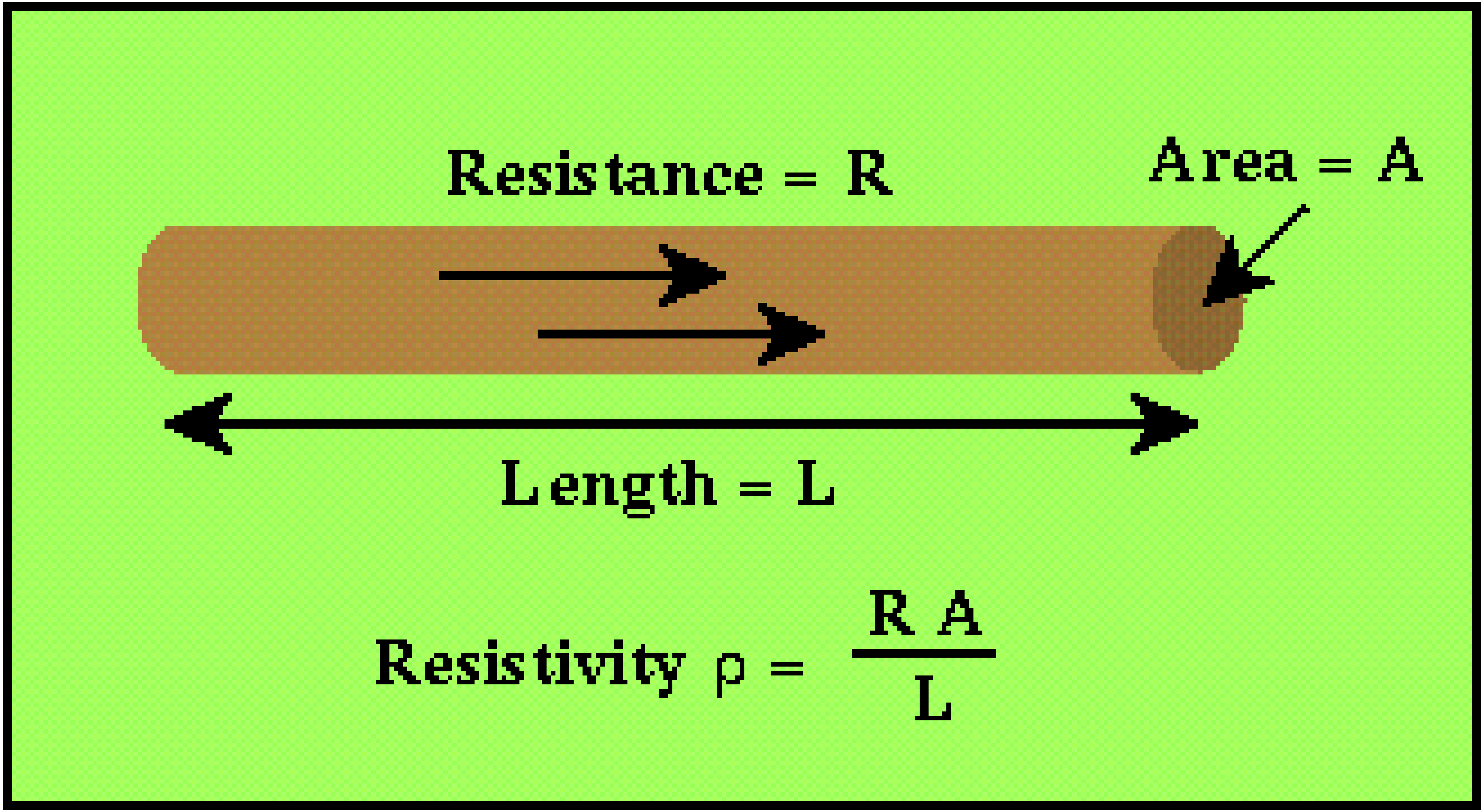


Recording Neurons with electrodes on human subjects

Metal semi micro electrodes need to be thin, long and

have a very thin tip approximately the size of neurons

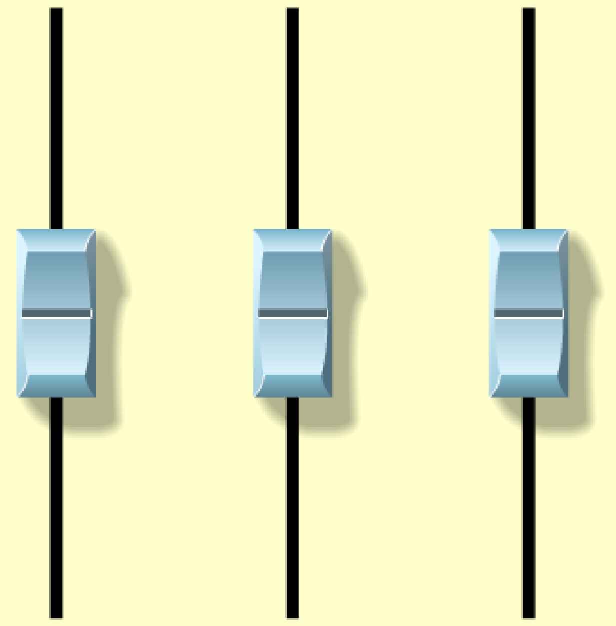
Electrode impedance results from its tip length, surface and conductivity properties


Resistance = R
Area = A
Length = L
Resistivity $\rho = \dfrac{R\,A}{L}$

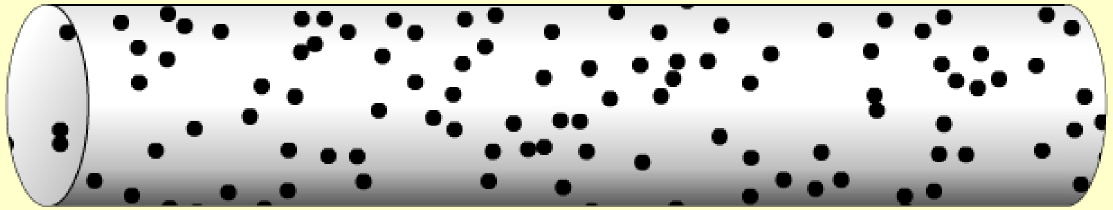
电阻 = 1.25 欧姆

$$R = \frac{\rho L}{A}$$

Ω厘米	厘米	厘米^2
0.5	10	4.01



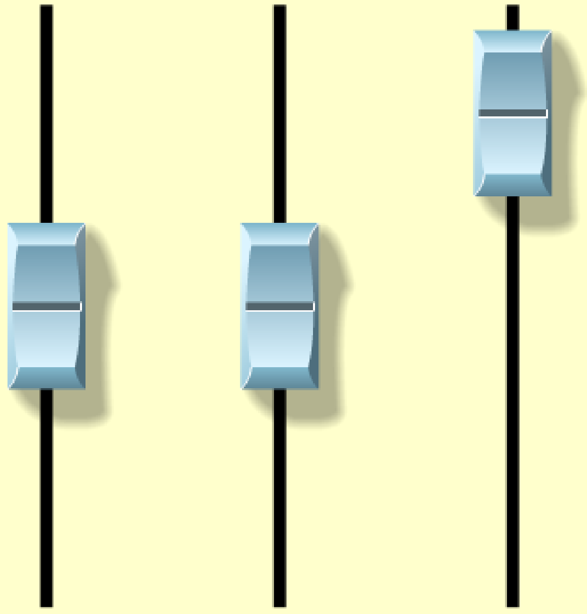
ρ	L	A



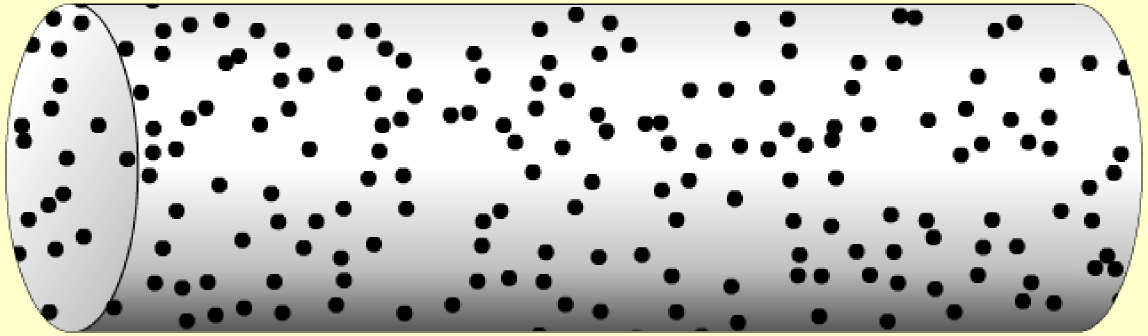
电阻 = 0.46 欧姆

$$R = \frac{\rho L}{A}$$

Ω厘米	厘米	厘米^2
0.5	10	10.77



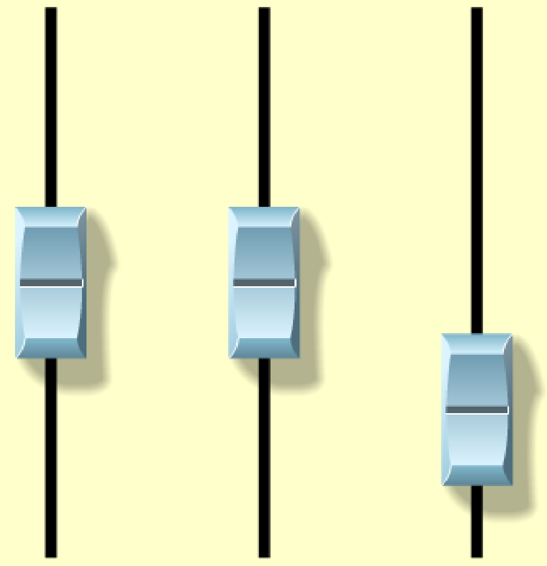
ρ	L	A



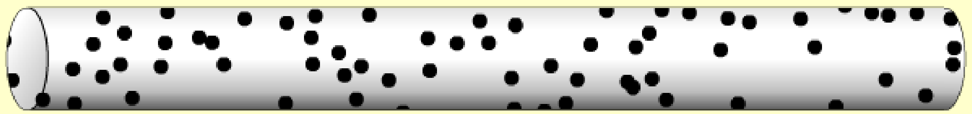
电阻 = 3.95 欧姆

$$R = \frac{\rho L}{A}$$

Ω厘米	厘米	厘米^2
0.5	10	1.26



ρ　L　A



How to record neurons action potentials ?

Membrane action potentials creates electrical fields diffusing into extracellular space.

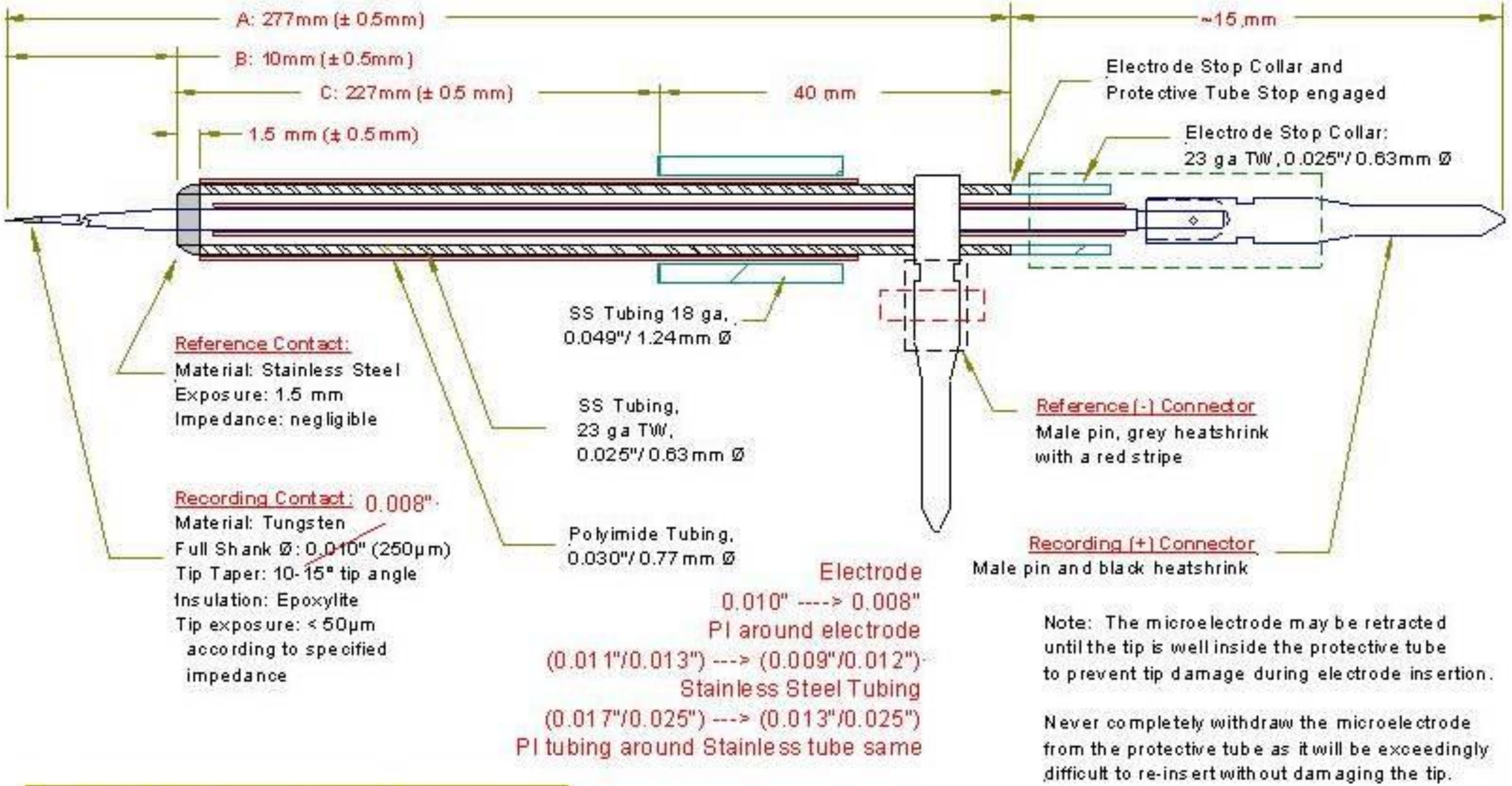
Decrease of electrical field is inversely proportional to the square of the distance (1/r2)

Close to the axone emergence, a micro electrode records potentials of less about 0.5 mV

Effect of electrode impedance on neurons signal recording

- very thin electrode tip surface => High impedance
=> recording of single or a few neurons action potentials

- larger electrode tip surface => Low impedance
=> more signals from different neurons
= less discrimination of action potentials
(decrease of signal to noise ratio)



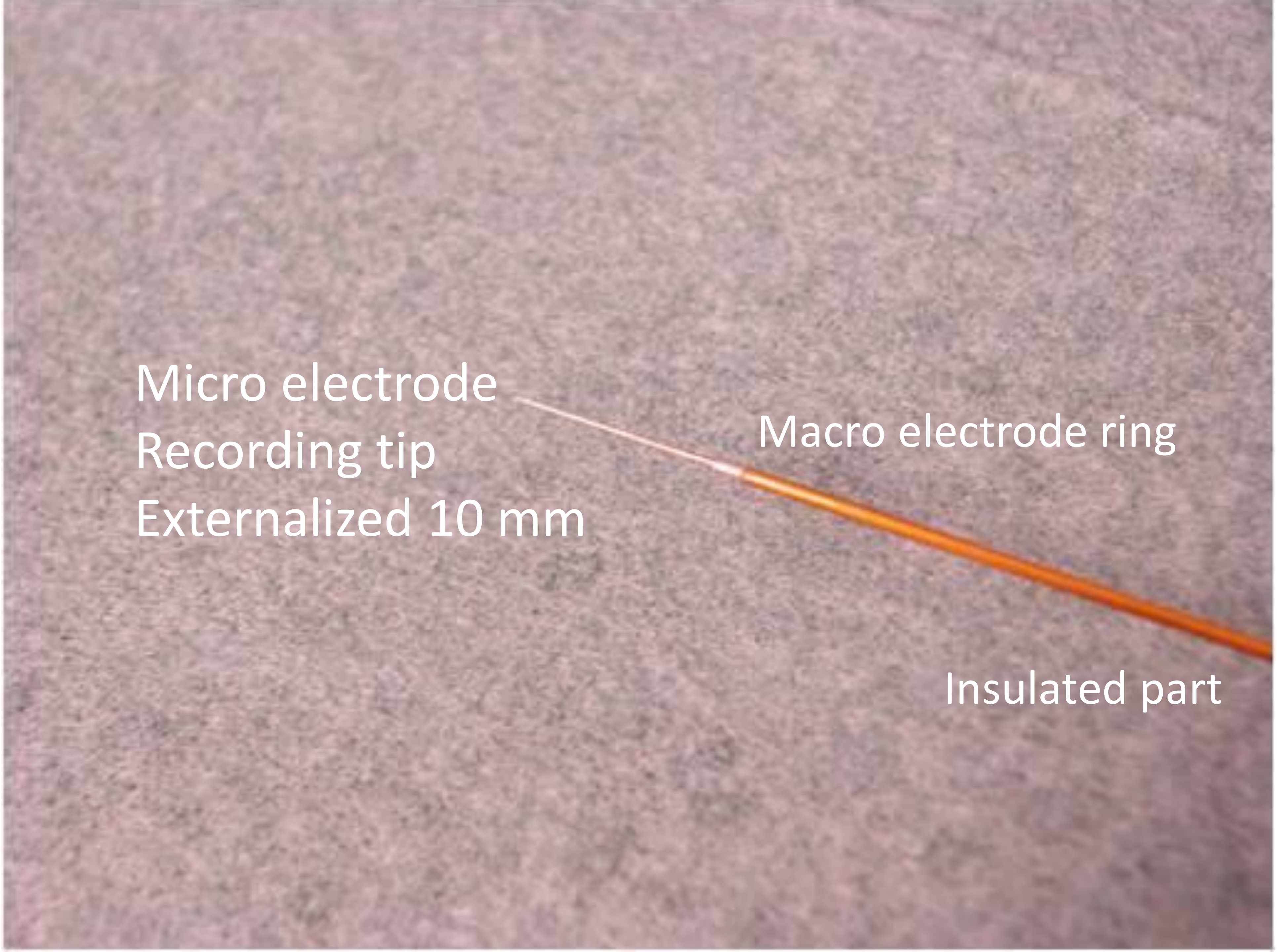
A: Electrode length: __277__ mm (±0.5 mm)
B: Differential Length: __10____ mm (±0.5 mm)
C: Protective Tube Length: __227__ mm (±0.5mm)
3: Impedance @1KHz, 1mm: __10____ M-ohms (±20%)
4: Packaging: Sterilization Tray _____ Non: _X___

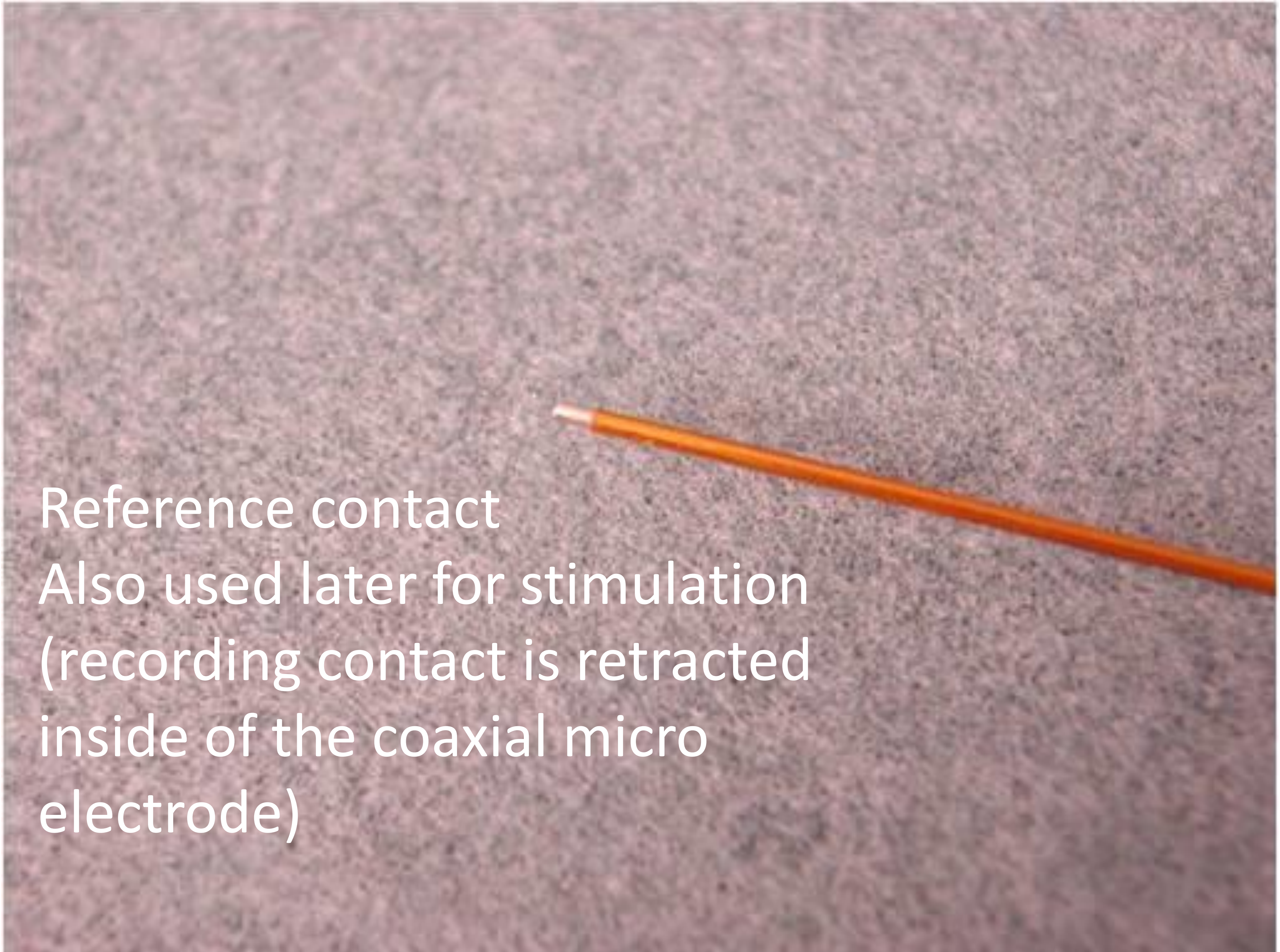
Inspected by: ____________ Date: ___/___/___

Sheet 1
Catalog Drawing
Customer Copy

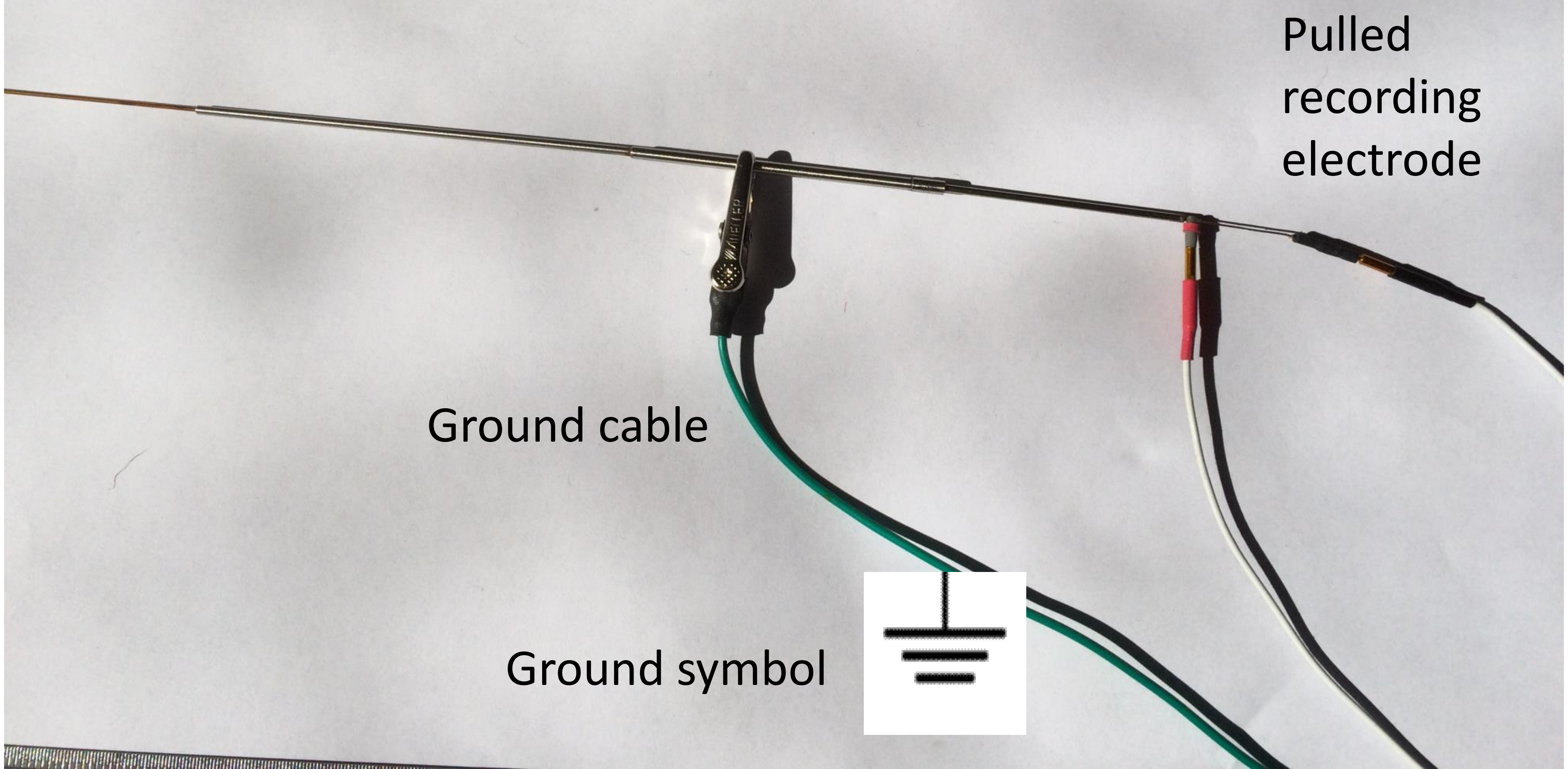
Not to scale.
All dimensions in millimeters (except where noted).

FHC	~~IOWVGGSE5BP6~~		12/8/00
	Electrode: Type BP 1.5mm metal exposure	File: IOWVG ESE5BP6.cad	

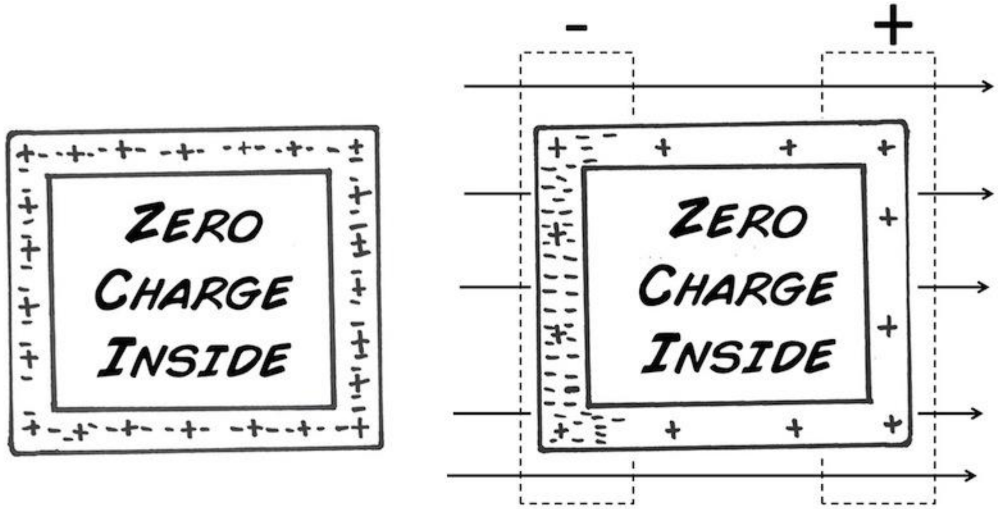

Micro electrode
Recording tip
Externalized 10 mm
Macro electrode ring
Insulated part


Reference contact
Also used later for stimulation
(recording contact is retracted
inside of the coaxial micro
electrode)

Micro electrode connections with recording wire (black connector) and reference wire (red connector)

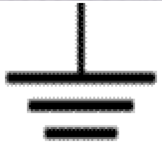


Faraday shield



NO EXTERNAL FIELD

WITH EXTERNAL FIELD

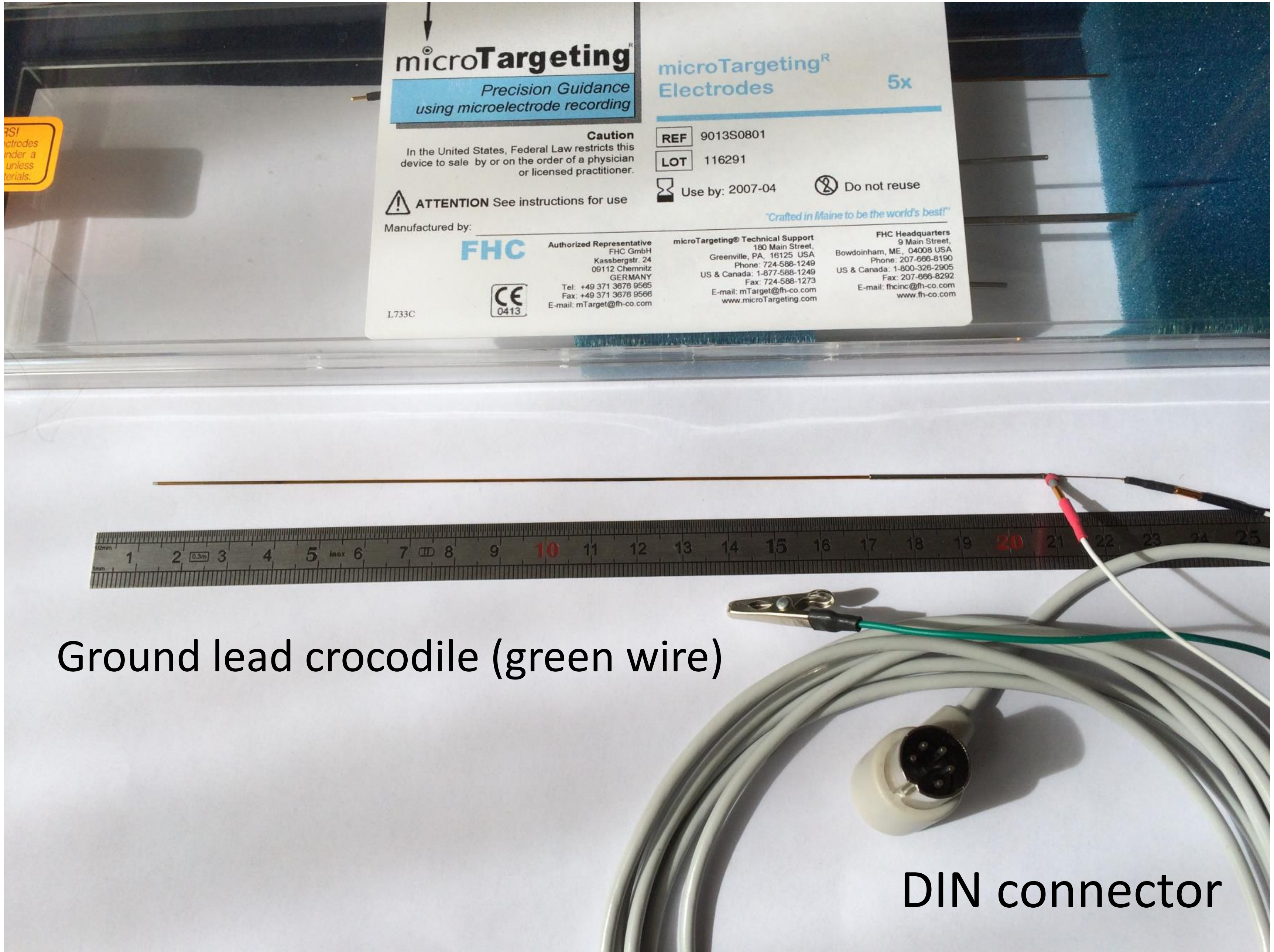


Connection to ground

Guiding tubes

- Guiding tubes provide electrode rigidity
- Straight trajectories
- shield insulation to avoid interferences from electromagnetic fields

3 leads cable connecting electrode to amplifiers



Active lead (black)

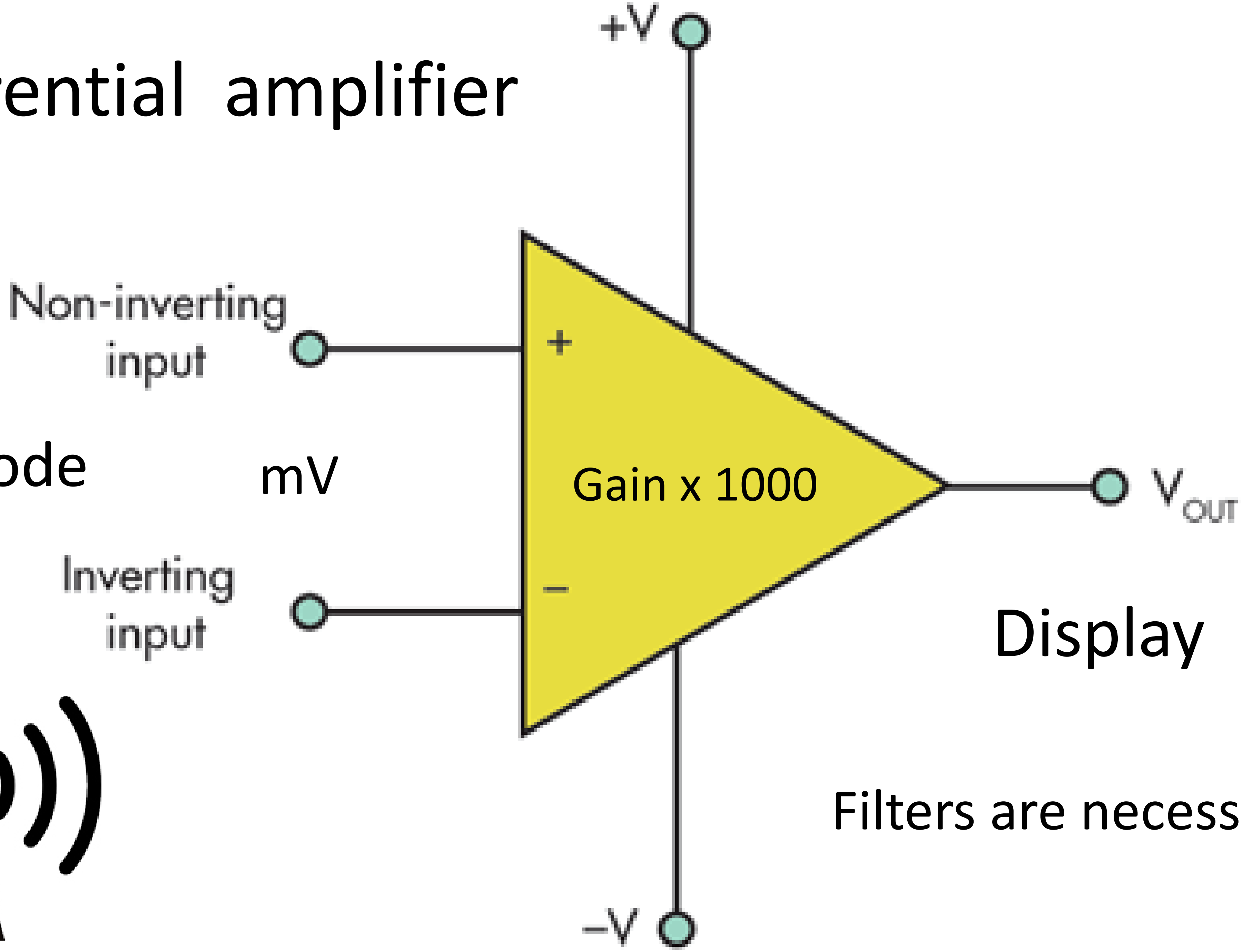
Reference lead (red)

Ground lead crocodile (green wire)

DIN connector

Connecting box

Differential amplifier



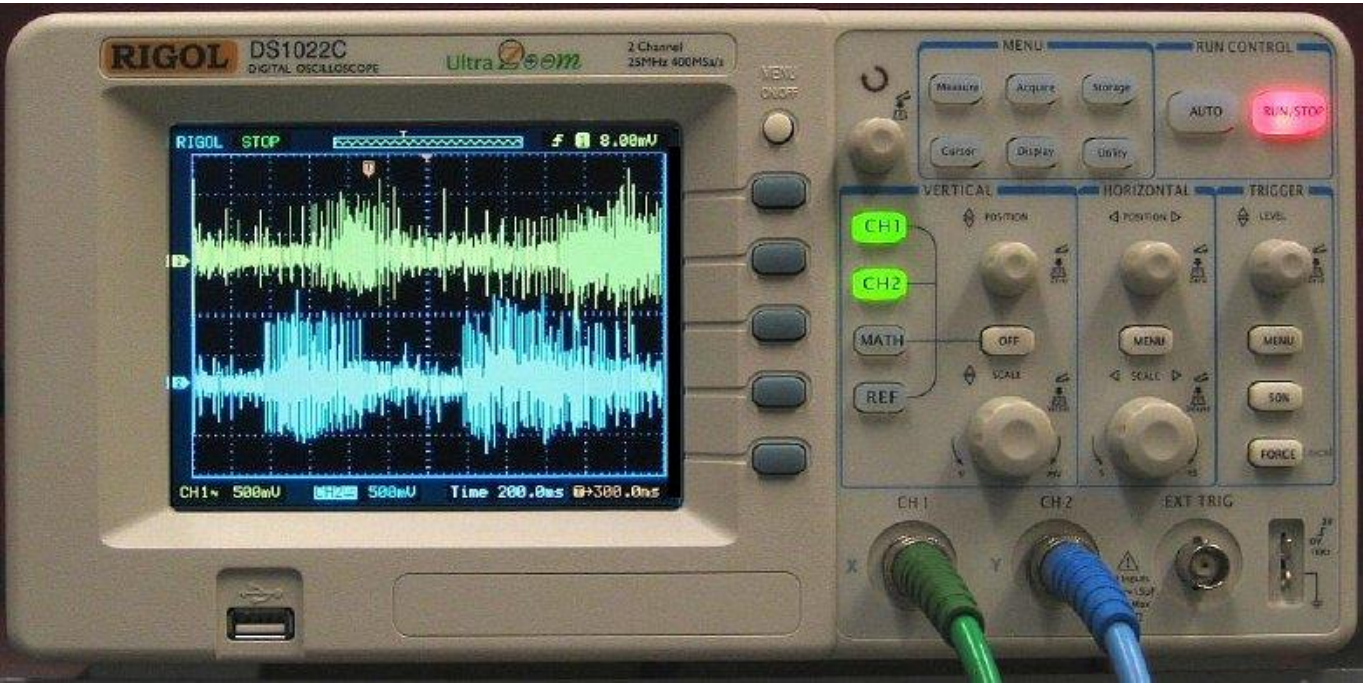
Electrode

mV

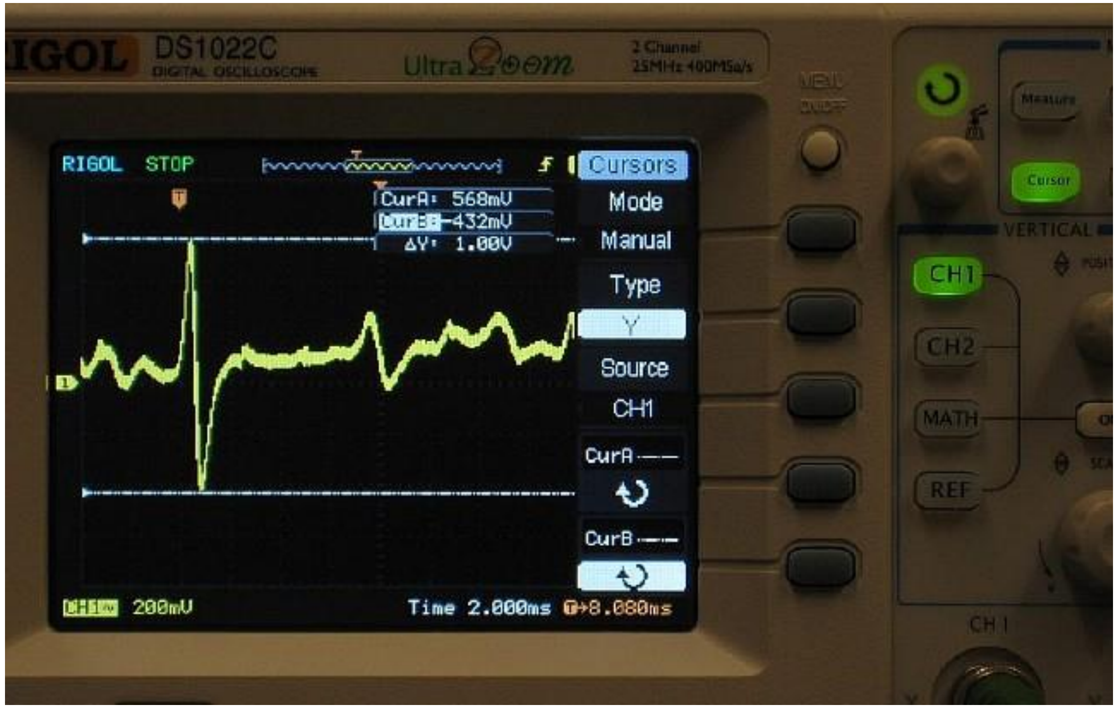
Display

Filters are necessary

Neurons action potentials visualization on oscilloscope

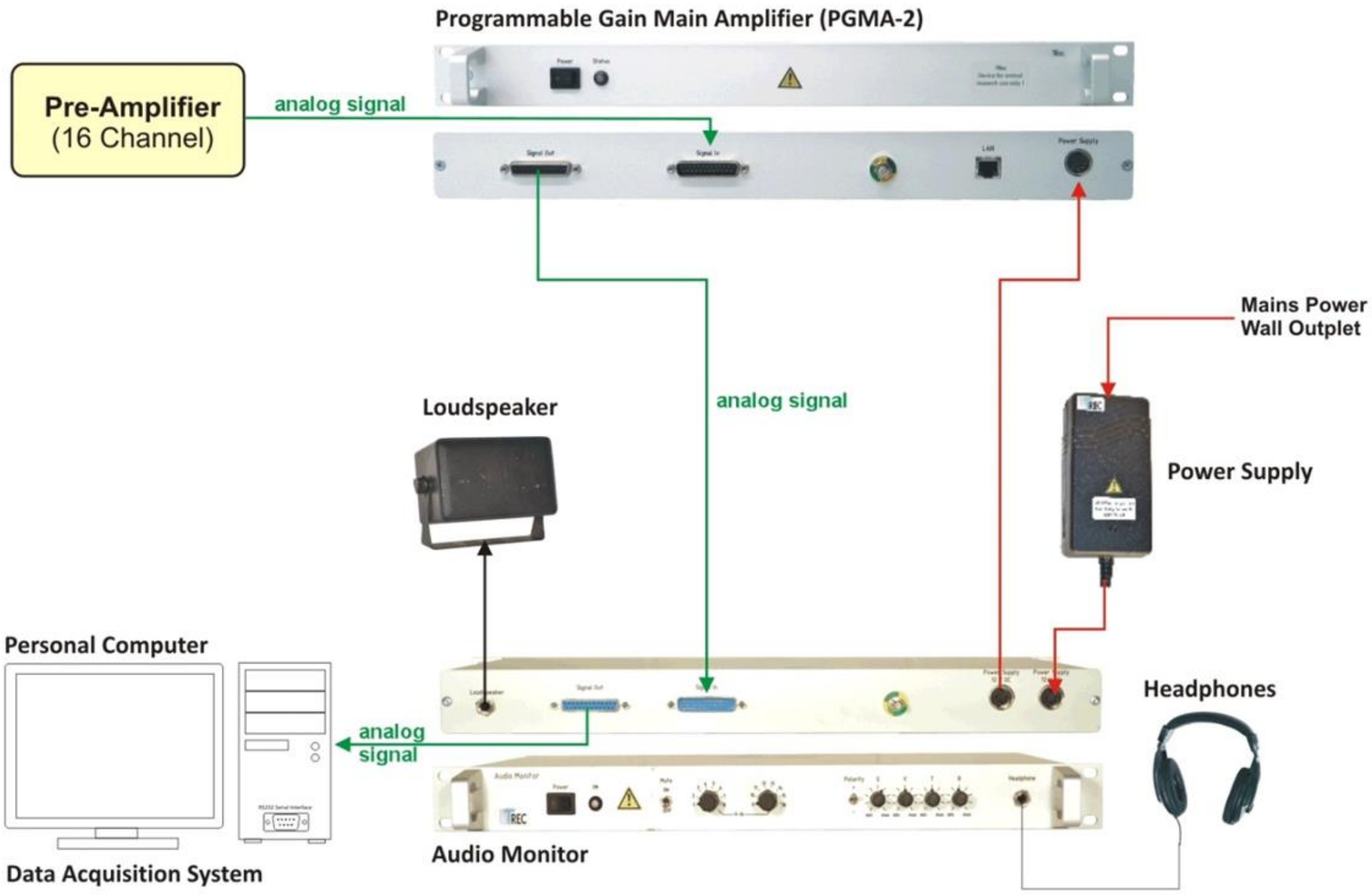


Low sweep speed : multiple action potentials



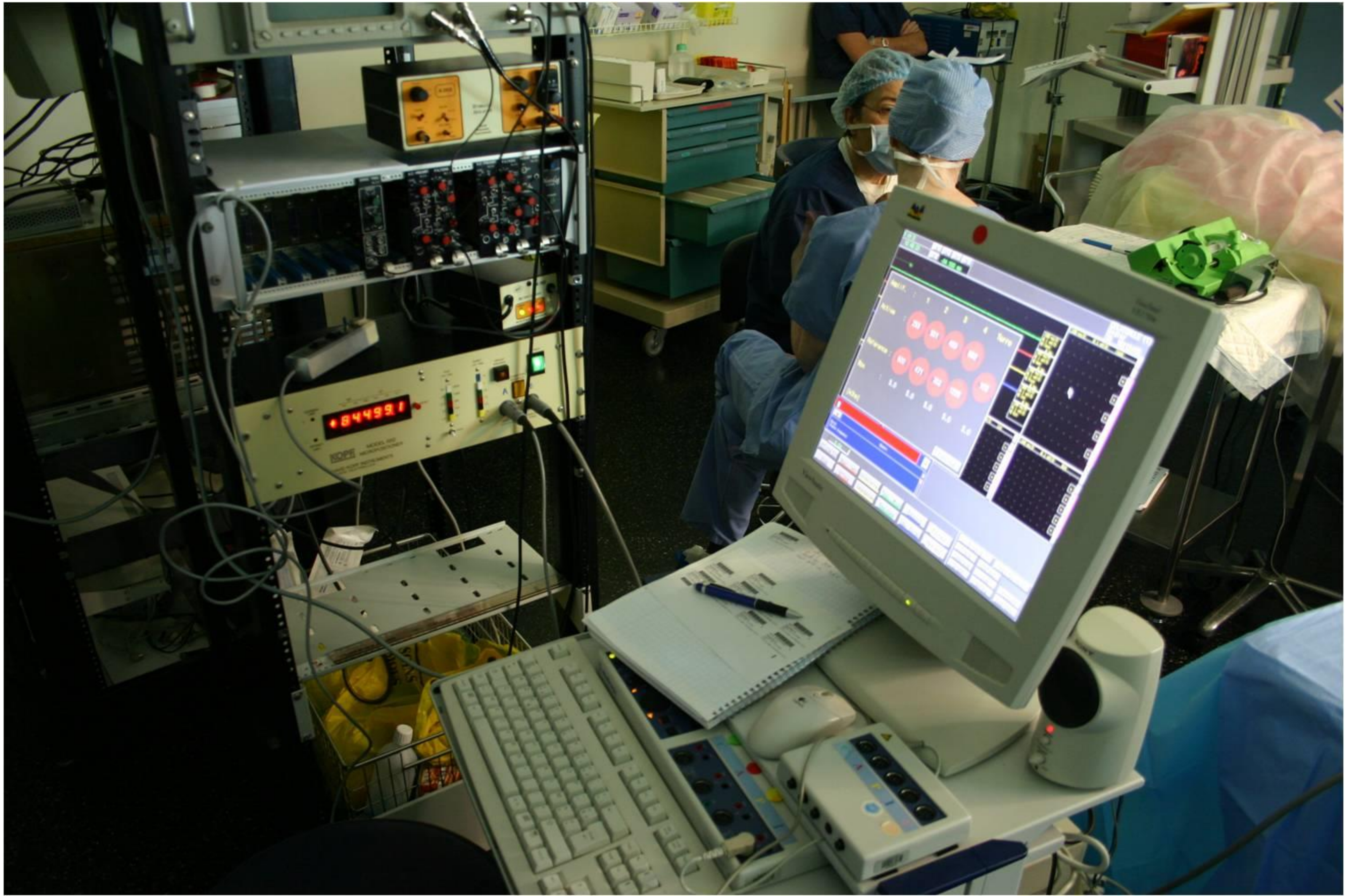
Fast sweep : single action potentials

Neurons action potentials audio monitoring

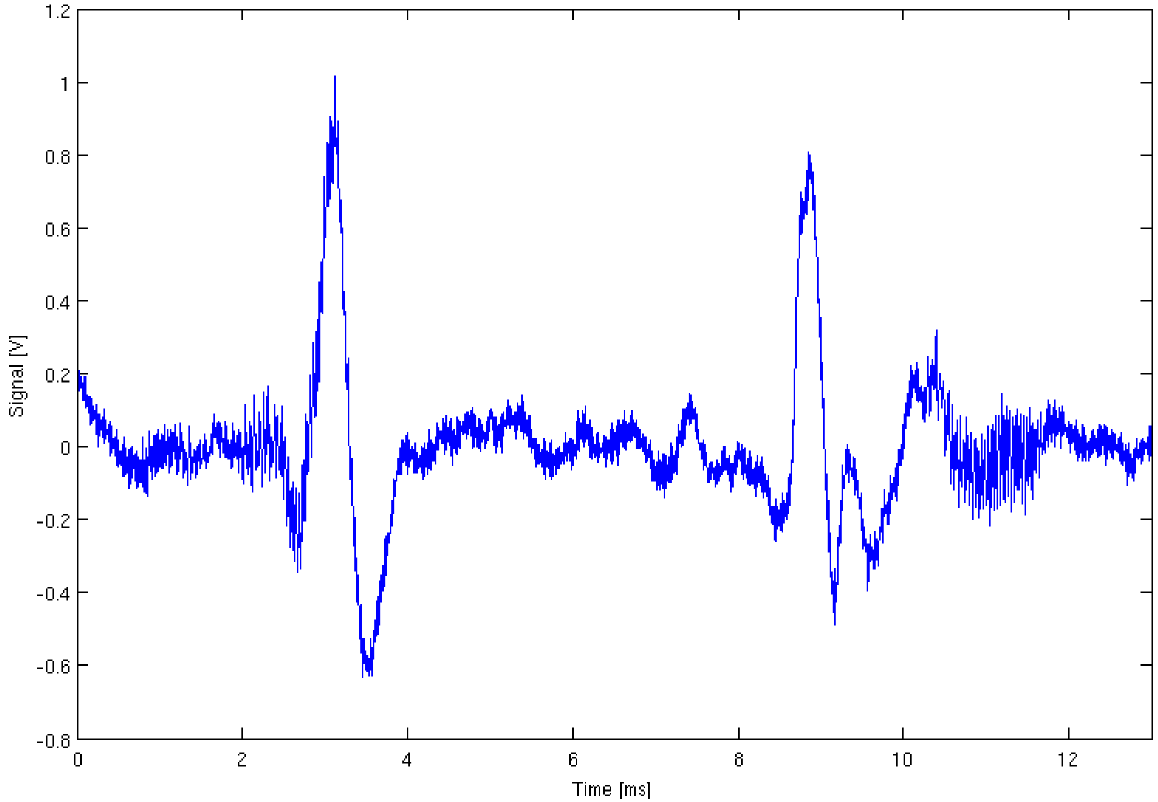


Connecting all things together …

Two generations of recording and stimulating devices



Analog signals

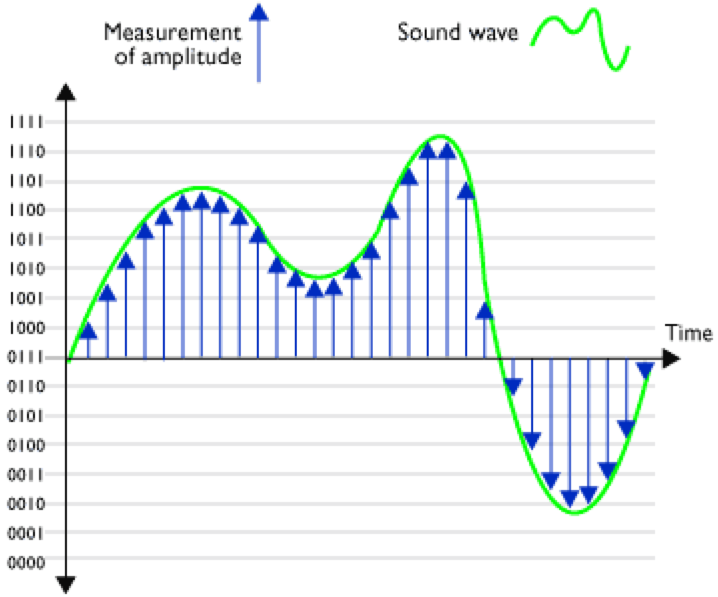


Analog signals are continuous change of alternative voltage varying in time

Action potentials (extracellular) are characterized by low amplitudes and short durations : micro volts, milliseconds

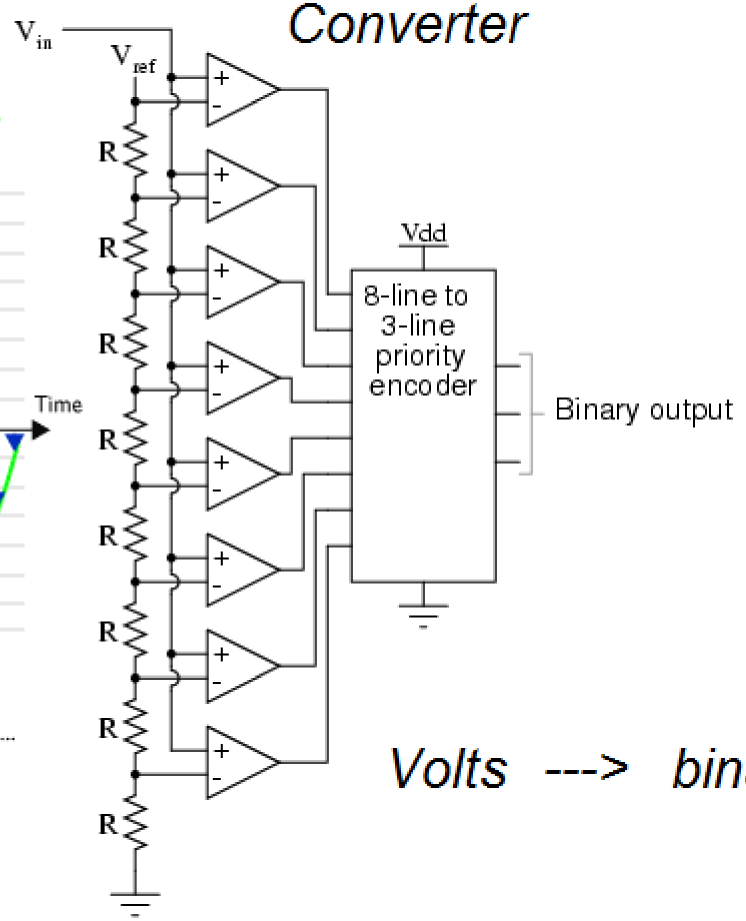
ANALOG TO DIGITAL CONVERTION

Analog signal



Each measurement is assigned a number (byte) according to its amplitude. The end result is a file comprising a string of bytes, eg ...
1001 1110 0001 1010 0111 0100 1111 1101 etc

Converter



Bits

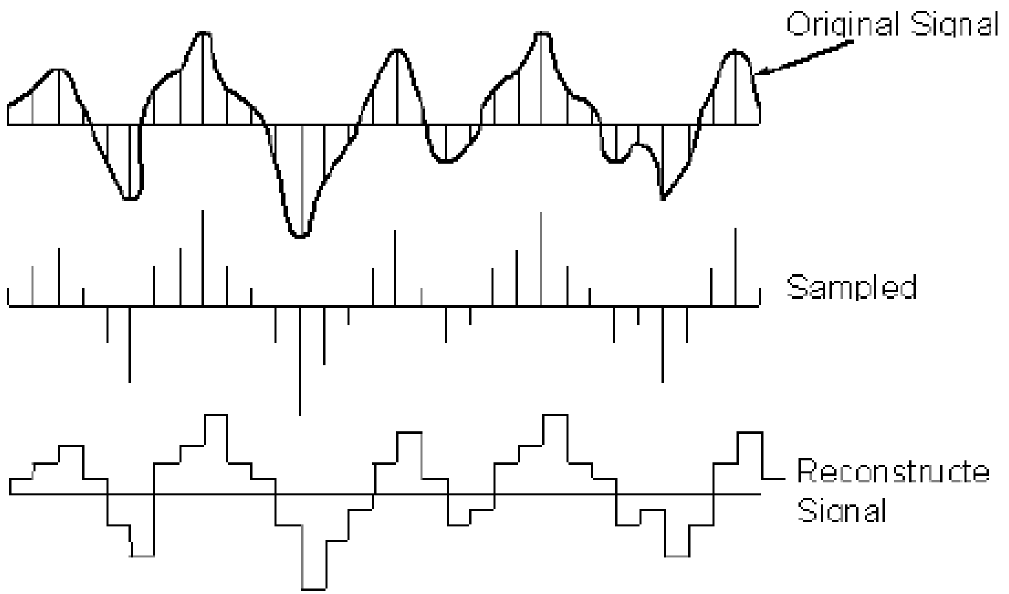
voltage	Binary
0.00 V	000
-1.25 V	001
-2.50 V	010
-3.75 V	011
-5.00 V	100
-6.25 V	101
-7.50 V	110
-8.75 V	111

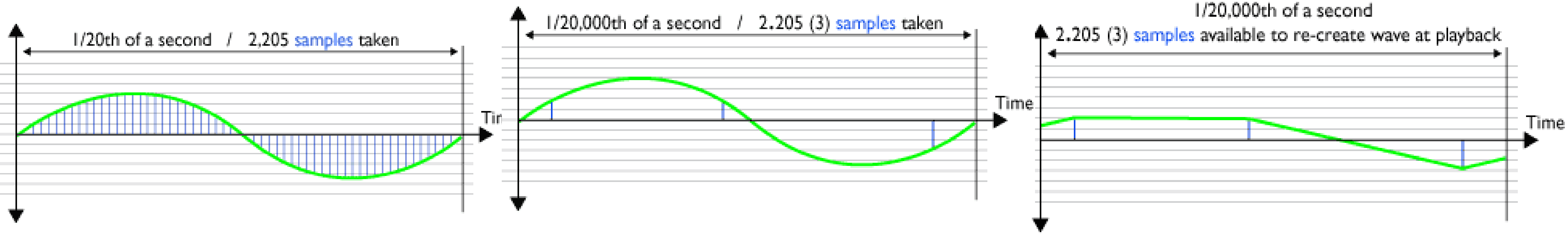
Volts ---> binary digits numbers

Sample frequency

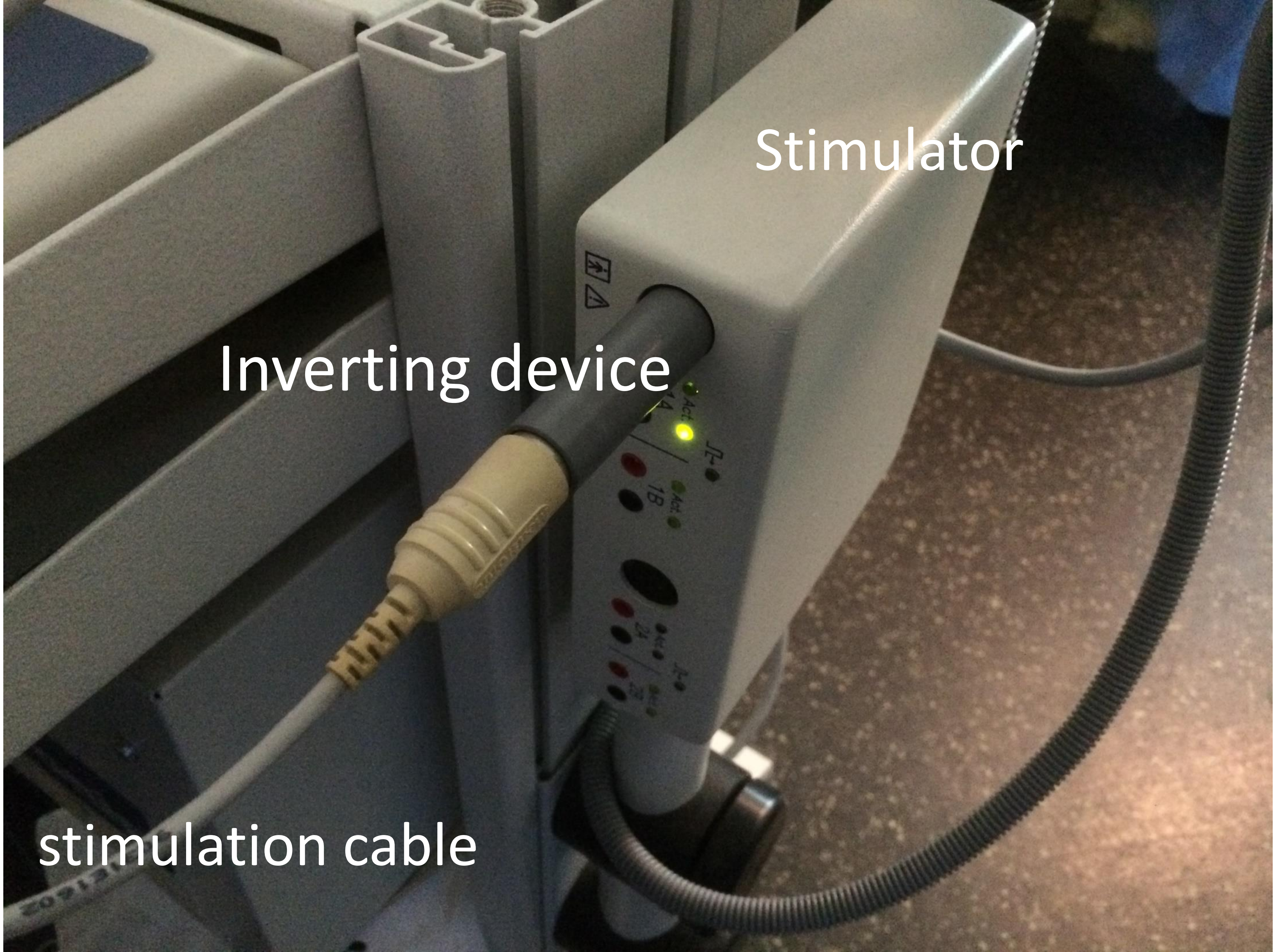
Amplitude coding on 3 binary digits

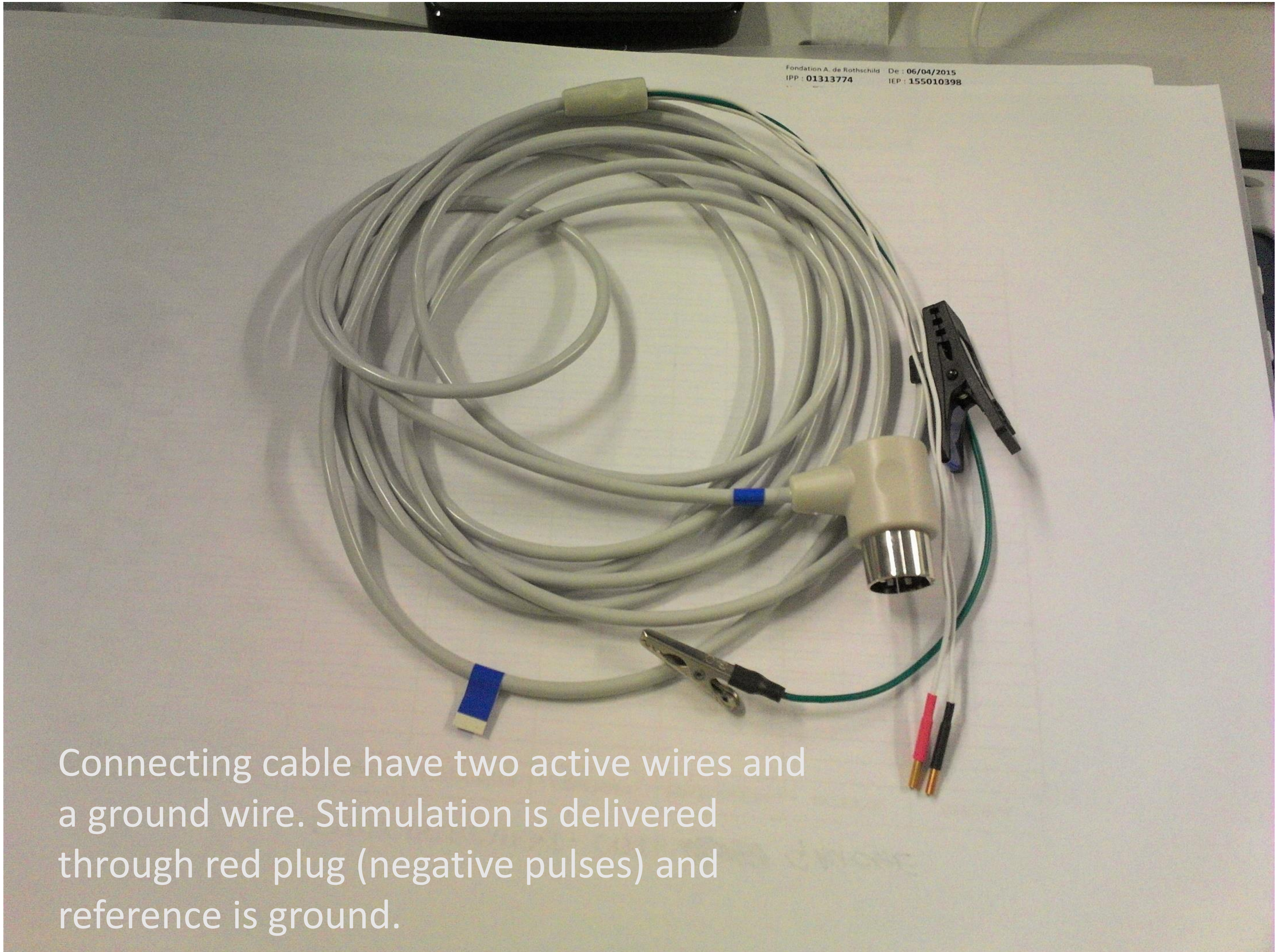
Frequency sampling



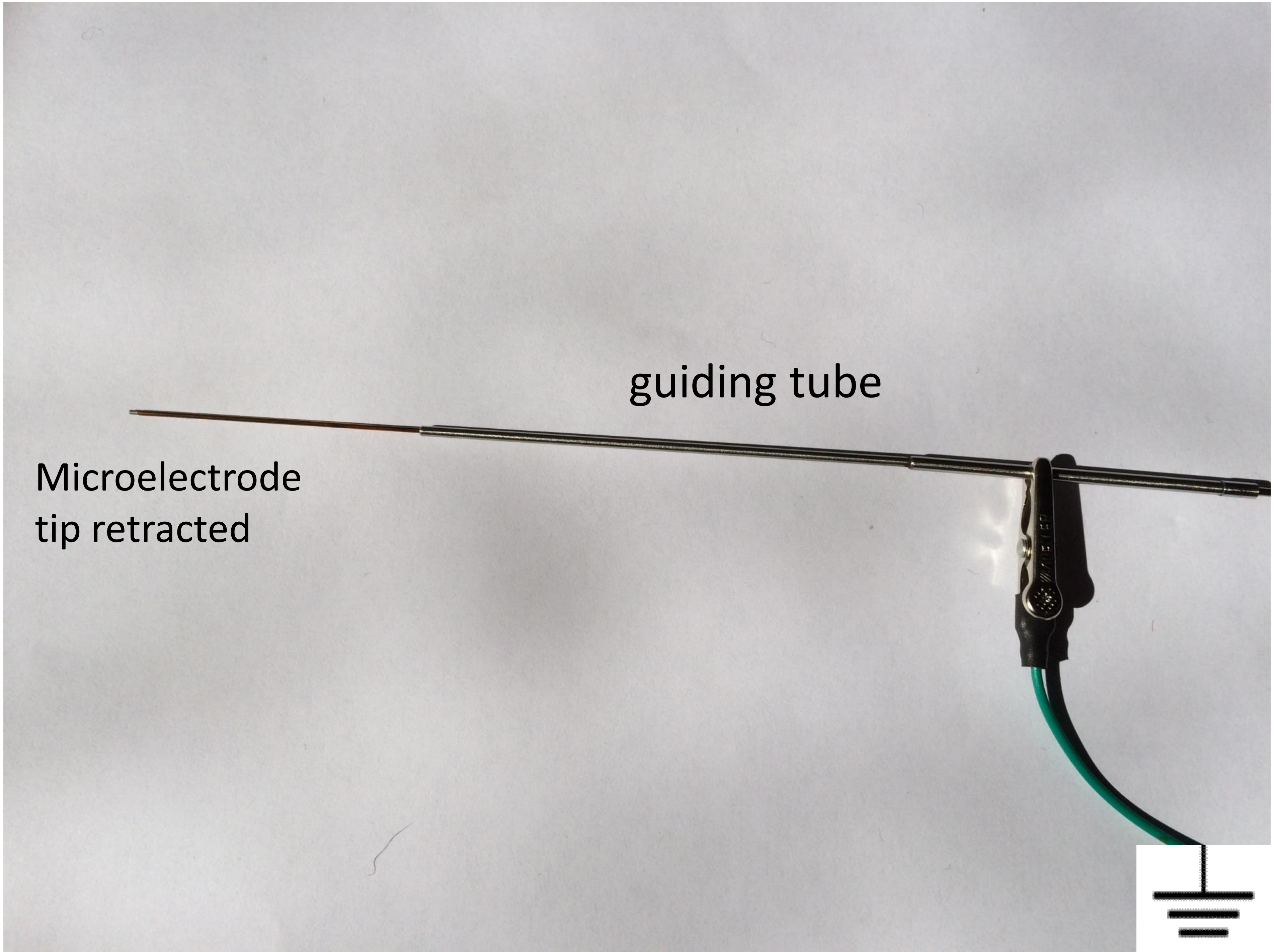



Medtronic
PHILIPS
rive - P

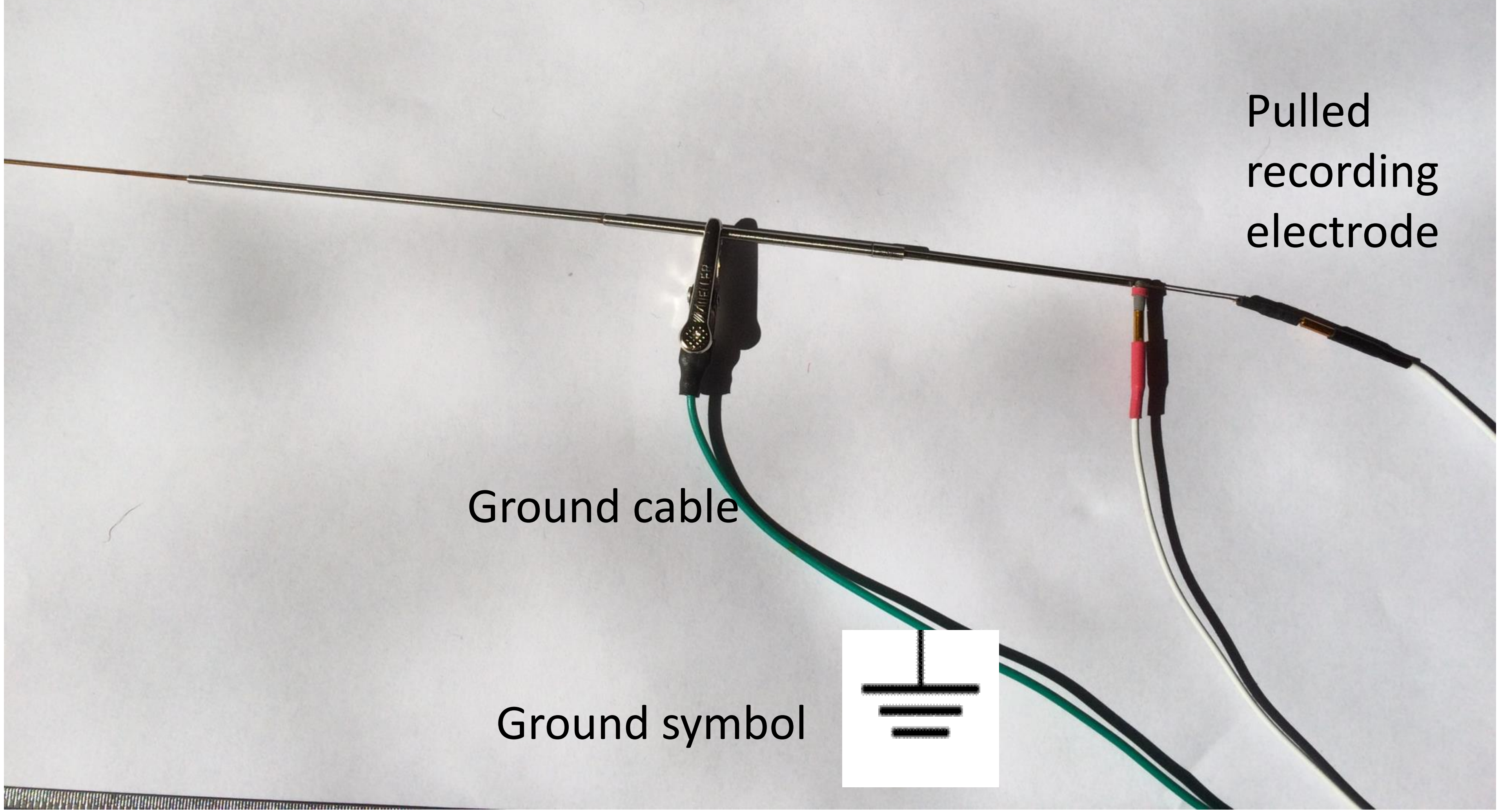

Stimulator
Inverting device
stimulation cable



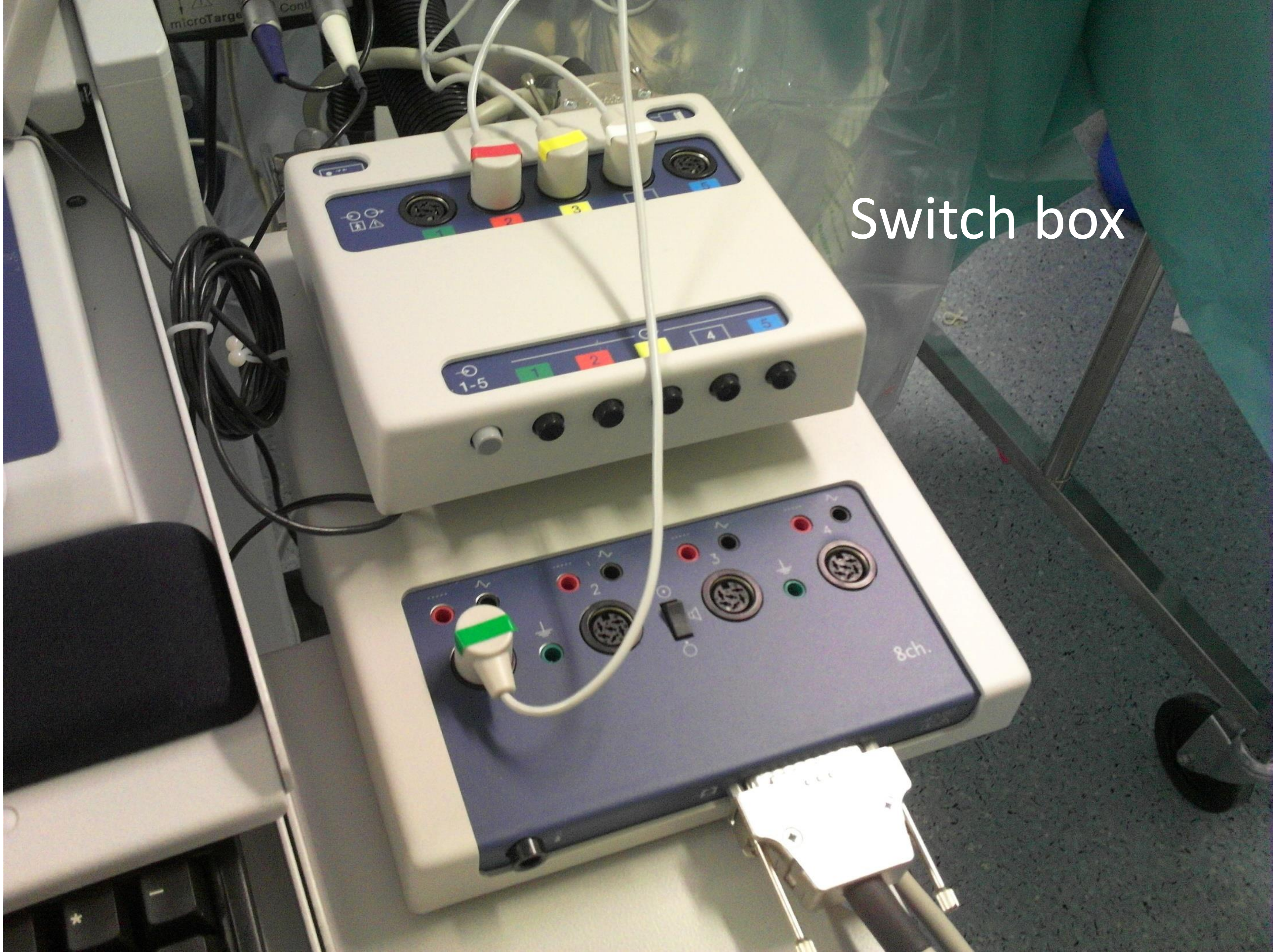
Connecting cable have two active wires and a ground wire. Stimulation is delivered through red plug (negative pulses) and reference is ground.


guiding tube
Microelectrode
tip retracted

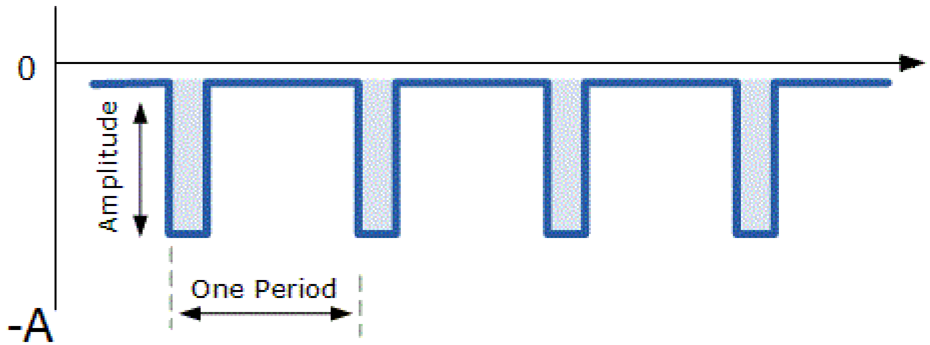
Macro electrode connections with stimulating wire (red connector)



Switch box



Per op stimulation parameters

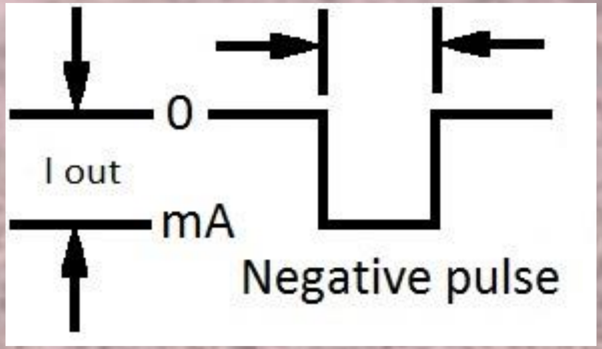


- Current 0-10 mA
- Monopolar pulses

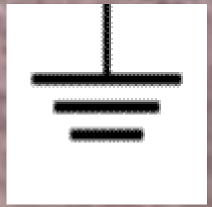
    Polarity : negative

    Duration : 100 µs

    Frequency (inverse of period) 130 – 185 Hz



Macro contact
used to deliver
negative current – stimulating
pulses (~~ 0-8 mA)
Reference contact is ground +



Goals of Intra-operative Stereotactic clinical neurophysiology

- localize the limits of target nucleus (STN) with the best precision (< 1 mm) ;

- find nucleus functional area giving the best clinical efficiency on clinical symptoms : akinesia, rigidity, or tremor

- localize functional target (optimal therapeutic effect and minimal adverse effects induced by per operative stimulation)

Gold standard procedure for best results

Patient awaked during recording and stimulation (!)

Microelectrode recording on five trajectories

Macro stimulation where recording showed targeted nucleus activity

Use of guiding tube for permanent electrode positioning

All steps under radiological control

Ludovic 11/05/12 Dr S. NAVARRO

T1	CA	CP	M
X =	103,0	102,3	102,5
Y =	103,9	79,2	102,4
Z =	118,3	116,2	77,5

d CA-CP : 25,2 mm

GPi g	**GPi d**
X = 121,5	X = 83,5
Y = 93,5	Y = 94,5
Z = 120,0	Z = 119,5
A = 105°	A = 84°
B = 56,5°	B = 60°

Movement Disorders, Vol. 21, Suppl. 14, 2006

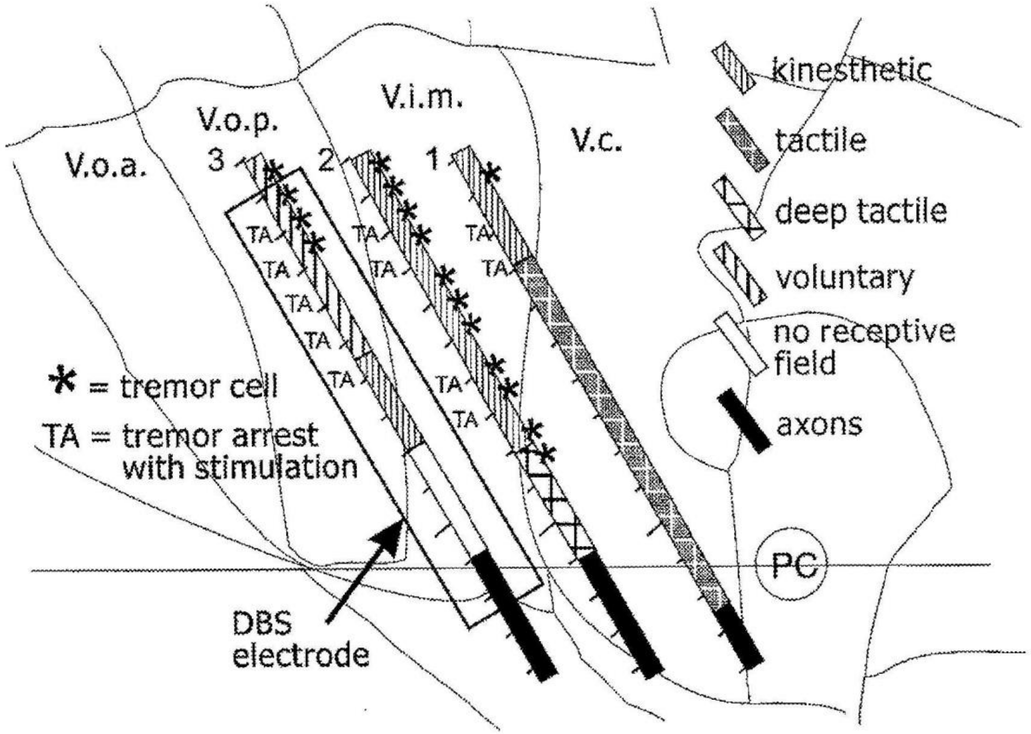
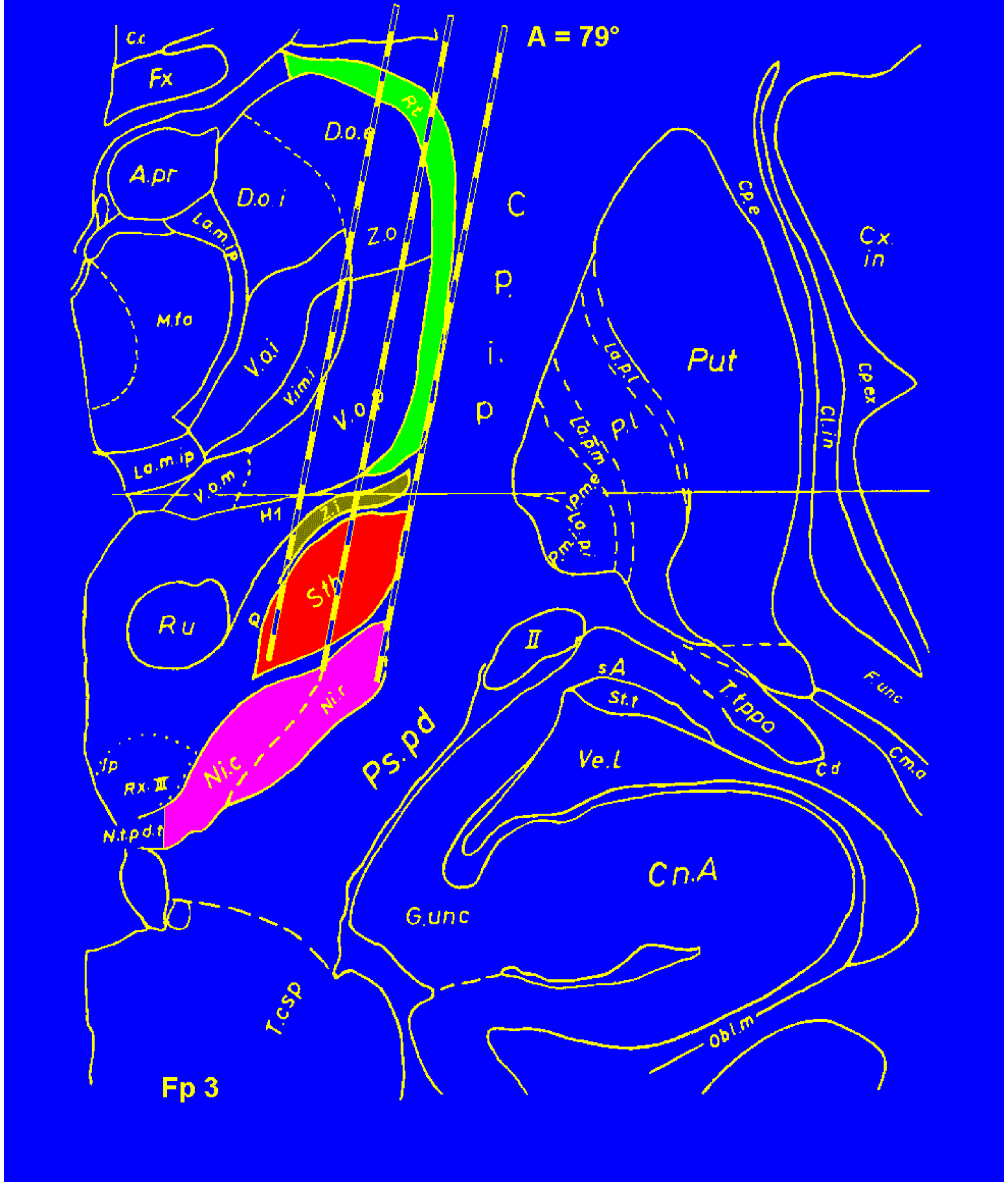
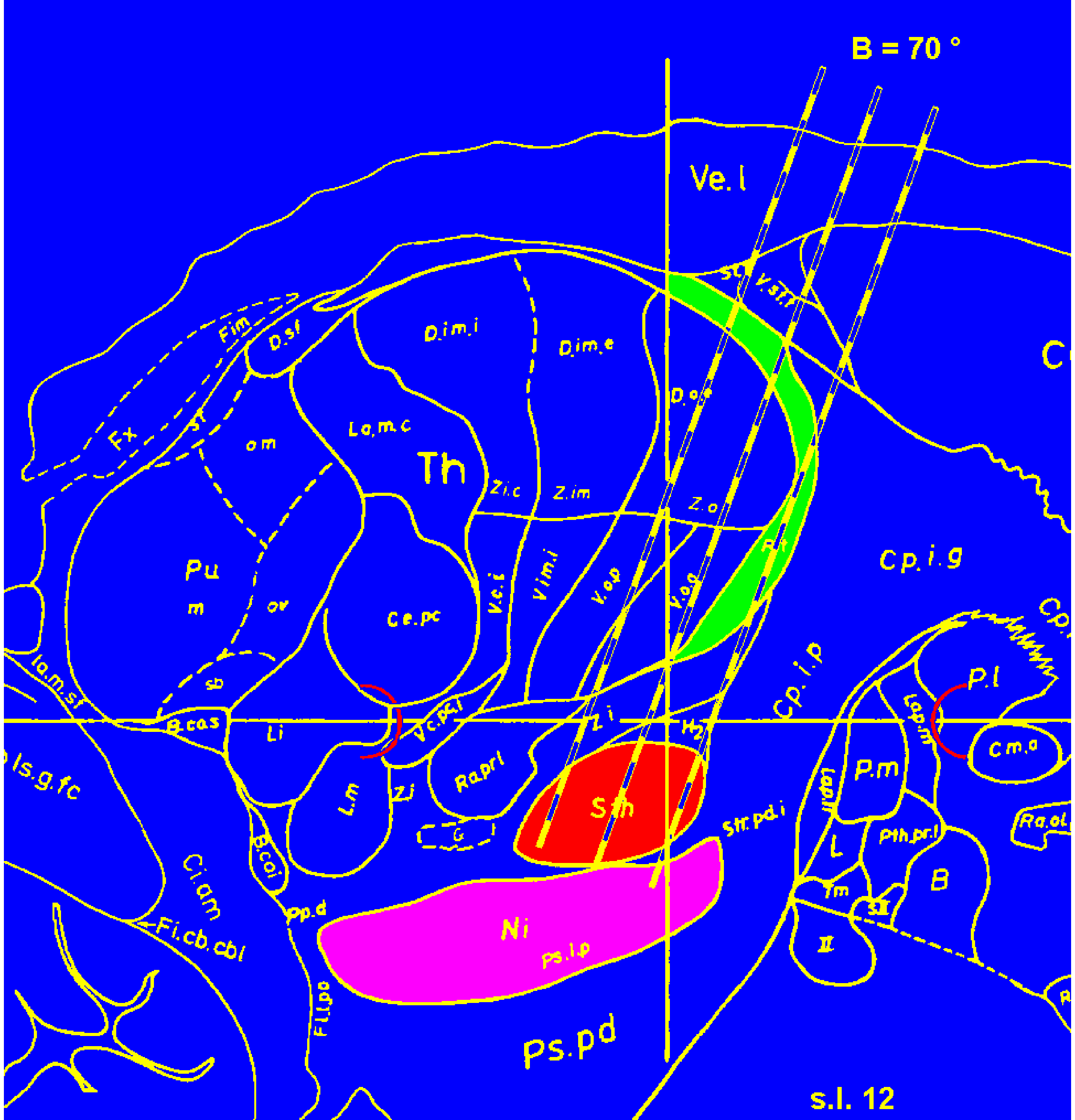
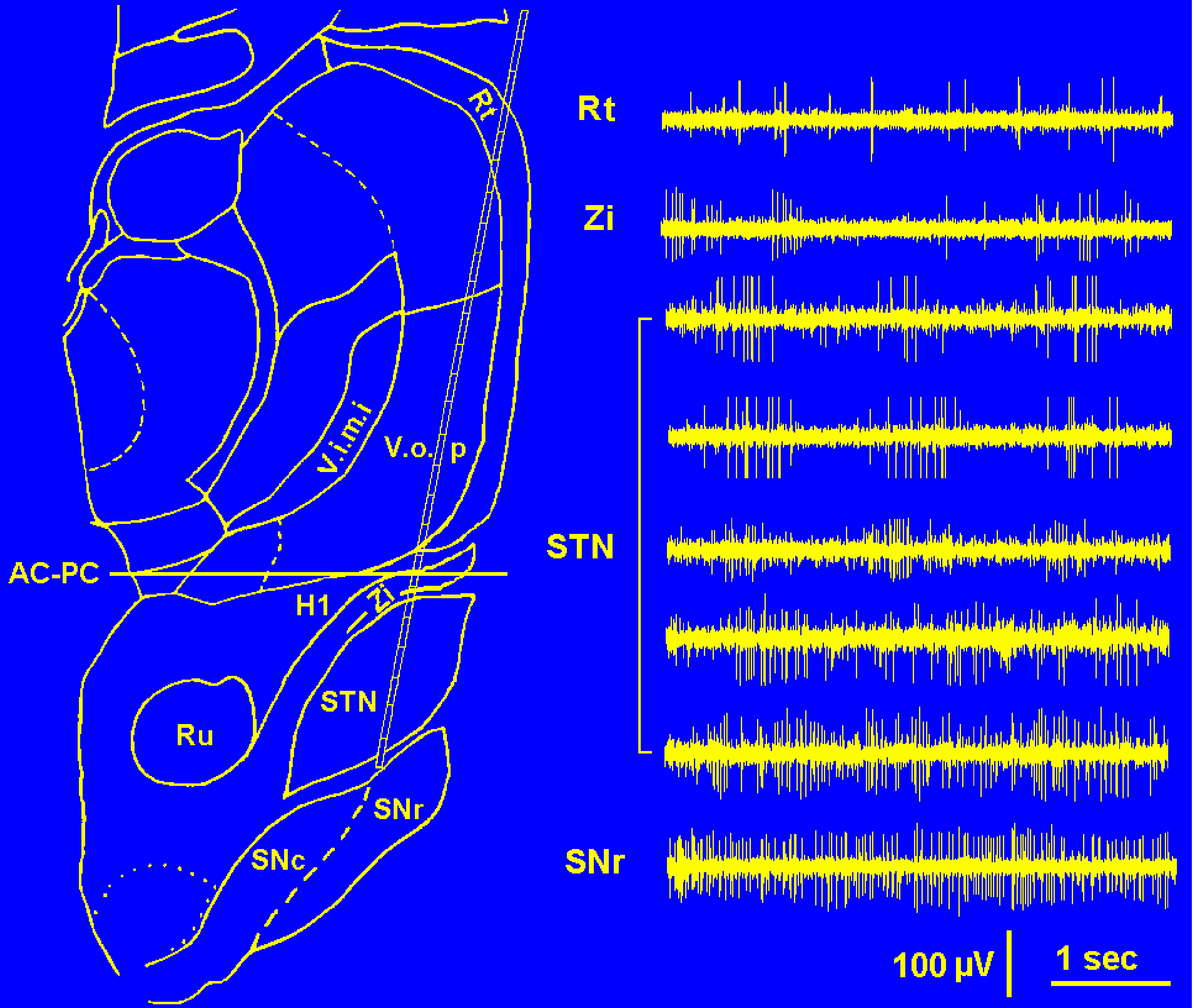


FIG. 5. Microelectrode mapping of the ventral intermedius nucleus. Typical microelectrode map during implantation of DBS into the Vim nucleus of thalamus. Three electrode tracks were performed to define the location of Vim and Vc prior to positioning the DBS electrode. Courtesy of W. Hutchison, University of Toronto.

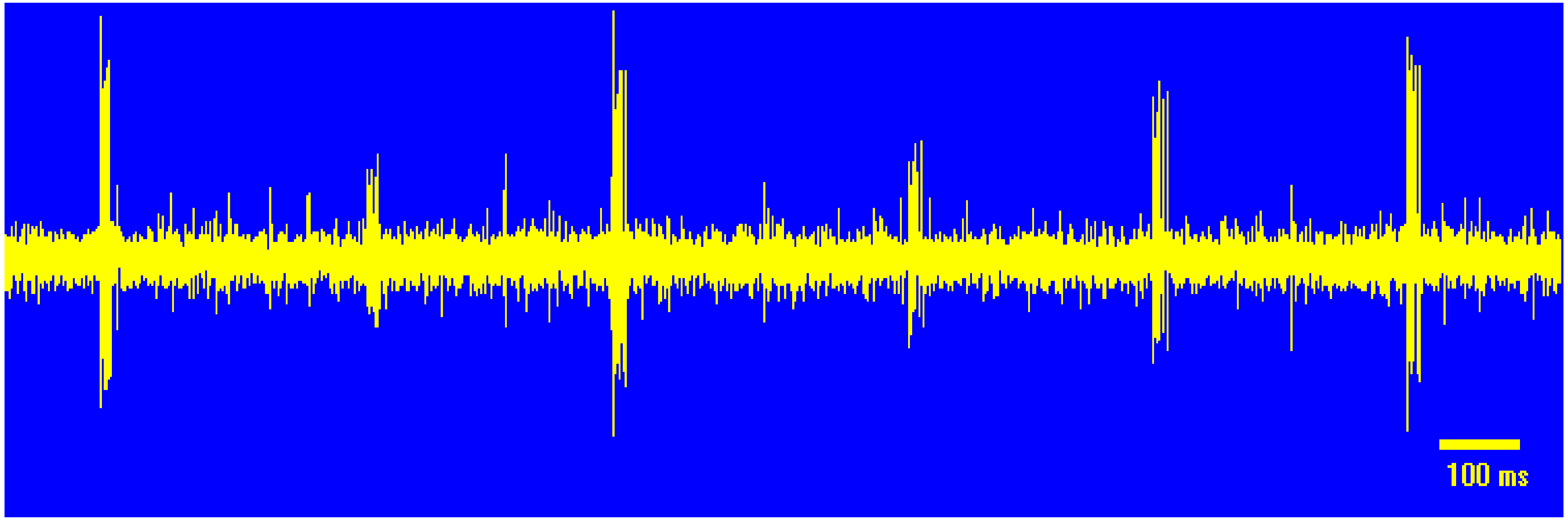

A = 79°
Cc
Fx
D.o.e
Rt
A.pr
D.o.i
C
La.m.ip
Z.o
Cx.
in
M.fa
p.
Put
V.o.i
i.
V.im.i
p
V.o.p
La.p.l
Cl.in
p.l
La.m.ip
V.o.m
H1
Z.i
Sth
Ru
II
sA
St.t
T.tppo
F.unc
Ni.r
Ni.c
Ps.pd
Ve.l
Cd
Cm.a
:ip
Rx. III
N.t.p.d.t
Cn.A
G.unc
T.csp
obl.m
Fp 3

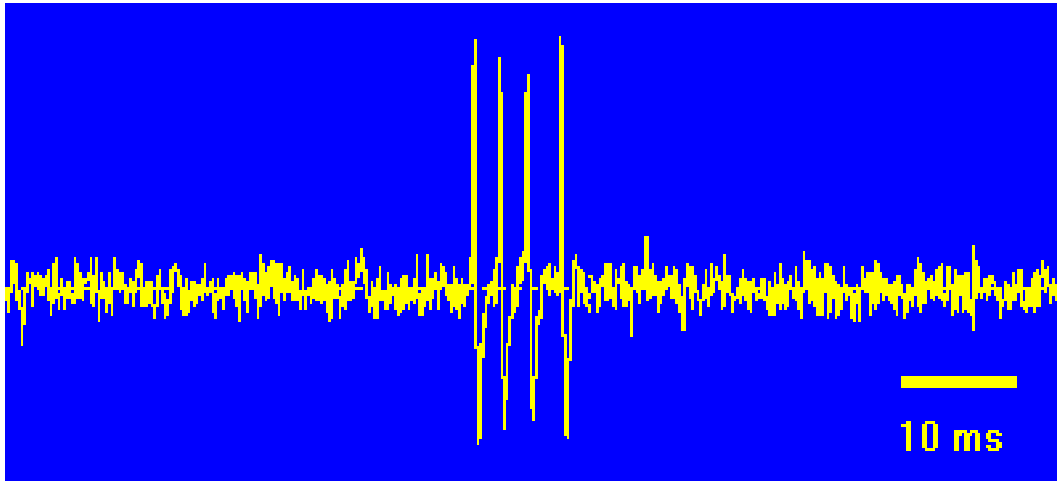

B = 70 °
Ve.l
Fim
D.sf
D.im.i
D.im.e
Fx
om
La.m.c
Th
Z.i.c
Z.im
Z.o
Pu
m
ov
Ce.pc
V.c.i
V.im.i
V.o.p
Cp.i.g
Cp.i.p
P.l
sb
B.cas
Li
Zi
H2
L.m
Sth
P.m
Cm.a
B.coi
Ci.am
Pp.d
Ni
Fi.cb.cbl
Ps.pd
L
Tm
B
II
s.l. 12



Rt
V.i.m.i
V.o.
p
AC-PC
H1
Zi
STN
Ru
SNr
SNc
Rt
Zi
STN
SNr
100 μV
1 sec

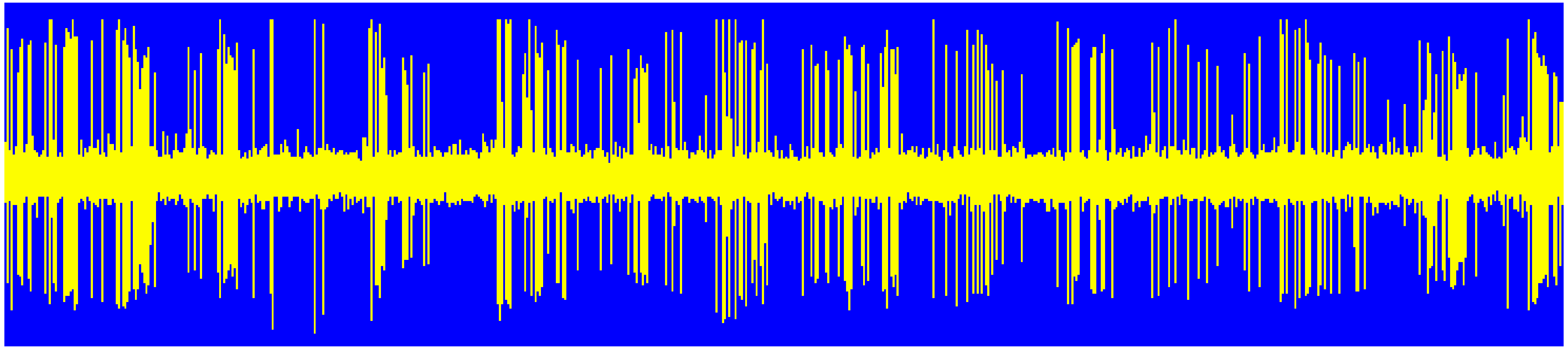
Thalamic reticular nucleus



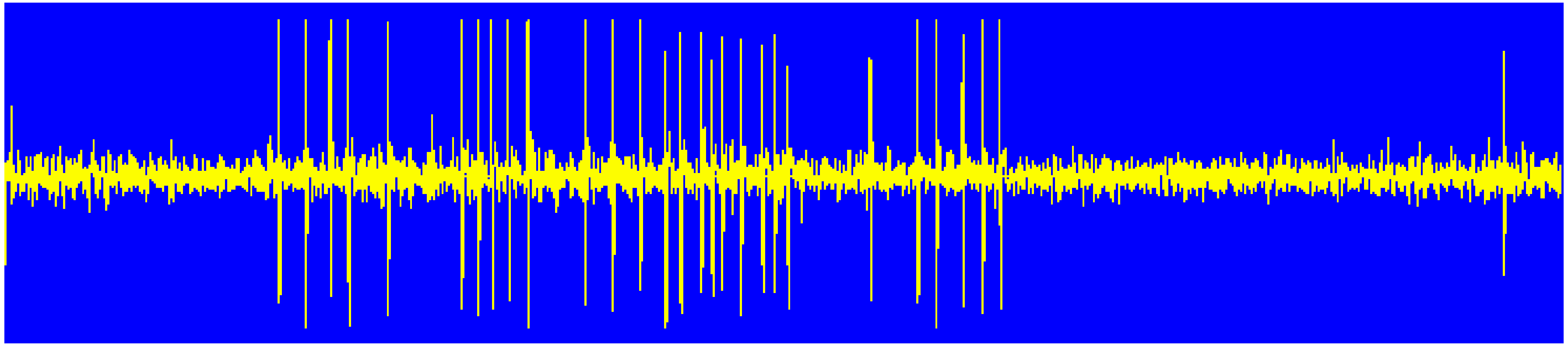


type B neurone
Raeva et al. 1991

Parkinson's Disease – Subthalamique Nucleus



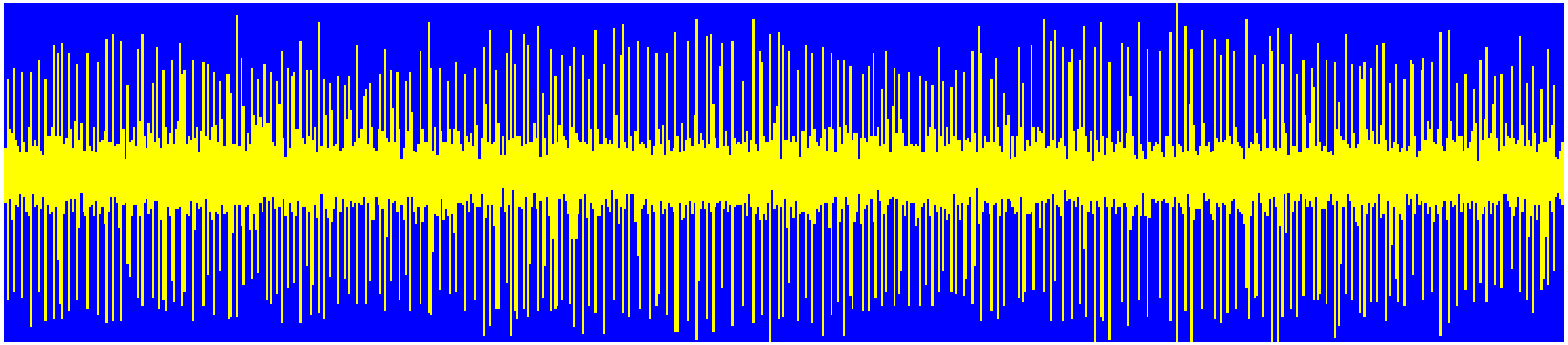
6 sec



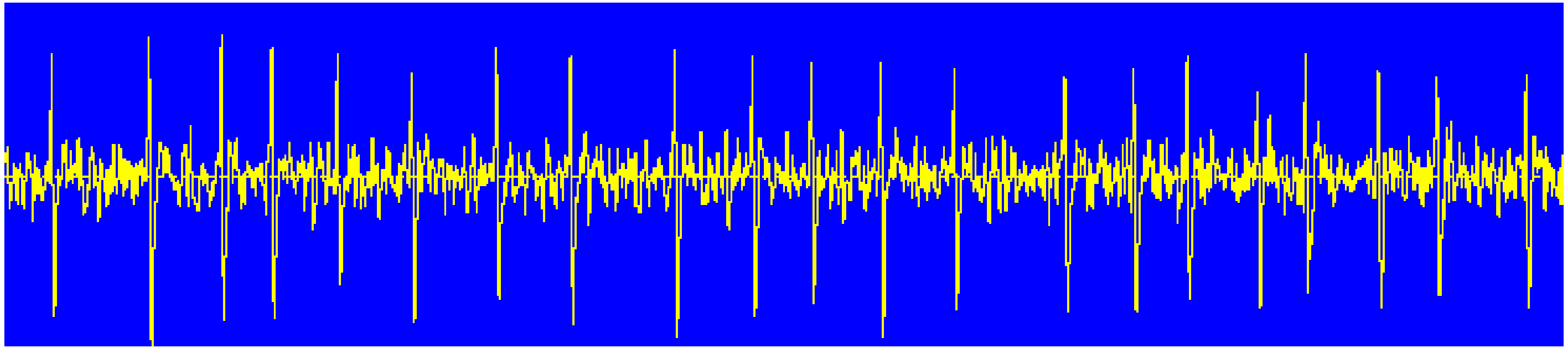
Single unit microelectrode recording

0,6 sec

Parkinson : substantia nigra single unit activity



2 sec



0,2 sec

10/2013

ENREGISTREMENT - COTE DROIT

Distance cible DT	Distance parcourue DD	Z radiologique	ANTERIEURE	CENTRALE	POSTERIEURE	INTERNE	EXTERNE
-9000	21000						
500							
-8000	22000						
500							
-7000	23000						
500							
-6000	24000						
500							
-5000	25000						
500							
-4000	26000						
500							
-3000	27000						
500							
-2000	28000						
500							
-1000	29000						
500							
CIBLE	30000						
500							
1000	31000						
500							
2000	32000						
500							
3000	33000						
500							
4000	34000						
500							
5000	35000						

SNr ?

SNR

SNR
SNR

10/01/12 G?i

RENEE (EN 08/02/12)
Ne(e):DEVYNCK
A 08/02/1944 () F 661223371 4

ENREGISTREMENT - COTE GAUCHE

Distance cible DT	Distance parcourue DD	Z radiologique	ANTERIEURE	CENTRALE	POSTERIEURE	INTERNE	EXTERNE
-9000	21000						
500							
-8000	22000						
500							
-7000	23000						
500							
-6000	24000						
500							
-5000	25000						
500							
-4000	26000						
500							
-3000	27000						
500							
-2000	28000						
500							
-1000	29000						
500							
CIBLE	30000						
500							
1000	31000						
500							
2000	32000						
500							
3000	33000						
500							
4000	34000						
500							
5000	35000						

[illegible] ∅
Z = 115

interne [illegible] pas [illegible] [illegible]

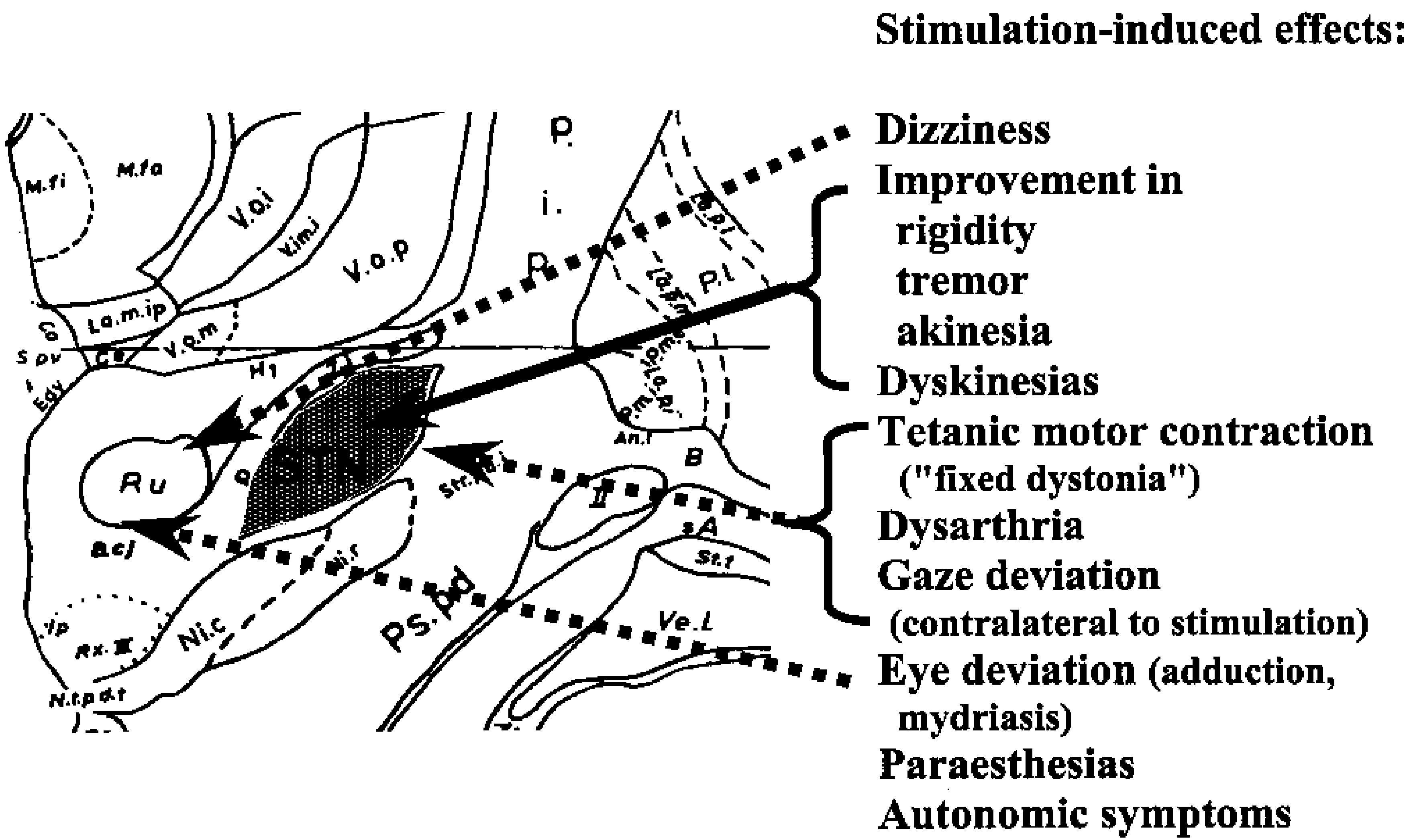


FIG. 2. Sites of stimulation-induced effects in the subthalamic nucleus region on a coronal view at 3 mm posterior to the mid-bicommissural line (from Schaltenbrand's atlas). STN, subthalamic nucleus. The site for paraesthesias is more posterior. The site for autonomic symptoms is more anterior.

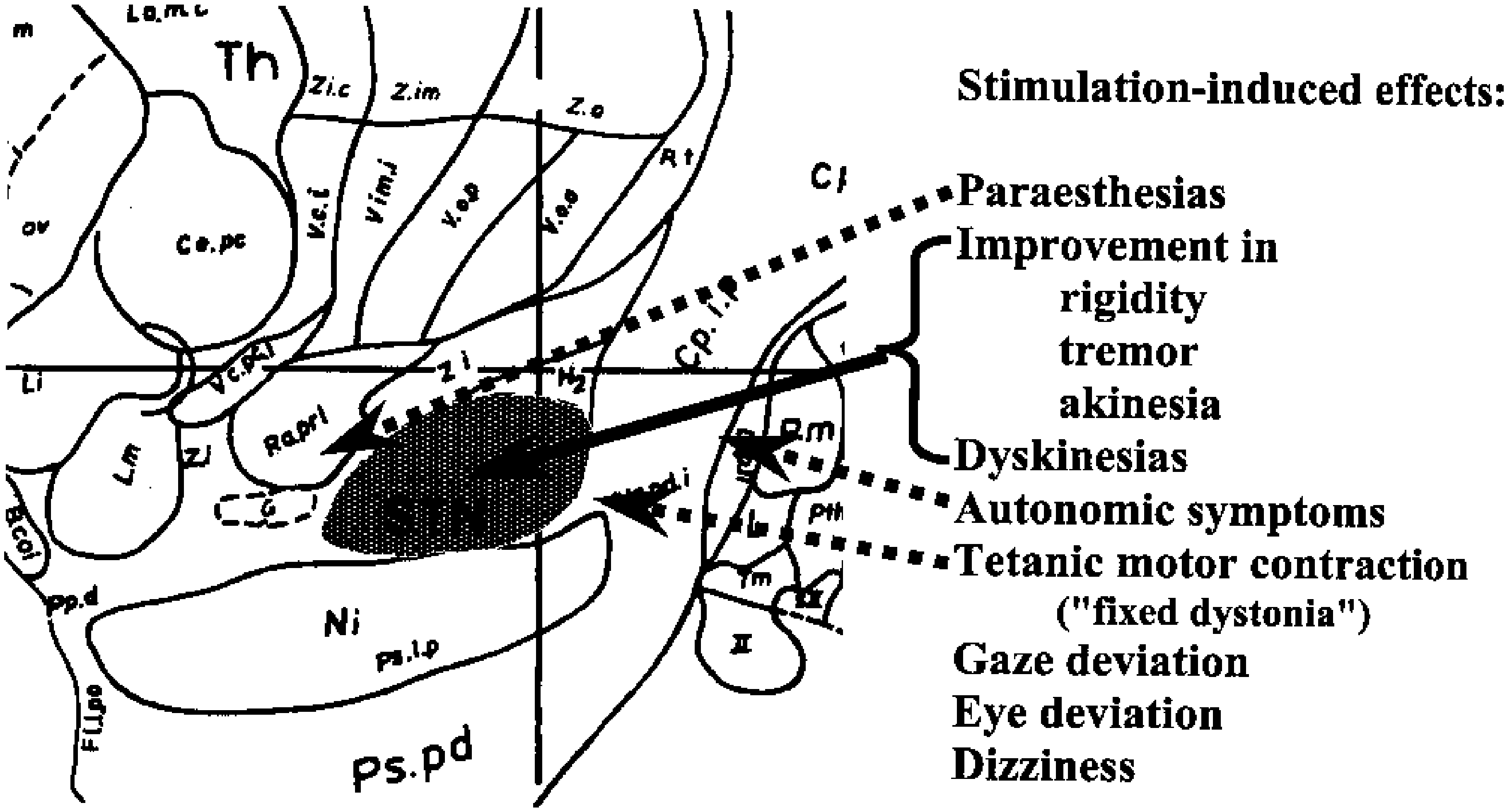
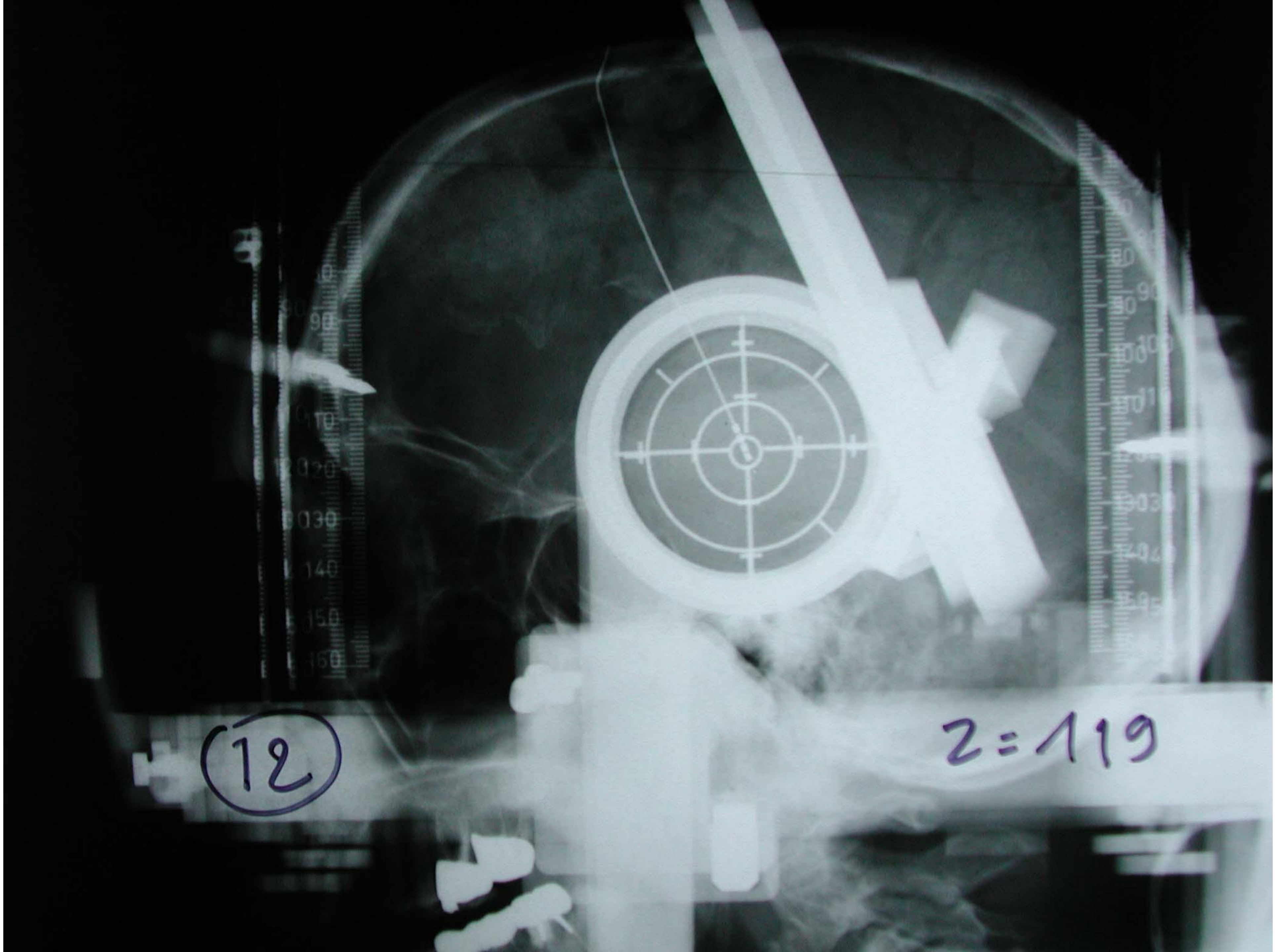
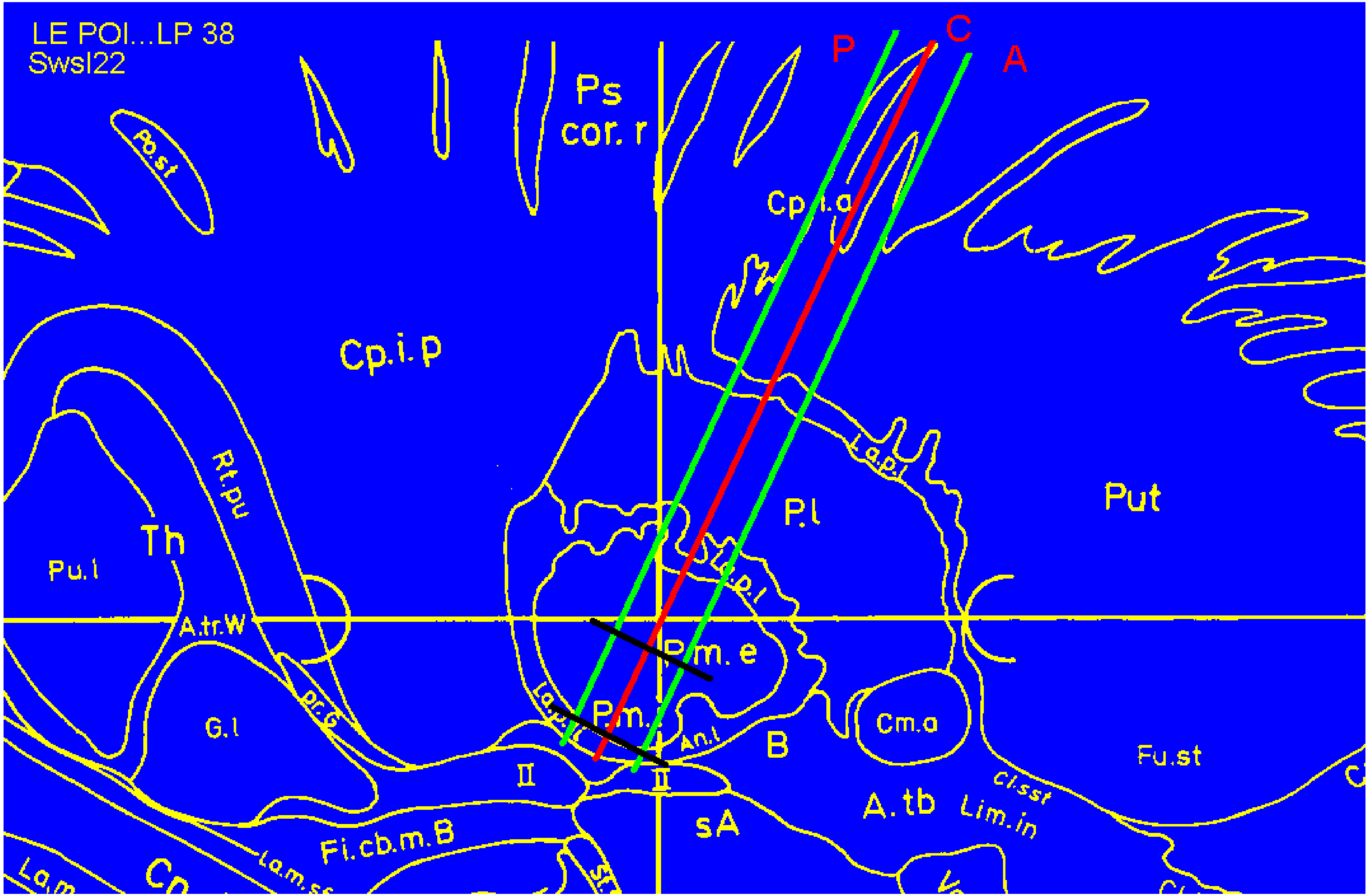


FIG. 1. Sites of stimulation-induced effects in the subthalamic nucleus region on a sagittal view at 12 mm of laterality (from Schaltenbrand's atlas) STN, subthalamic nucleus. The site for gaze deviation is imprecise. The sites for eye deviation and dizziness are more medial.


Rx n°9
Z = 121

11
Z=120


12
z = 119



LE POI...LP 38
Swsl22
P
C
A
Ps
cor. r
Po.st
Cp.i.a
Cp.i.p
Rt.pu
Th
Pu.l
La.p.l
P.l
Put
L.p.l
A.tr.W
Pm.e
Pm.i
G.l
pr.G
An.l
B
Cm.a
Fu.st
II
sA
A.tb
Cl.sst
Lim.in
Fi.cb.m.B
La.m.sc

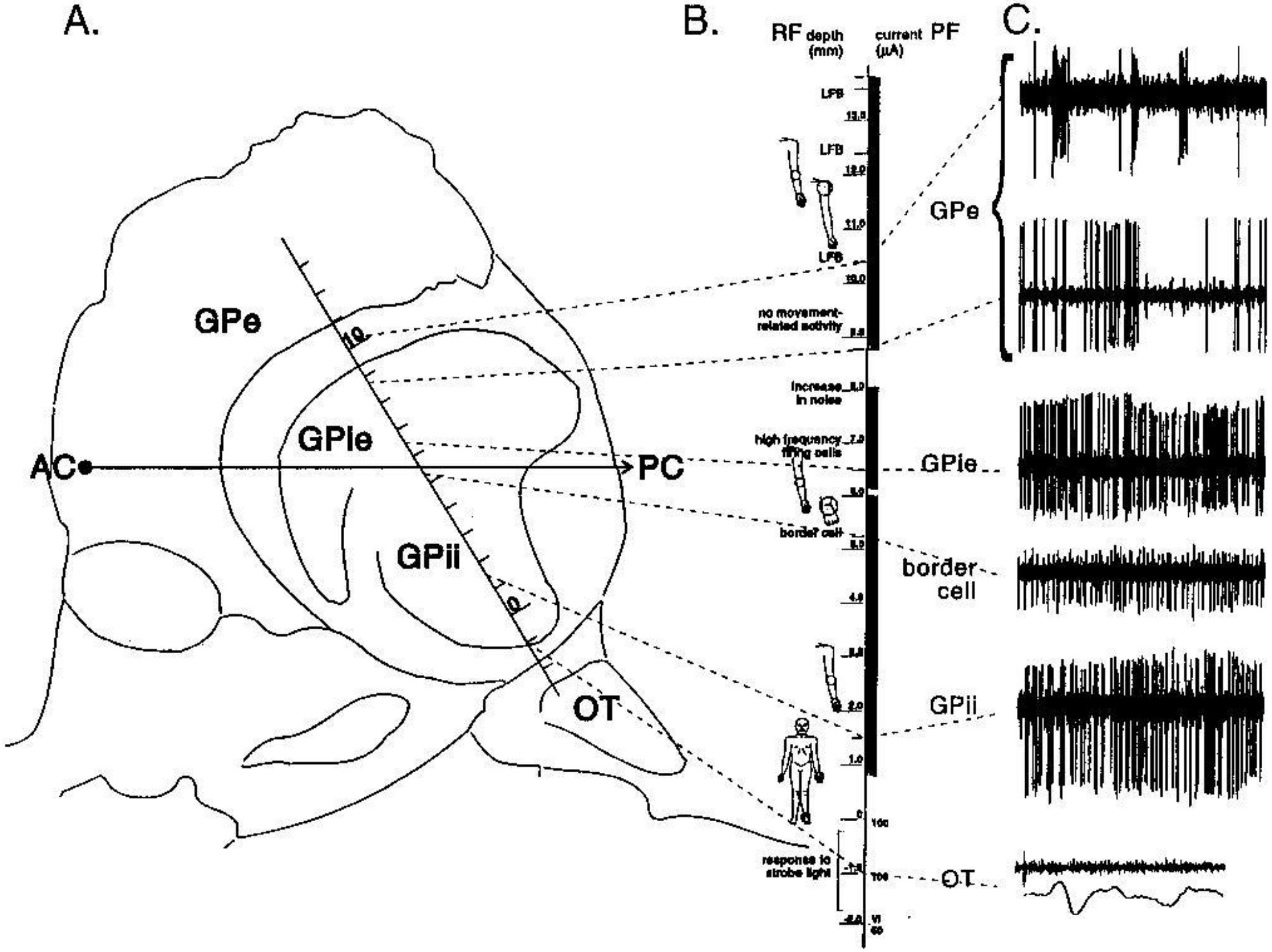
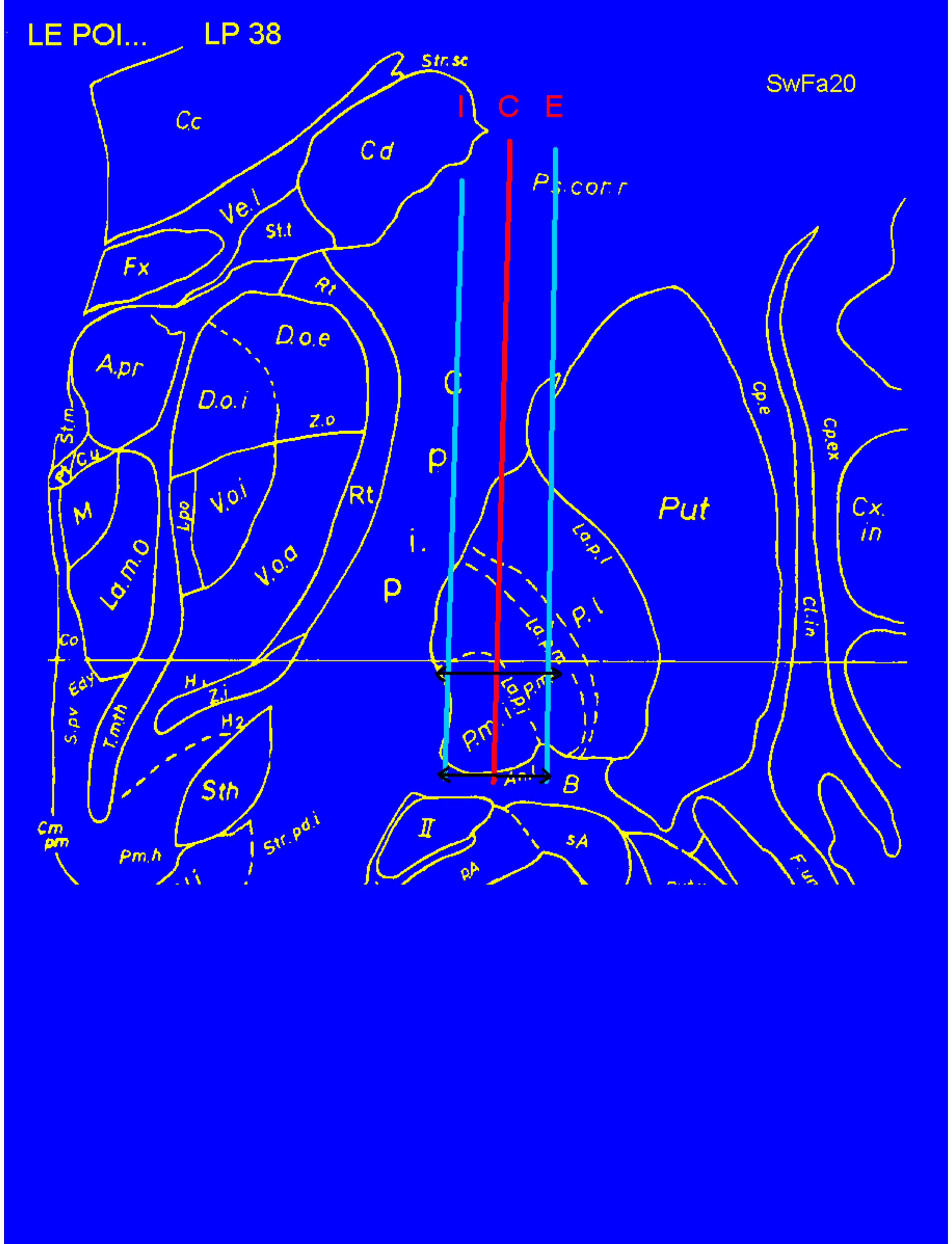
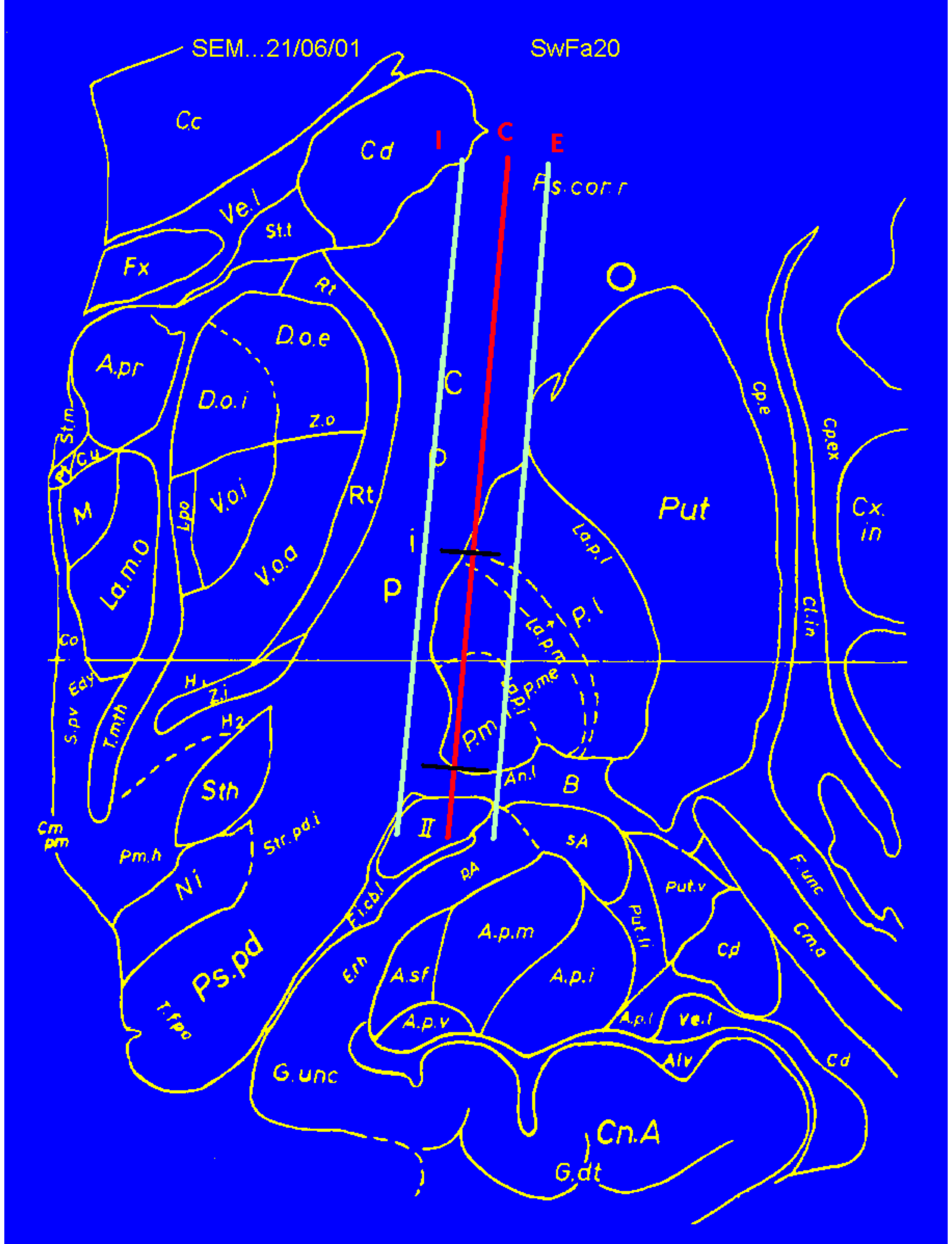


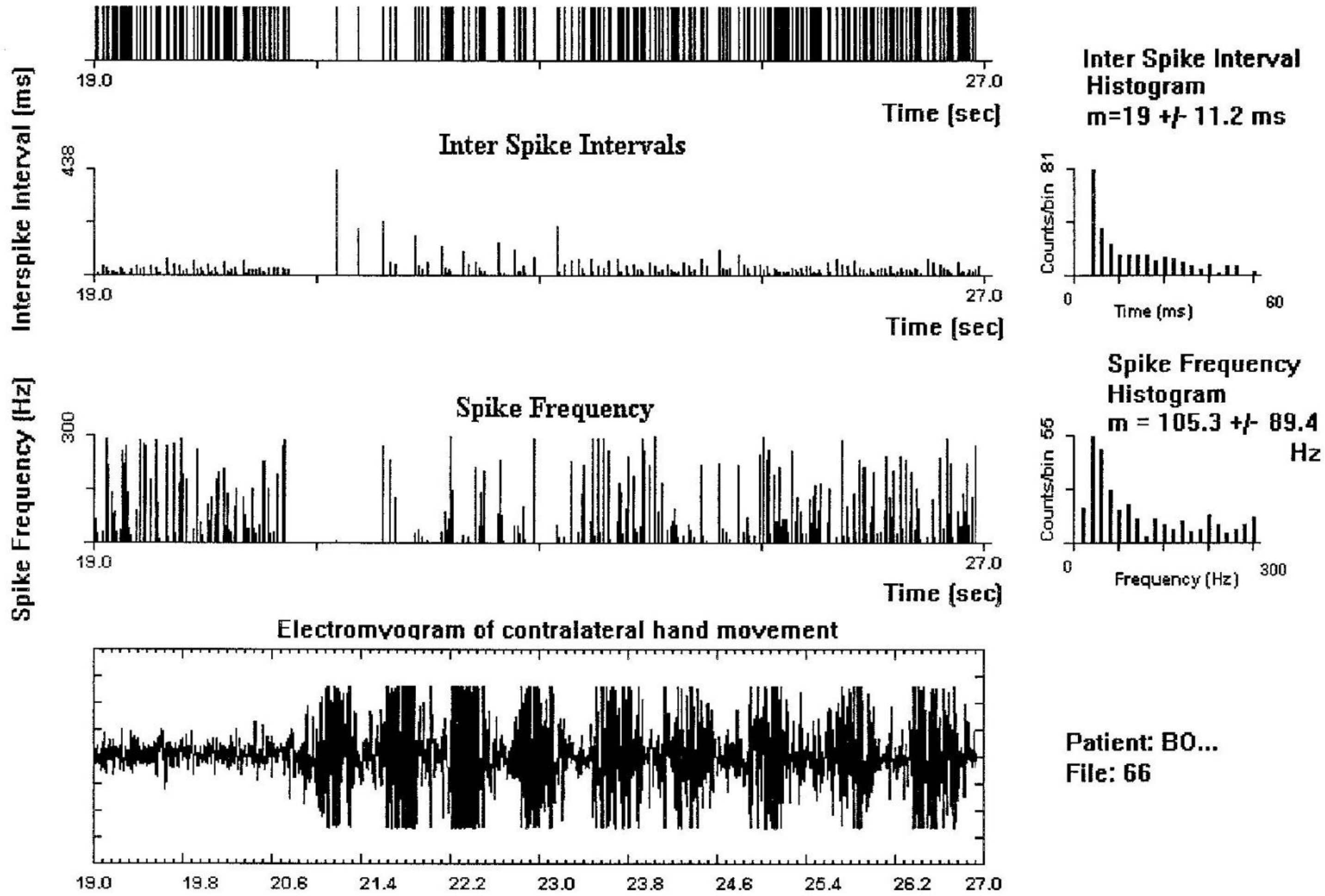
FIG. 2. A: Physiological data obtained from one trajectory through the globus pallidus and optic tract (OT), plotted on the 20-mm sagittal map from the Schaltenbrand and Wahren stereotactic atlas. B: The locations of neurons and their responses as well as intraoperative observations of the characteristics of recordings can be seen. C: Oscilloscope traces of representative examples of the neuronal types described in text. At the bottom is a single sweep of the filtered trace for which the optic tract field potential to visual stimuli was heard but not readily seen. With appropriate filter settings for visual evoked potential measurement from the optic tract, the visual evoked potential can be seen, as illustrated below (the smooth trace). LFB, low-frequency burst neuron; RF, receptive field; PF, projected field; AC, anterior commissure; PC, posterior commissure; GPii, internal segment of GPi; GPie, external segment of GPi. For other abbreviations, see legend to Figure 1. (Reprinted with permission from Lozano et al.[1])



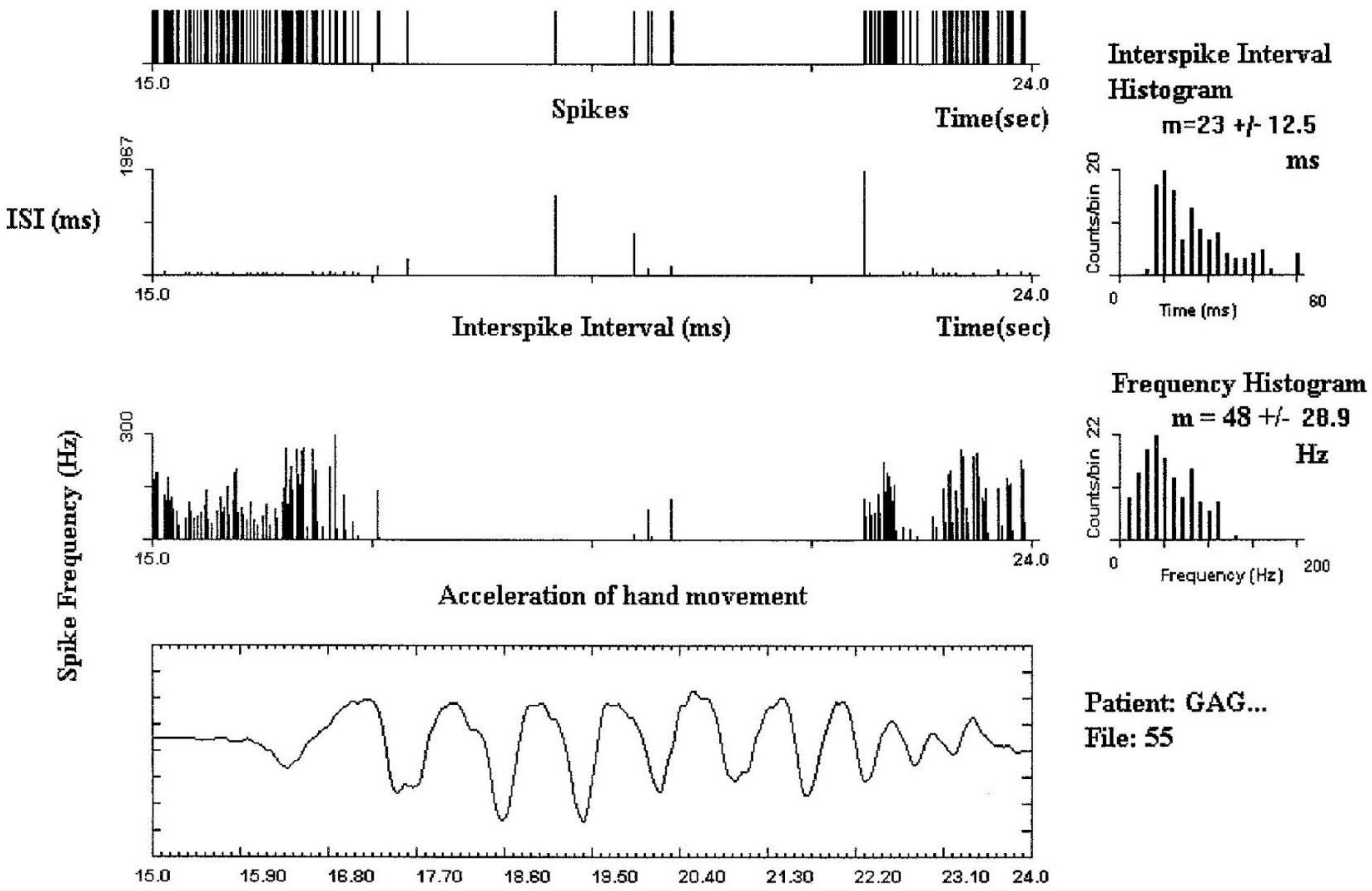
LE POI...
LP 38
SwFa20
I
C
E
Str.sc
Cc
Cd
Ps.corr
Ve.l
St.t
Fx
Rt
D.o.e
A.pr
D.o.i
Z.o
St.m
Cu
M
Lpo
V.o.i
Rt
V.o.a
La.m.o
C
p
i.
p
Put
Cp.e
Cp.ex
Cx.
in
La.p.i
P.i
La.p.m
Cl.in
Co
Edy
H₁
Z.i
H₂
S.pv
T.mth
Pm
Sth
B
II
sA
pA
Cm
pm
Pm.h
Str.pd.i


SEM...21/06/01
SwFa20
I
C
E
Cc
Cd
Ps.cor.r
Ve.l
St.t
Fx
Rt
O
D.o.e
A.pr
D.o.i
Z.o
C
O
St.m
Cu
Pf
M
V.o.i
Lpo
Put
Cp.e
Cp.ex
Cx. in
Rt
La.m.O
V.o.a
i
P
La.p.l
P.l
Cl.in
La.p.m
Co
Edy
H
Zi
La.p.me
P.m
S.pv
T.mth
H2
Sth
An.l
B
II
Cm pm
Str.pd.i
Pm.h
sA
Ni
pA
Put.v
F.unc
F.cb.l
Put.li
Cd
Cm.a
A.p.m
Ps.pd
E.rh
A.sf
A.p.i
T.fpo
A.p.v
A.p.l
Ve.l
Alv
cd
G.unc
Cn.A
G.dt

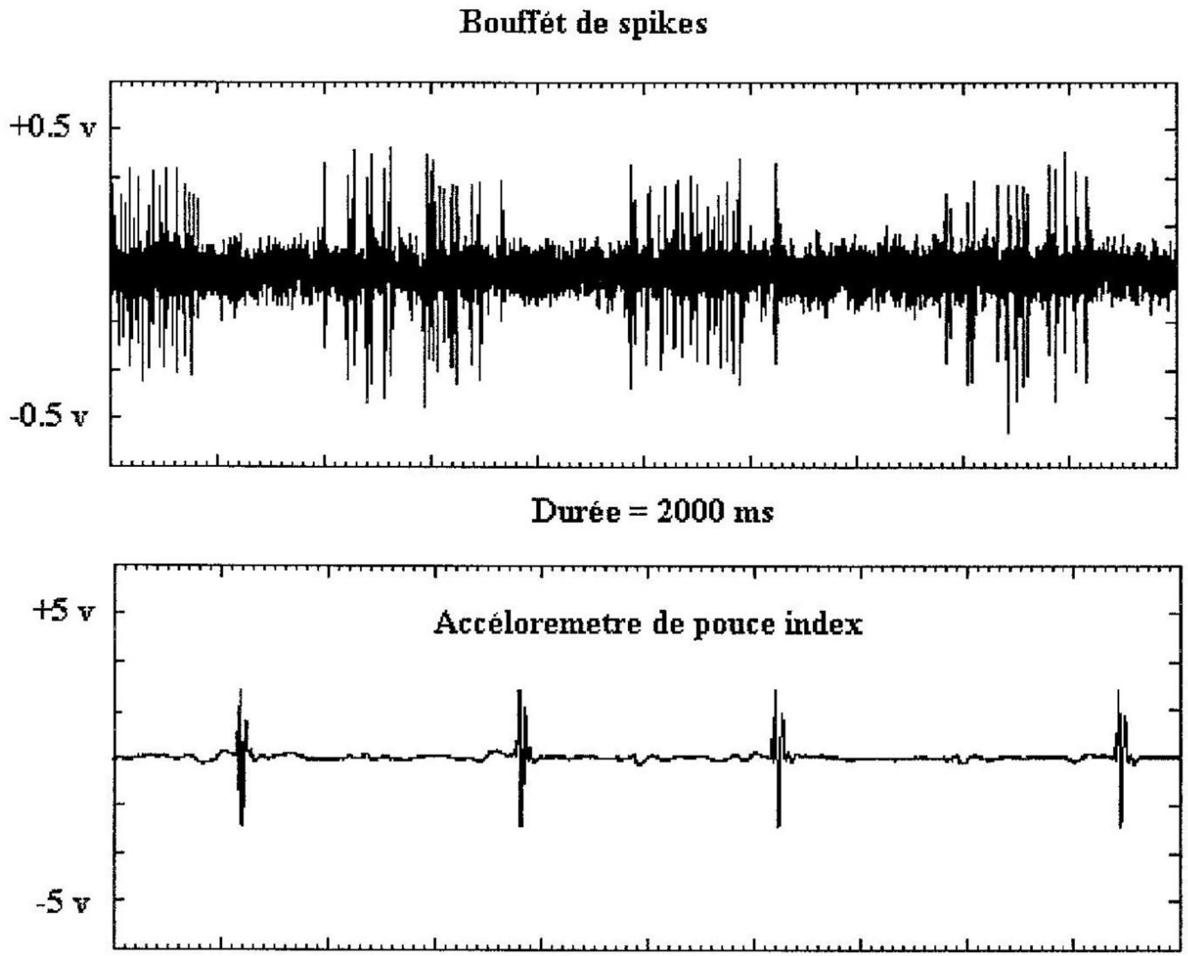
GLOBUS PALLIDUS SPIKES MODULATION BY CONTRALATERAL HAND ACTIVE FLEXION EXTENTION MOVEMENTS

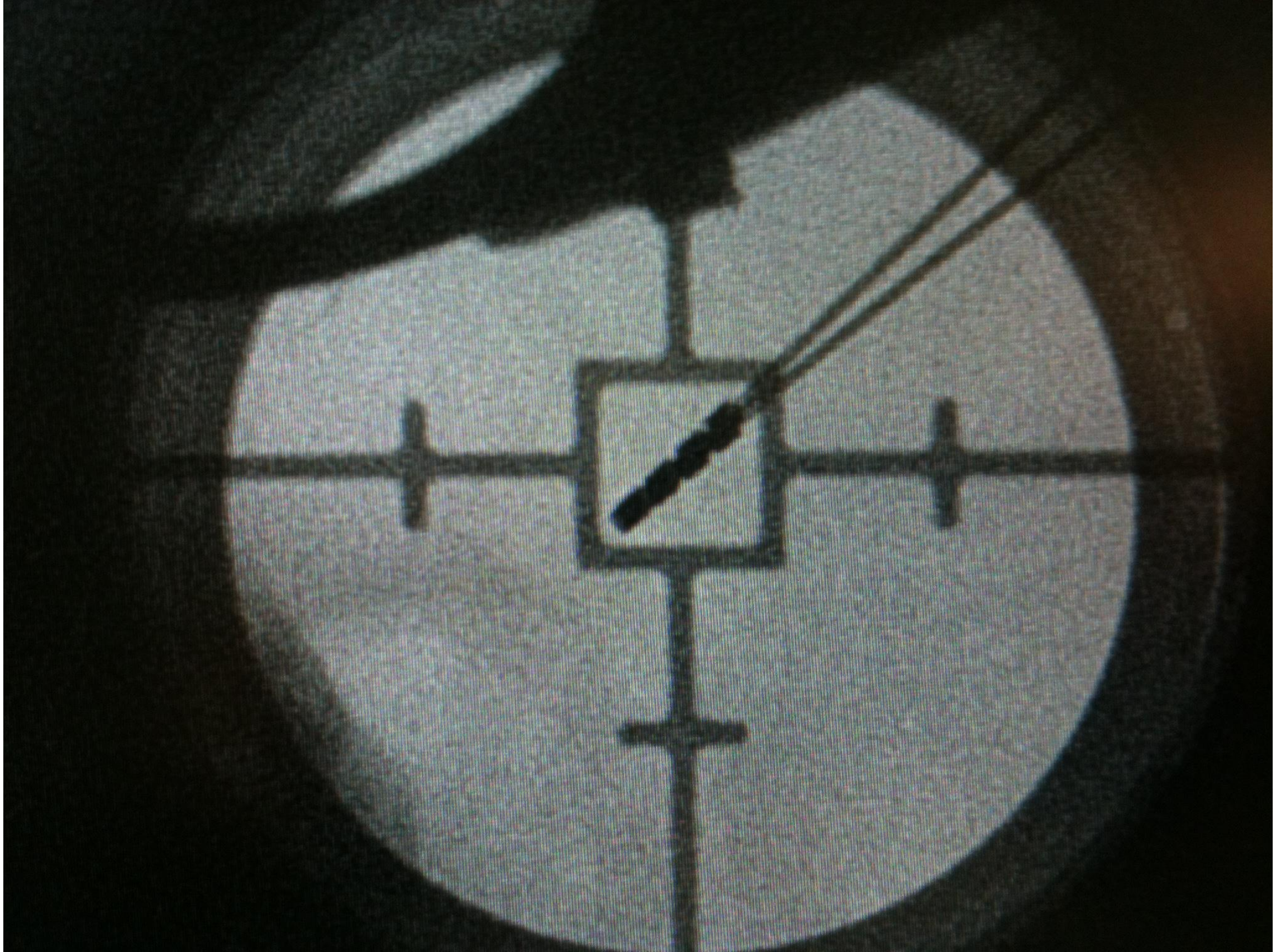


GP SPIKES INHIBITED BY CONTRALATERAL ACTIVE HAND MOVEMENT



Pallidal neurons activity and finger movements





Intra-operative stereotactic neurophysiology :

1. Confirms or adjusts the radiological target coordinates
2. Localizes with an extreme precision the spatial limits of nuclei (micro recordings)
3. Identifies their electrophysiological signatures
4. Defines the therapeutic contact position (macro stimulation, functional target).

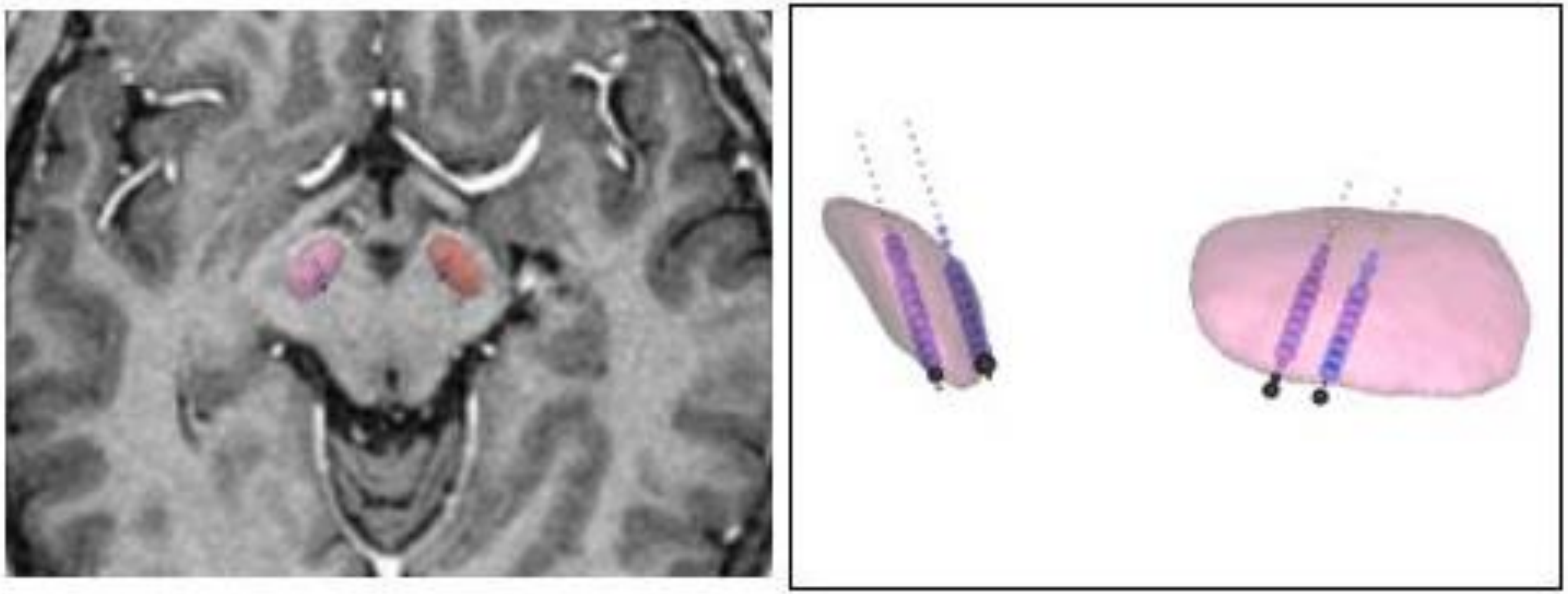
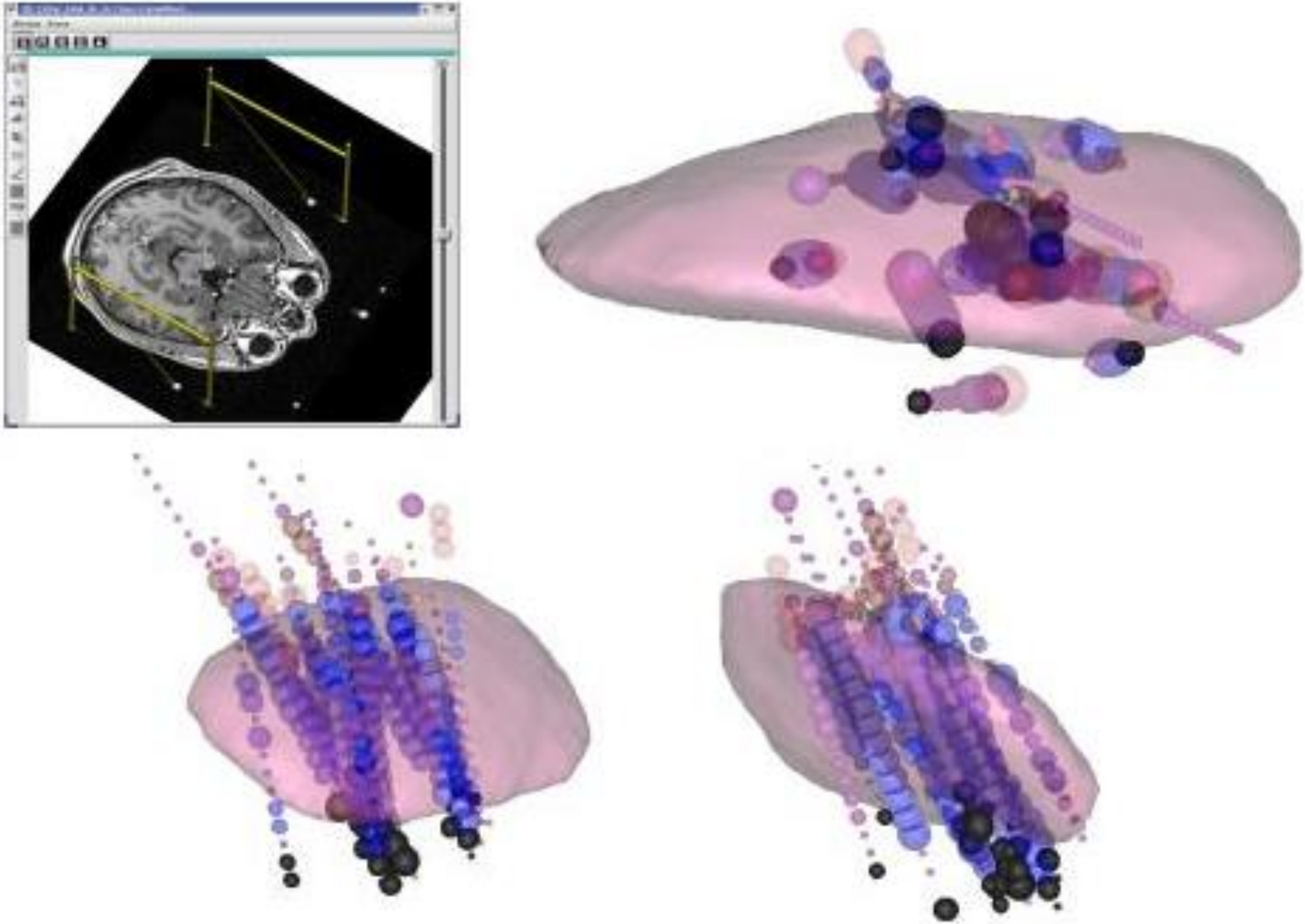
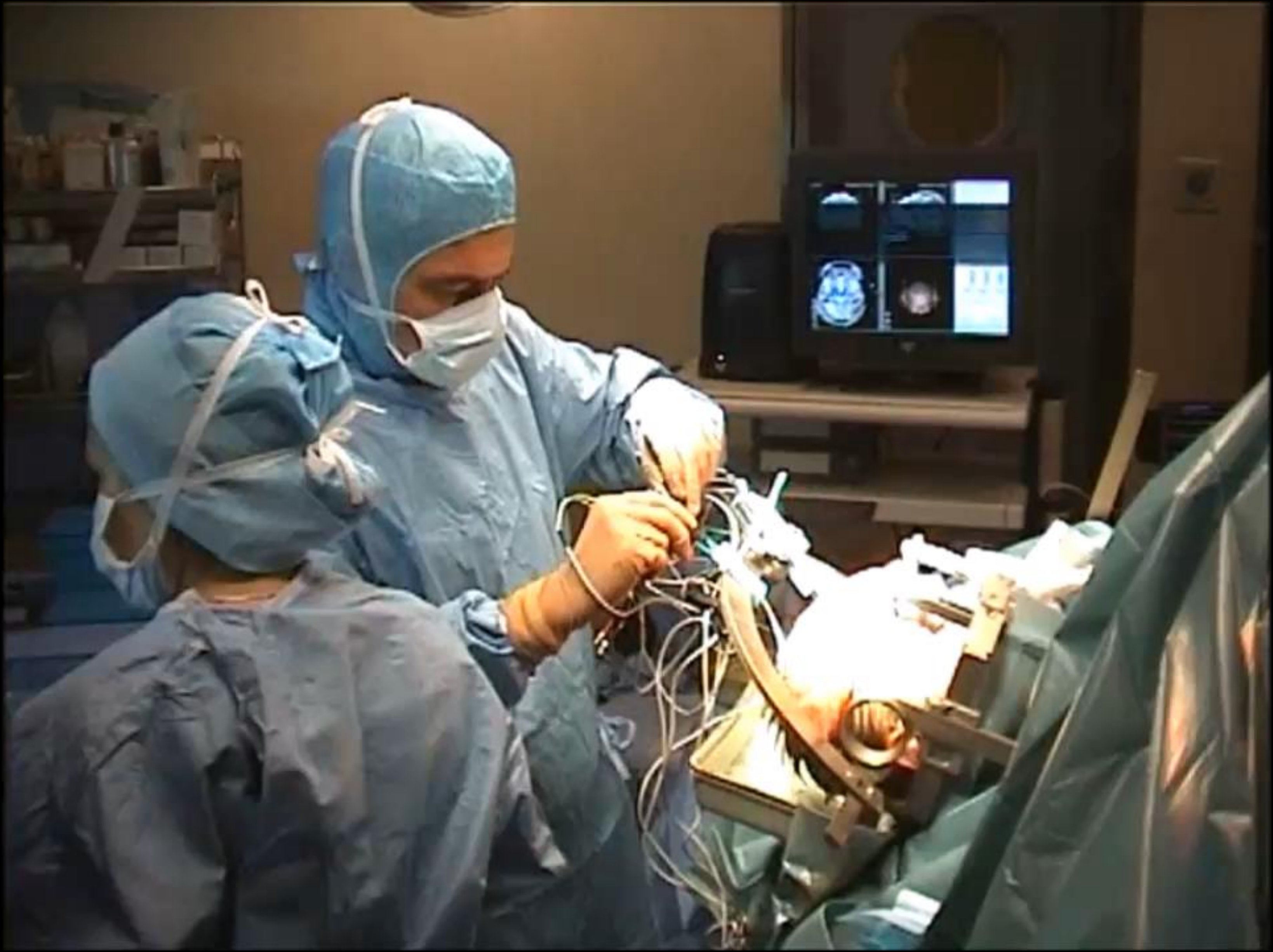
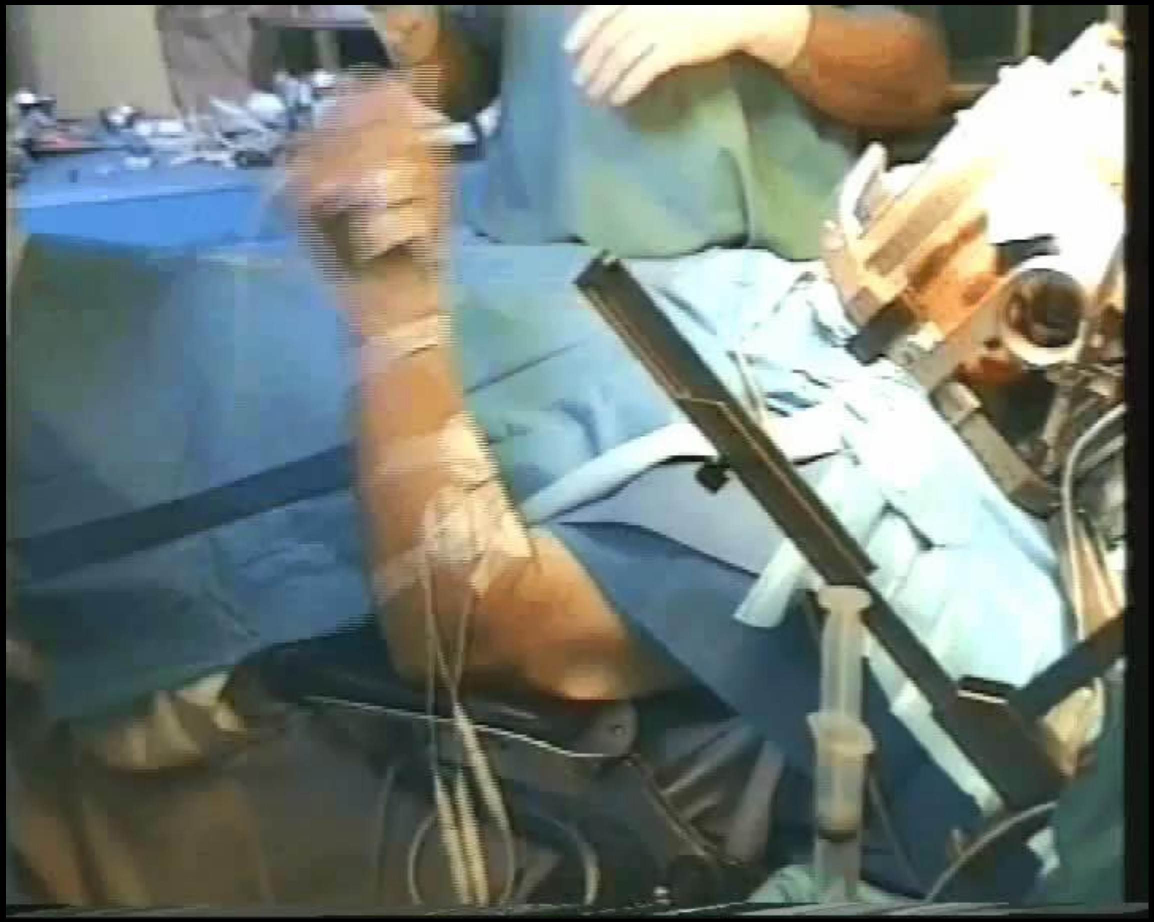


Fig.4. Confrontation of the atlas structures and electrophysiological per-operative recordings in the patient's pre-operative MRI. The blue spheres represent the recordings of ttwo microelectrodes by hemisphere identified as being within the STN by the electrophysiologist. Interval distance between twosuccessive spheres is 0.5 mm.

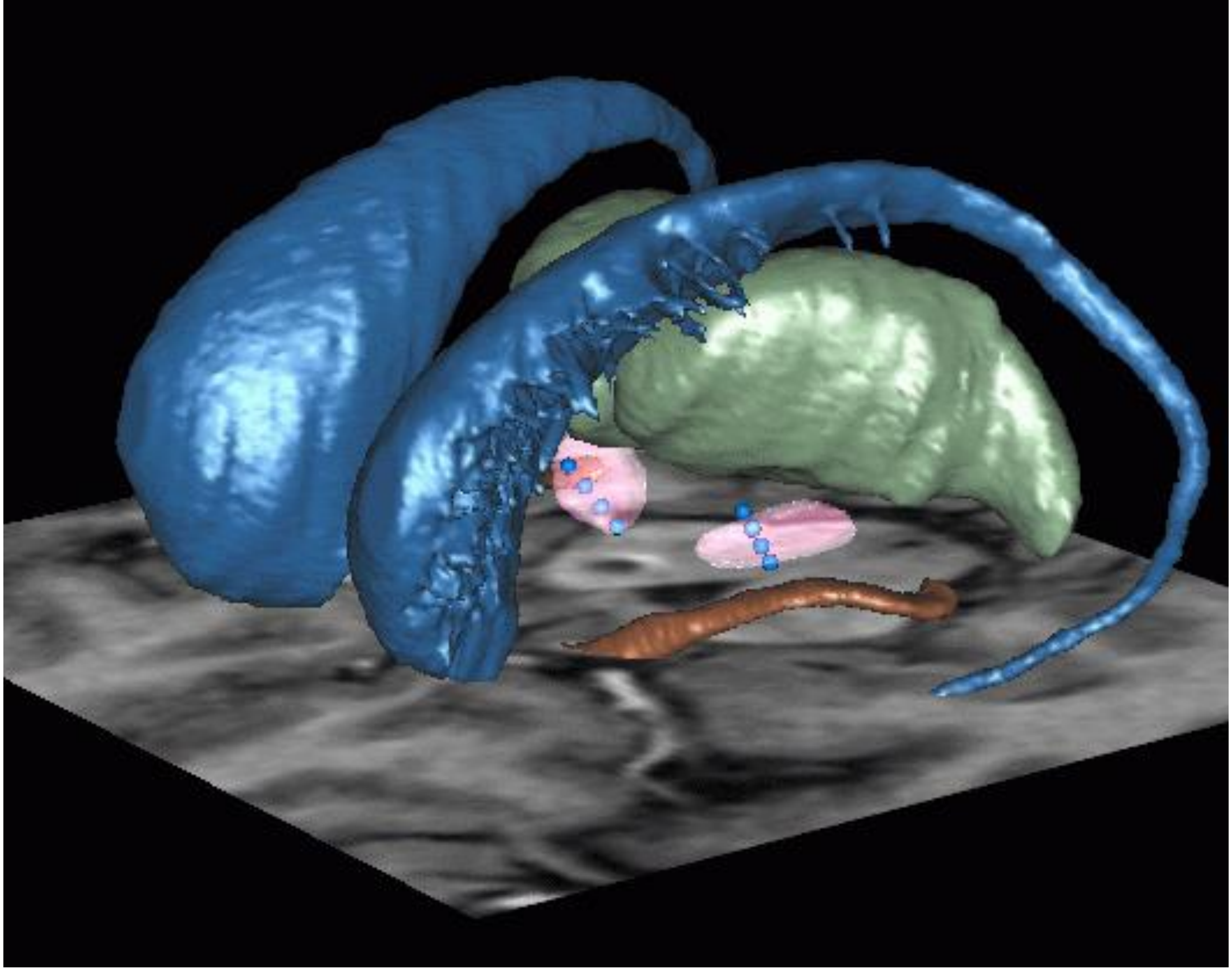


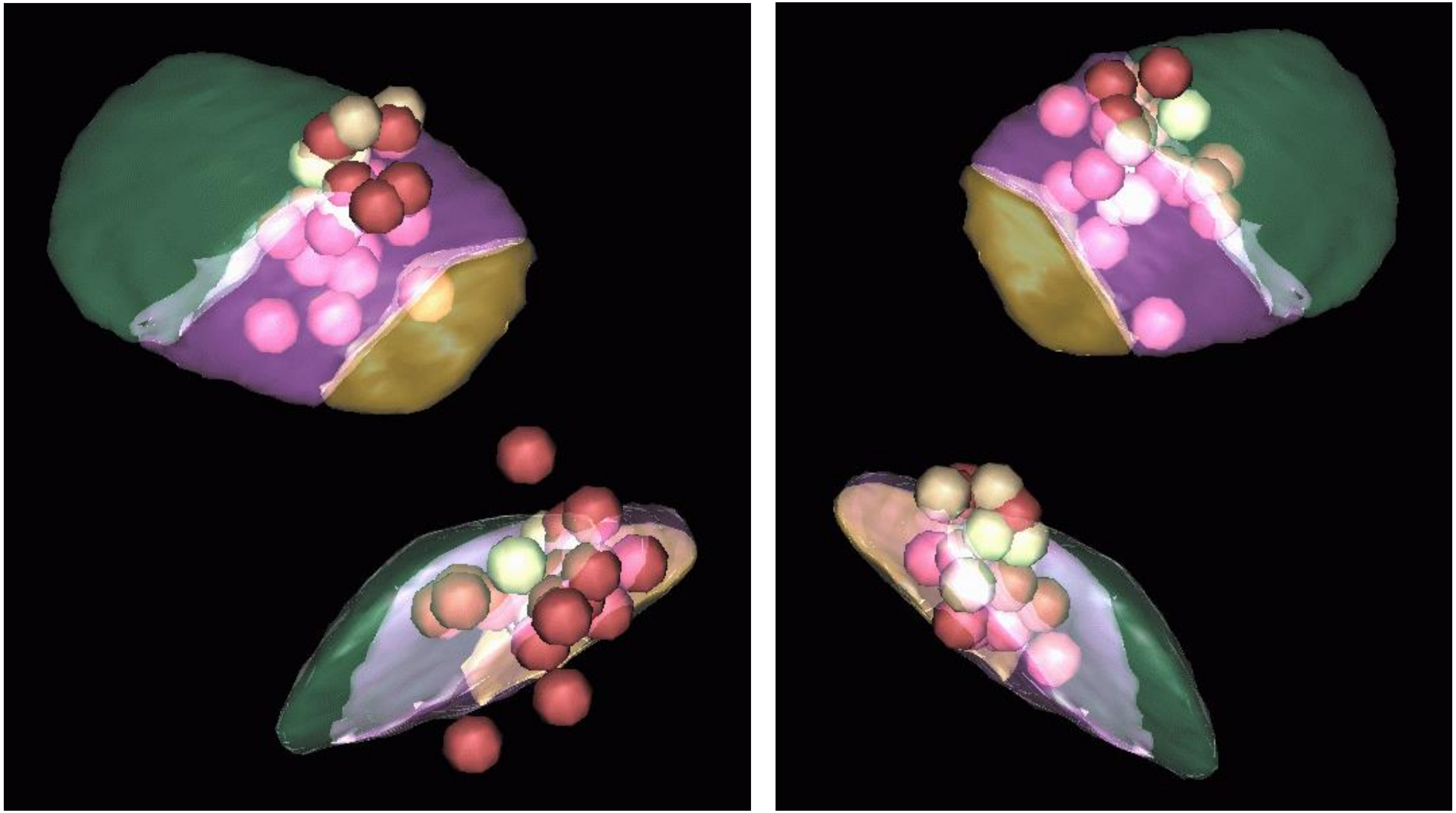


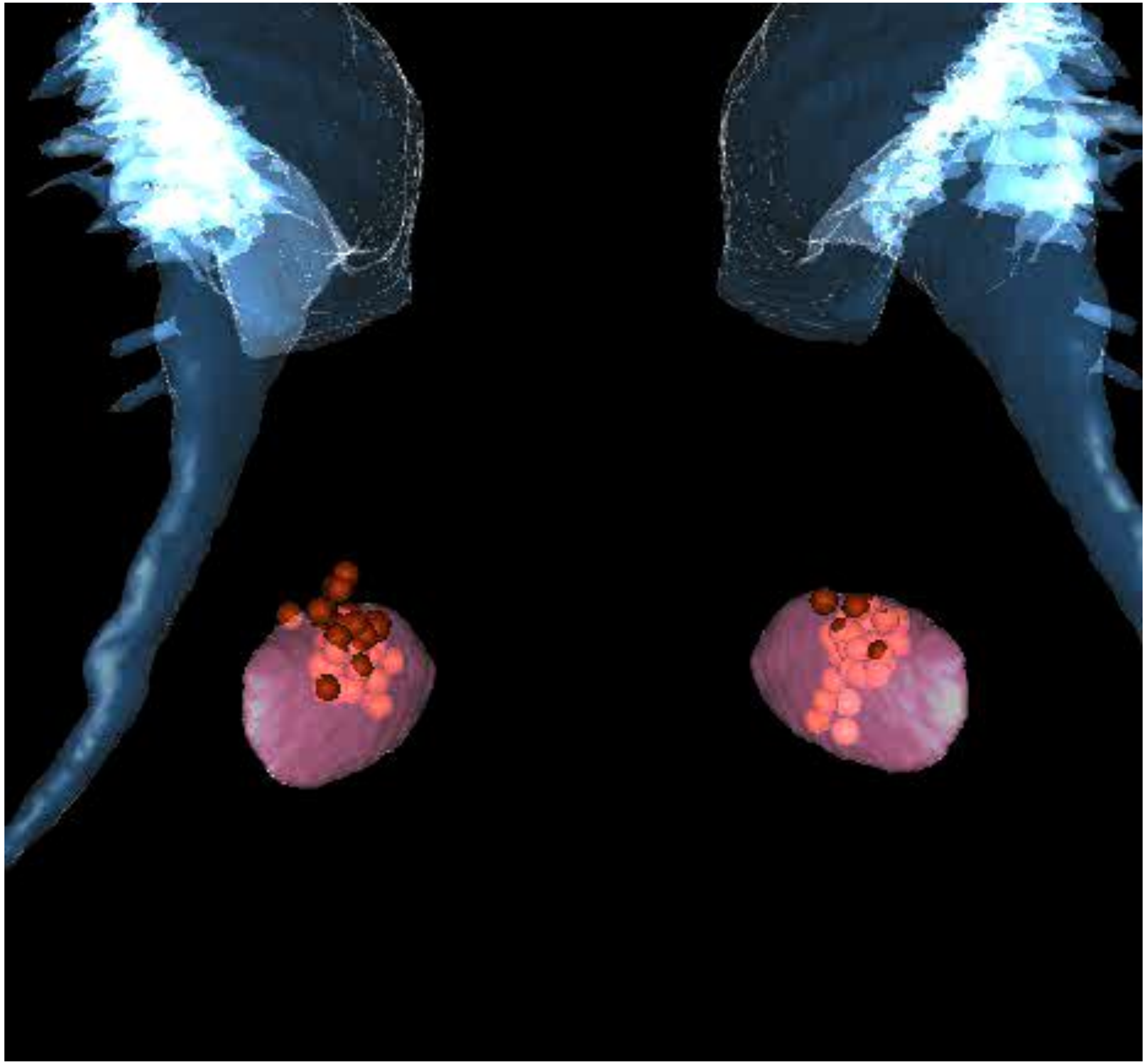



16:07:19


23-33 CM







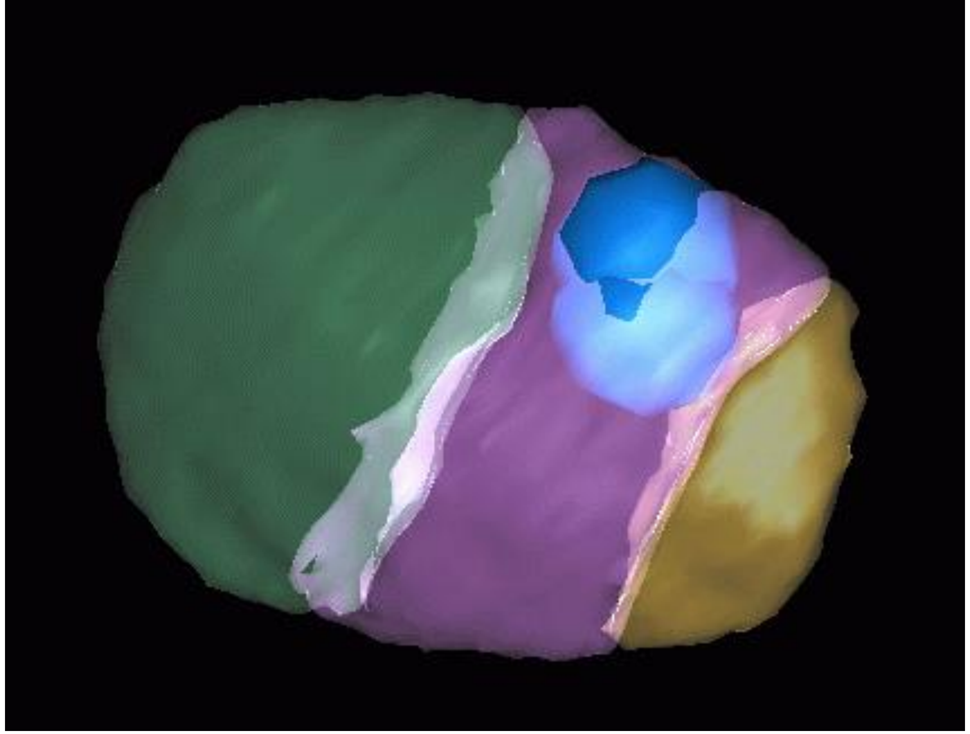
Coordinates of mean contact
(mean + std dev in mm)

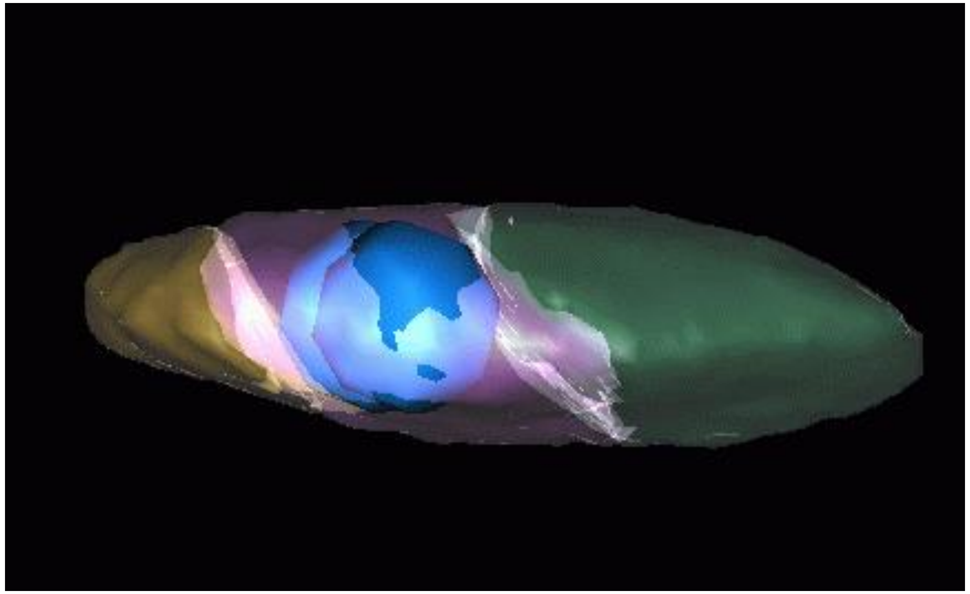
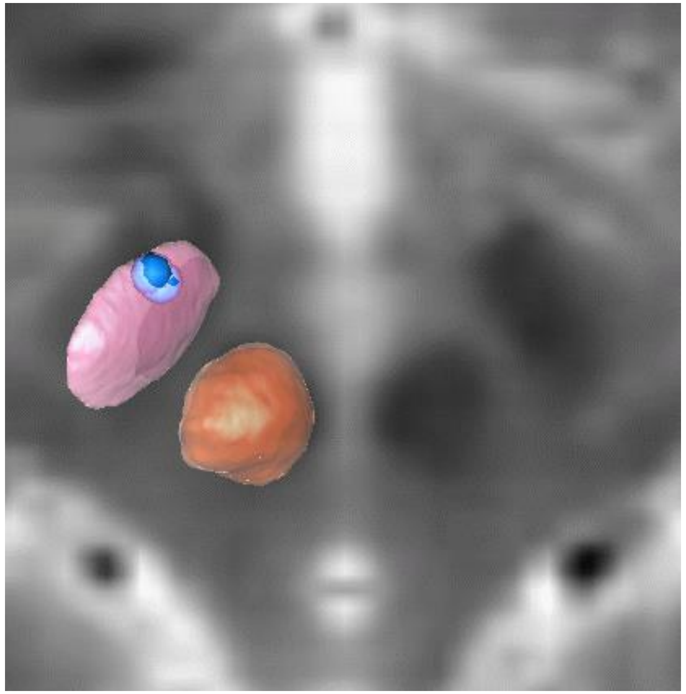
RH

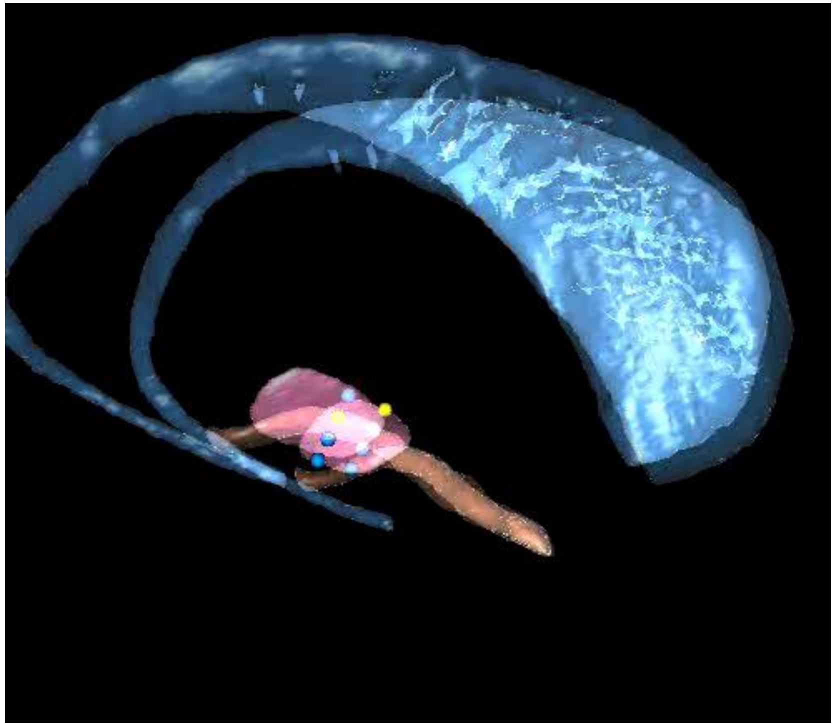
ML	11.25	***0.81***
AP	11.6	***1.05***
DV	3.9	***1.11***

LH

ML	11.6	***0.91***
AP	12.05	***1.34***
DV	2.9	***1.19***





谢谢您！