NANOCI

First steps towards a gapless auditory nerve – CI electrode interface

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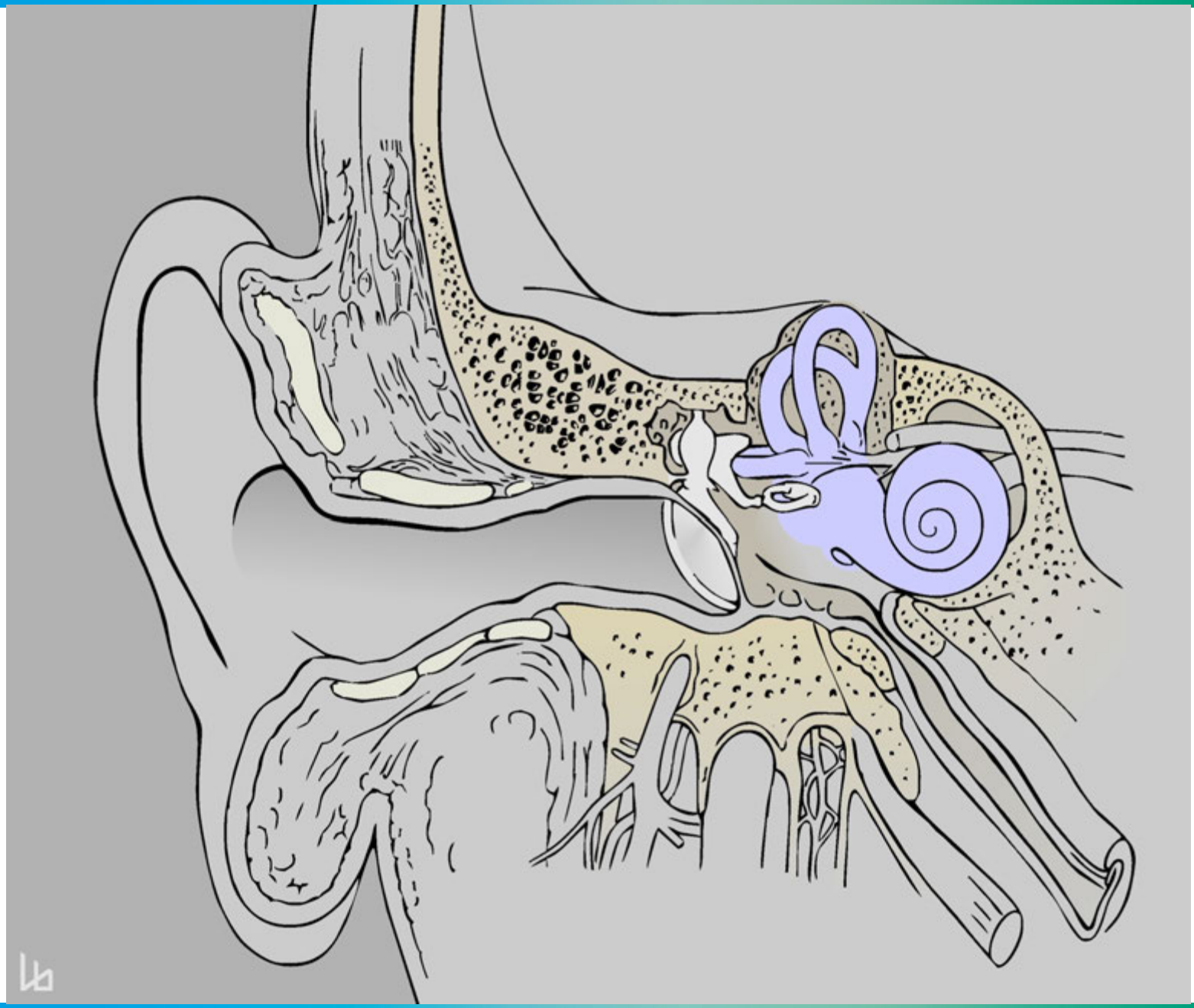
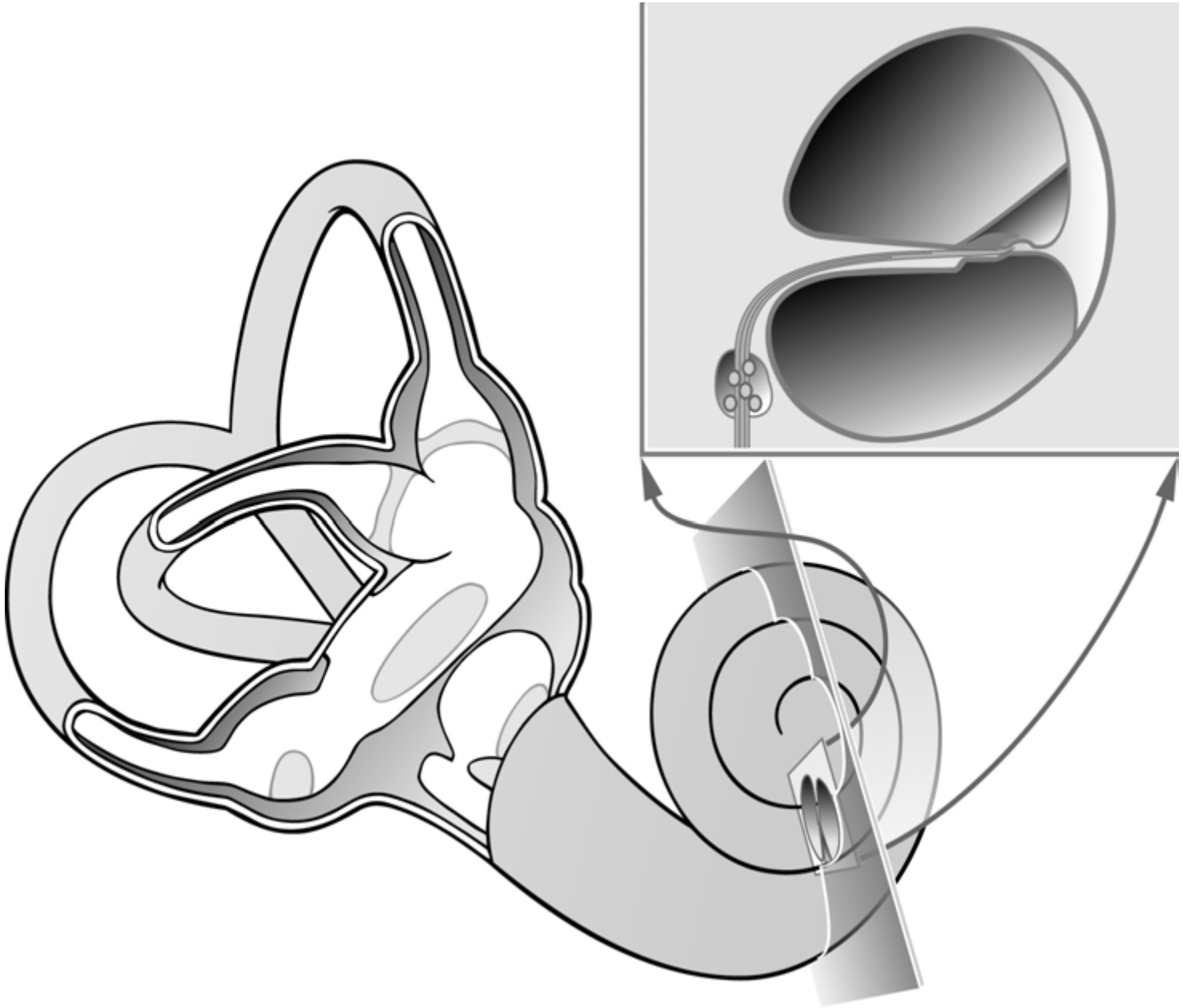
Geneva

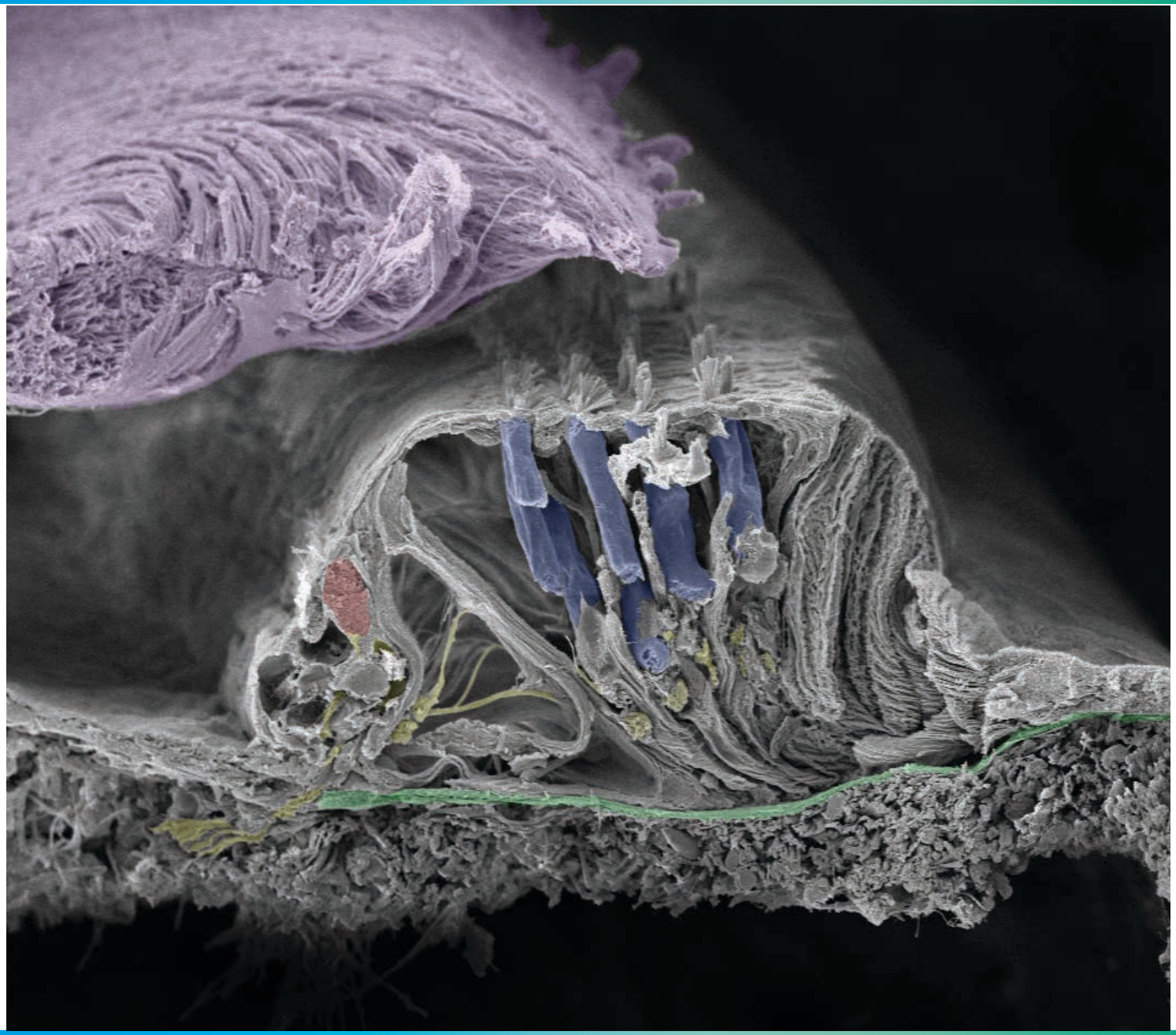
Bern

Content

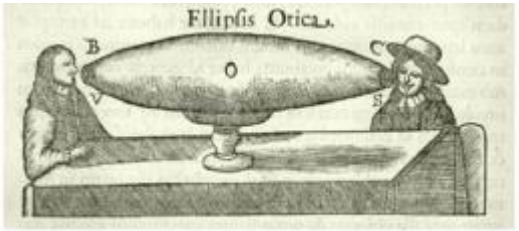
- Strengths & limitations of current cochlear implant (CI) technology
- NANOCI – background and concept
- Methods to explore the feasibility of the NANOCI concept
- Results in vitro and in vivo
- Summary and conclusion







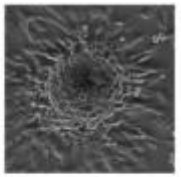
1700s



1900s

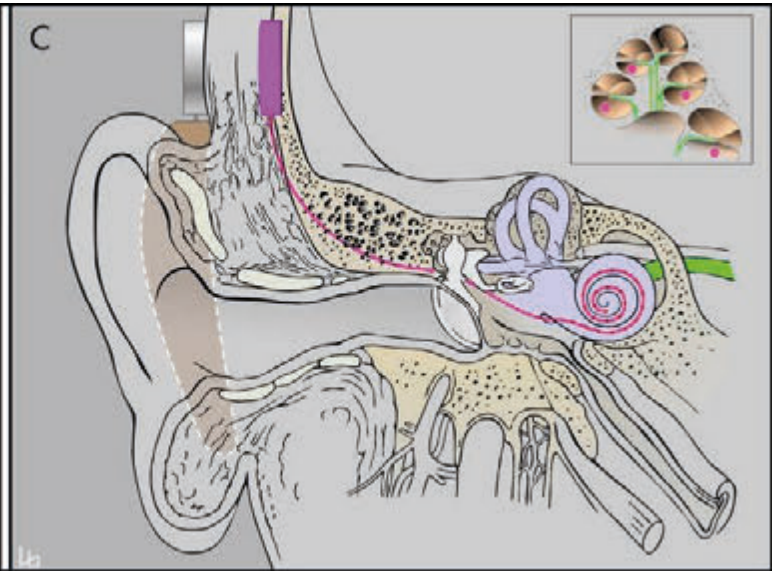
2000s

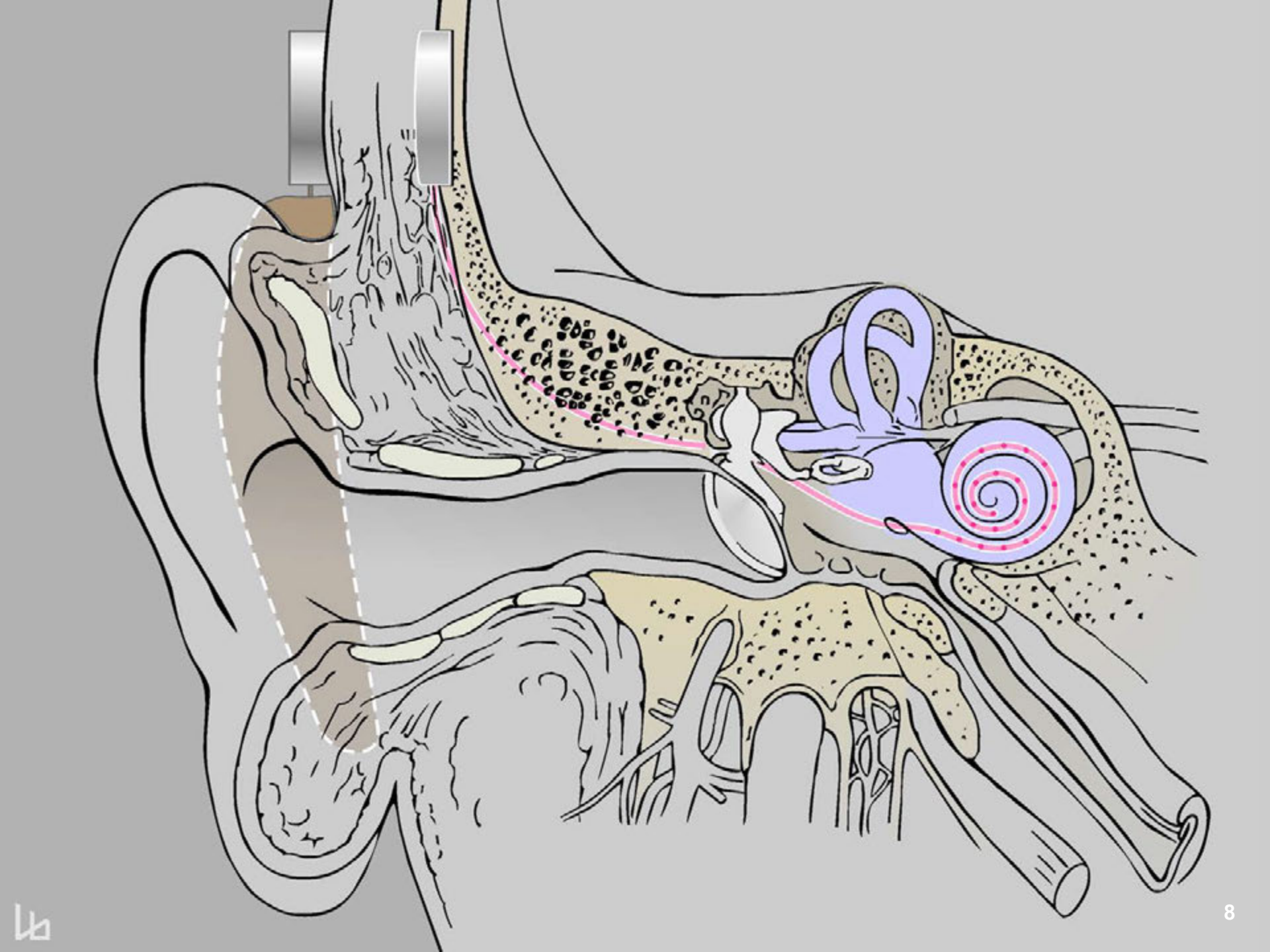
2100s

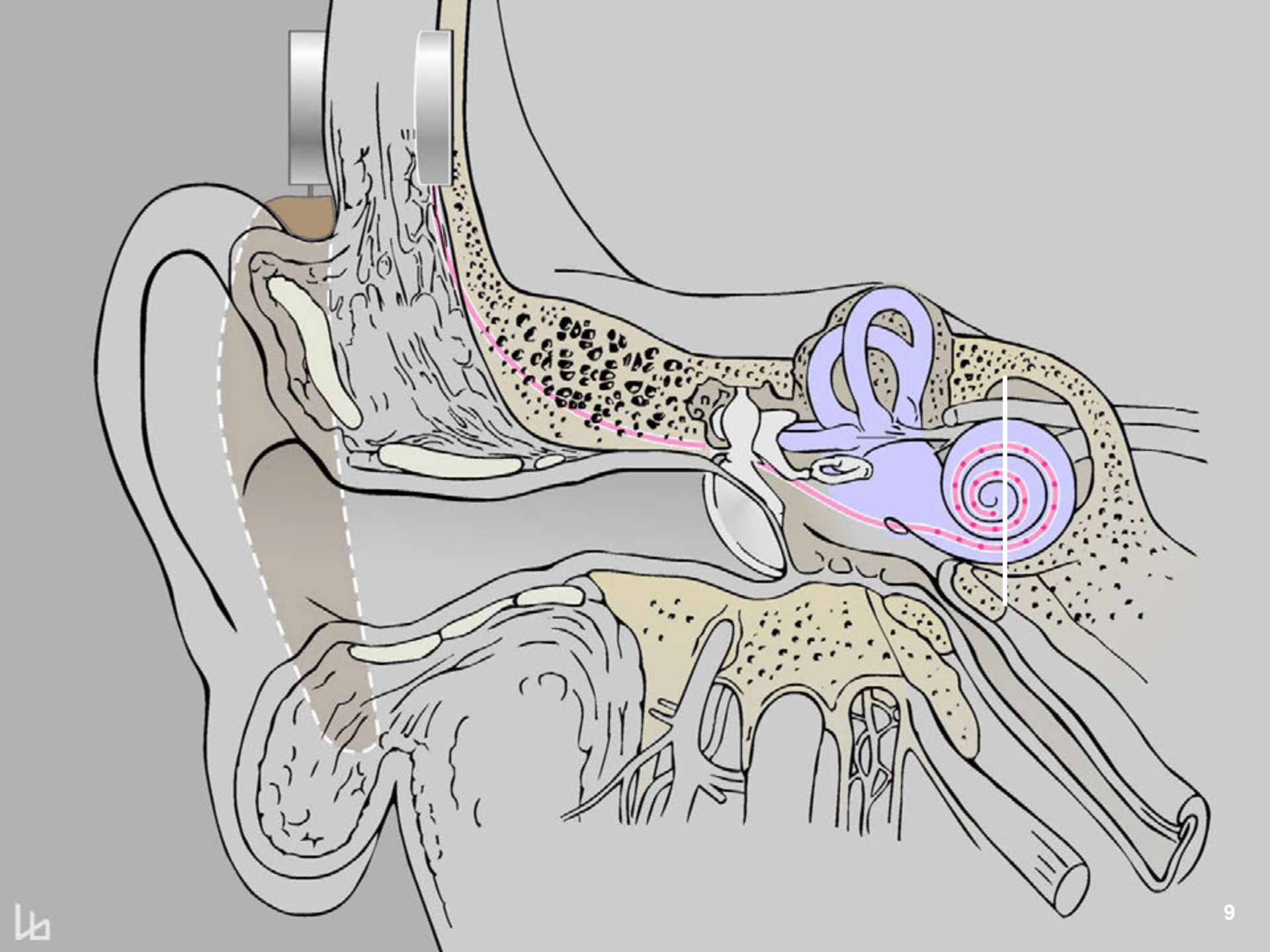


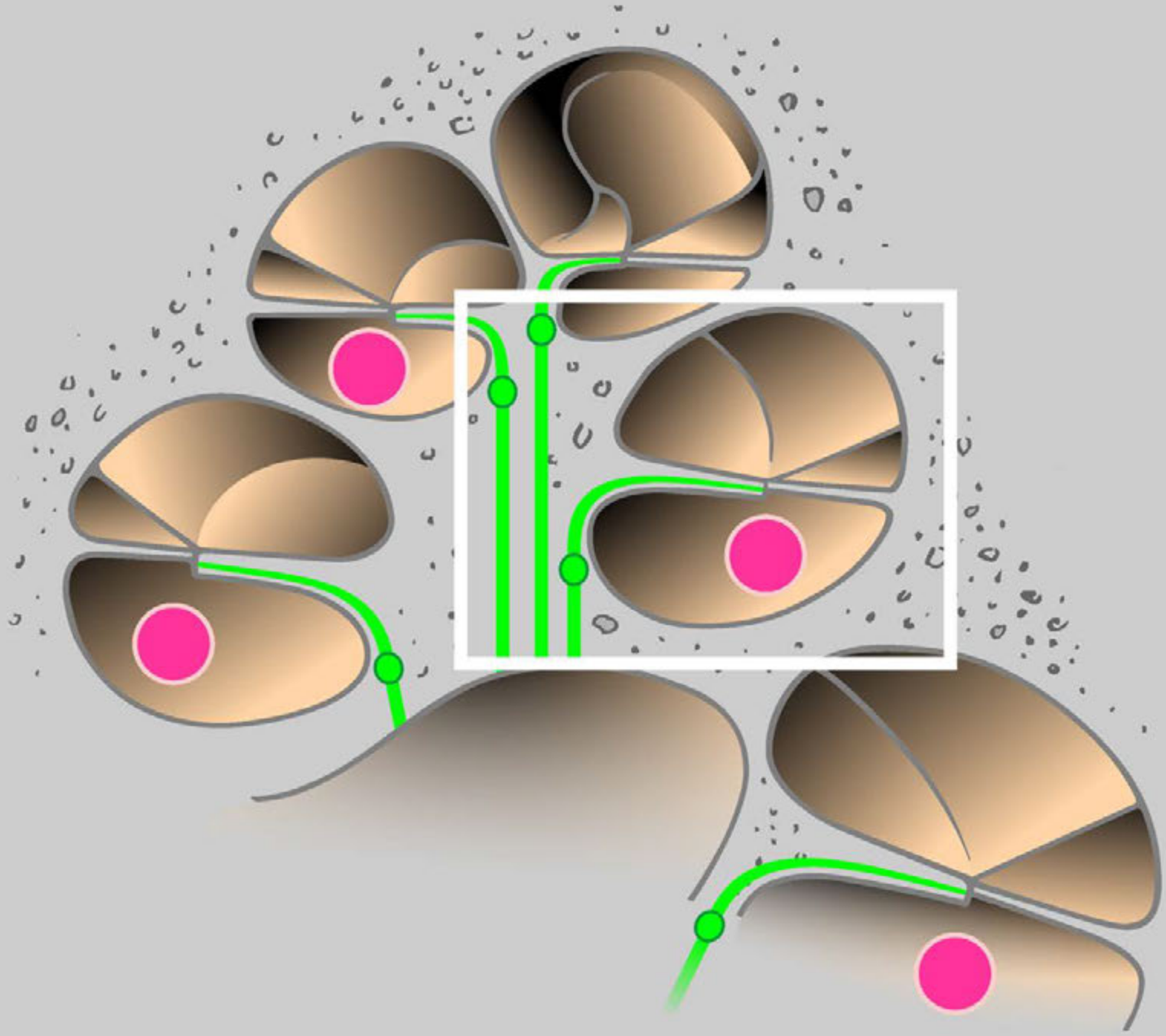

A
0 1 2 3 4 5 cm

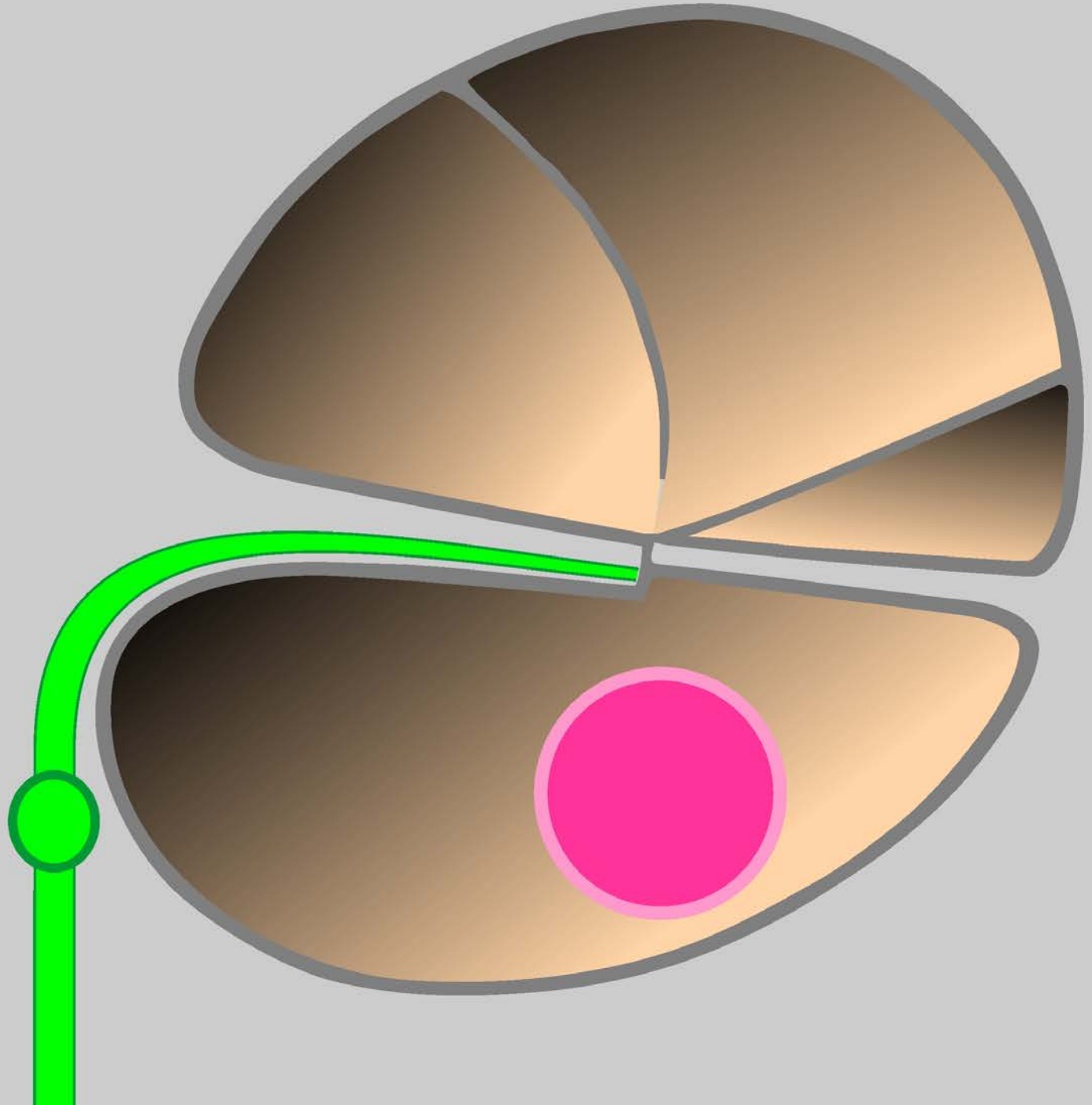

B


C





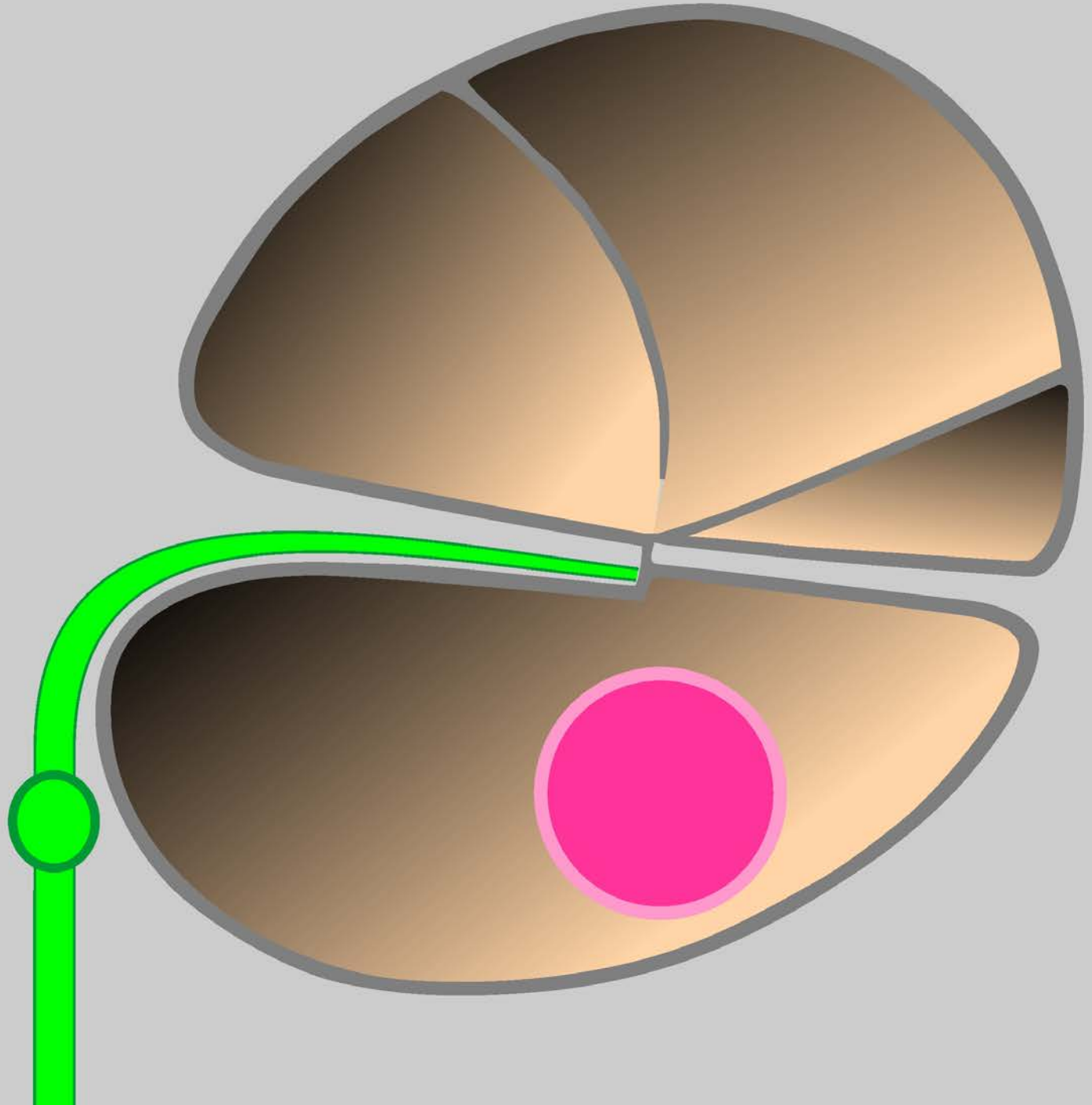


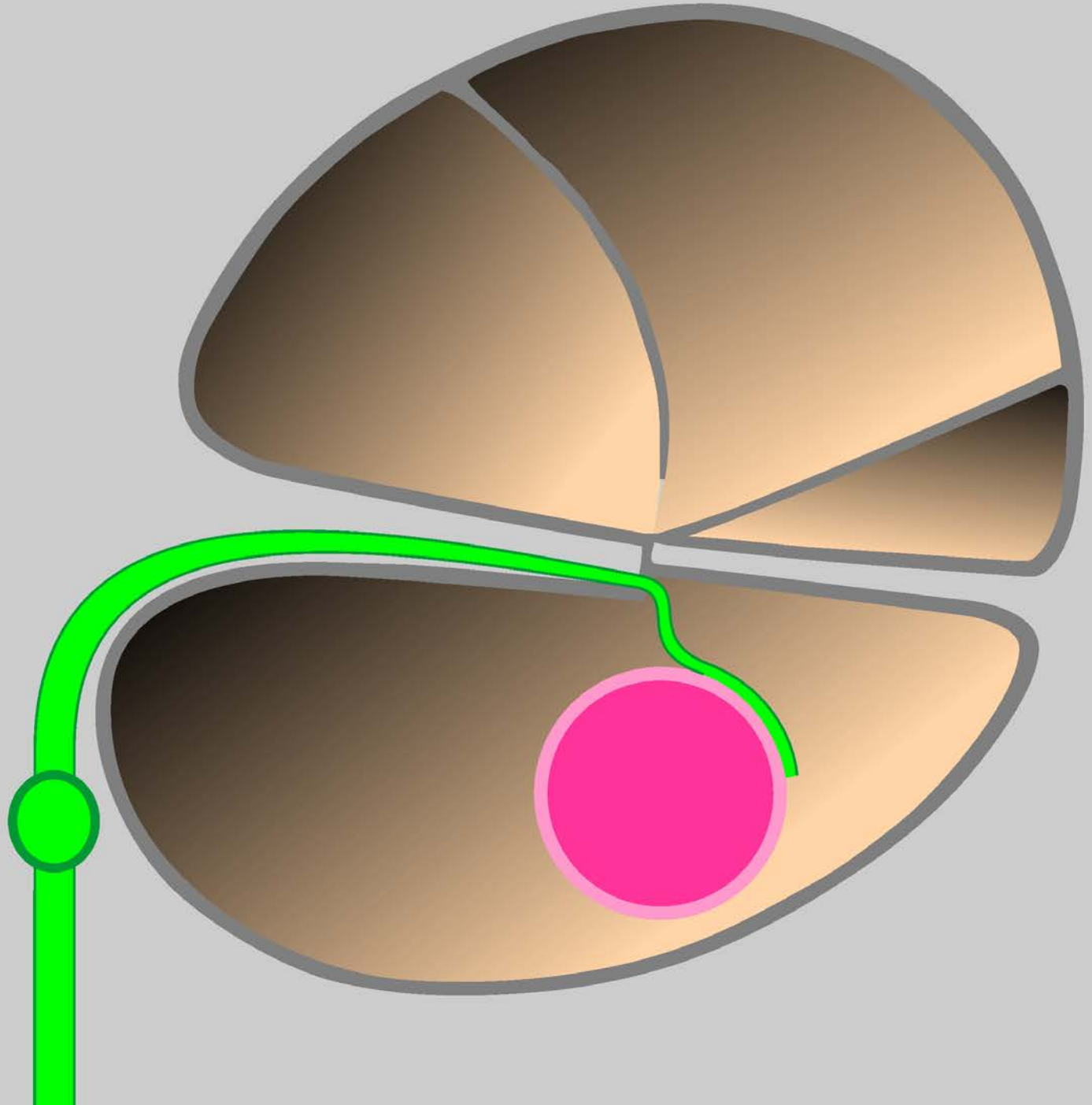


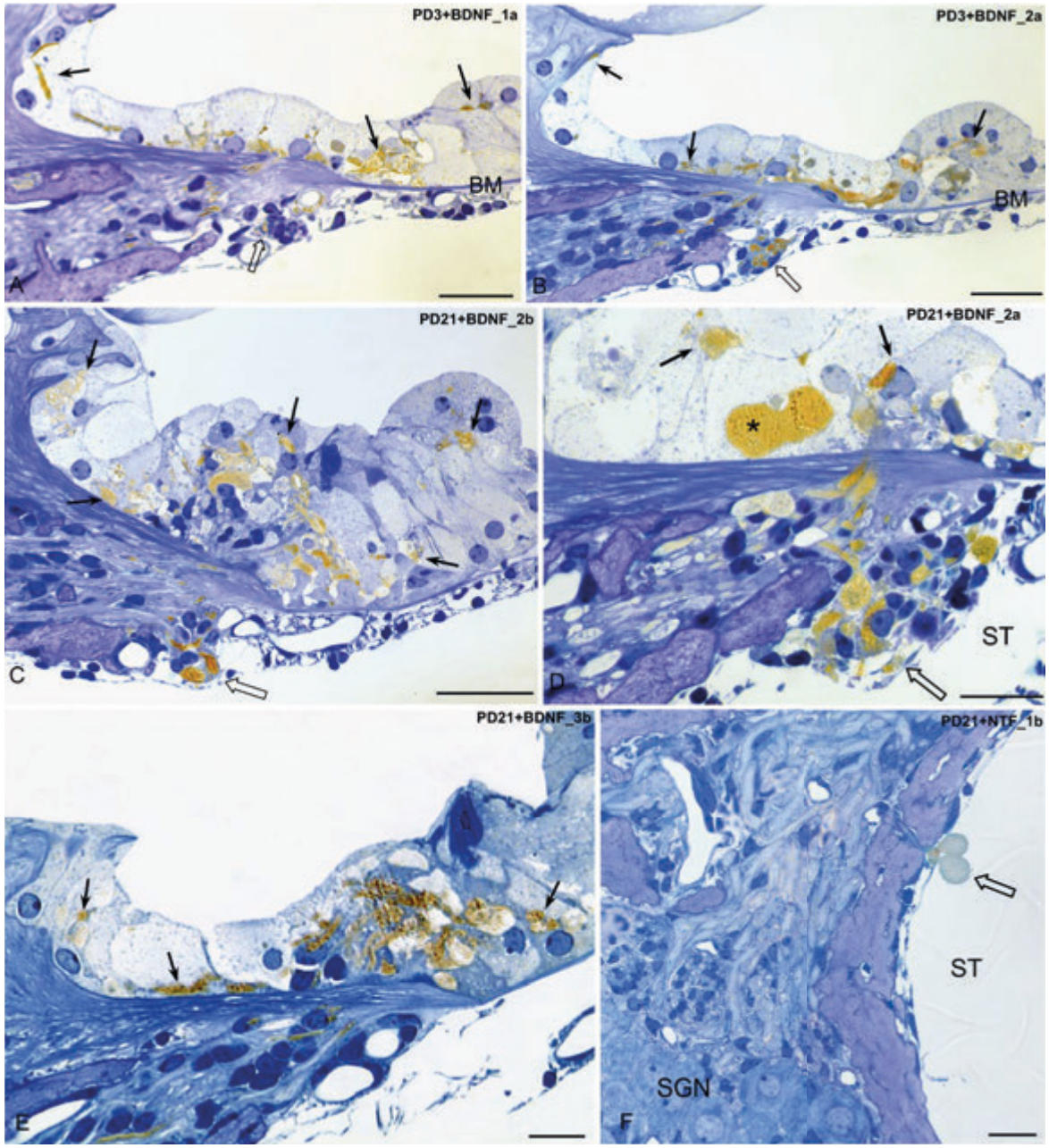
Limitations of current CI technology

- Limited auditory resolution – limited performance
  - Tonal languages
  - Listening in background noise
  - Music listening

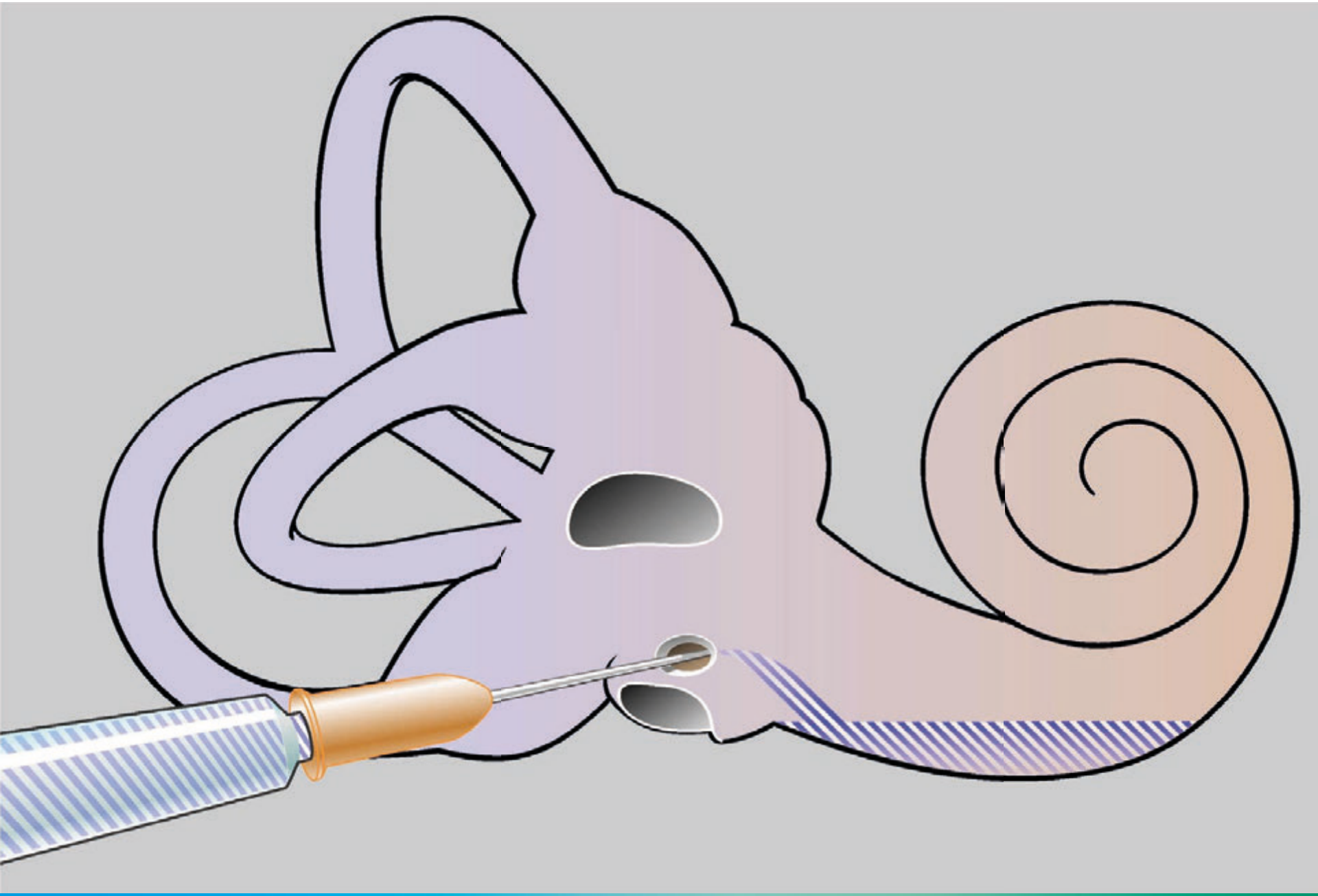
- High power consumption
  - High recurring costs (500 CHF per year for batteries per CI)
  - Responsible for large speech processor
  - Impeds development of fully implantable devices

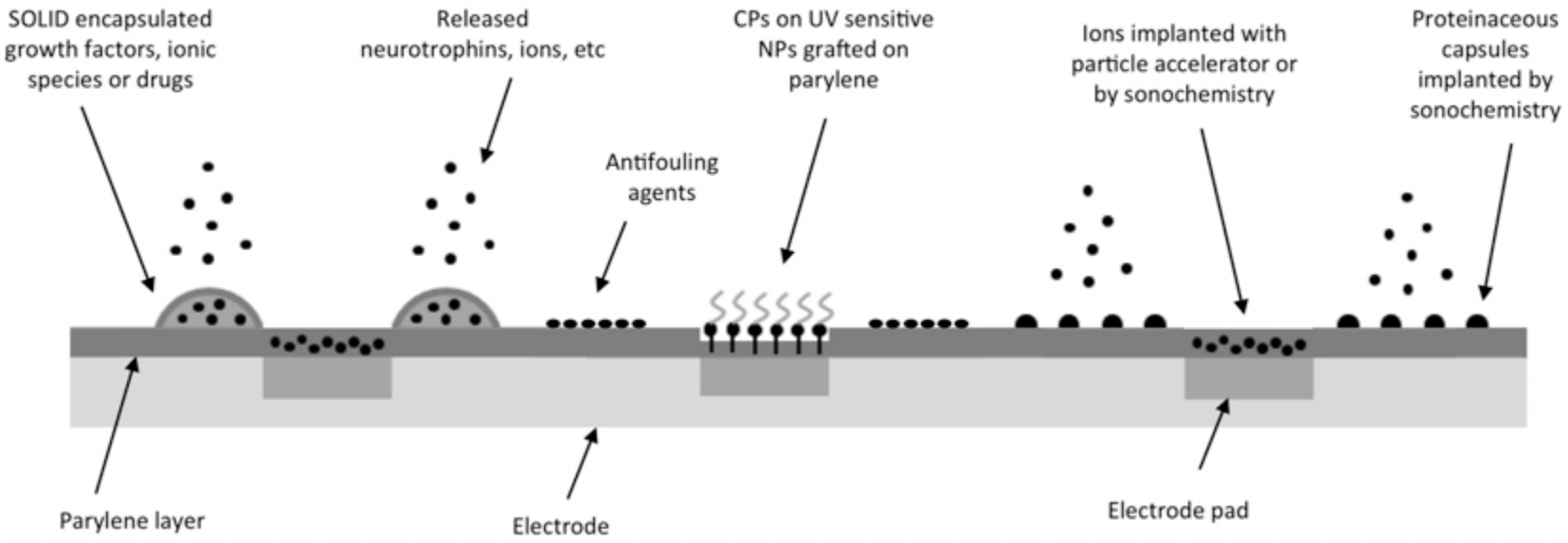


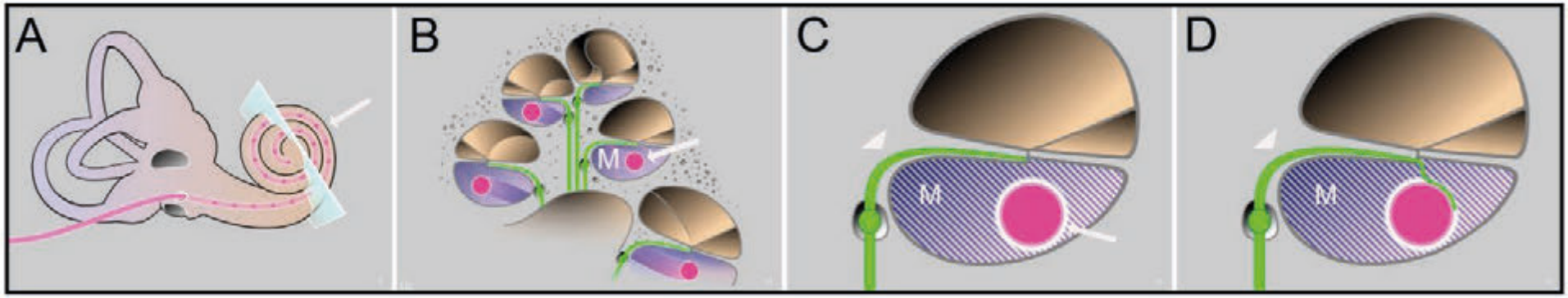


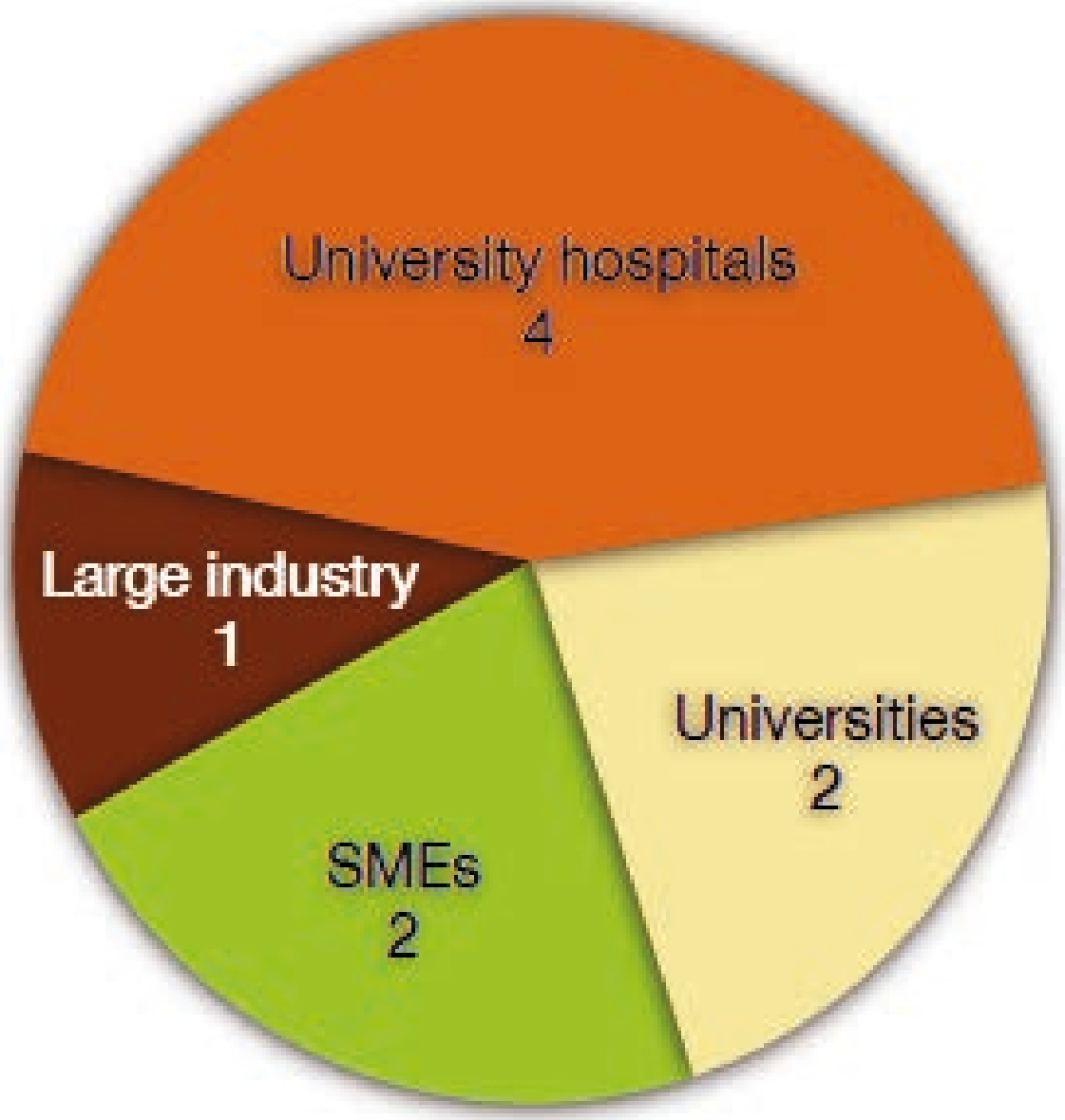


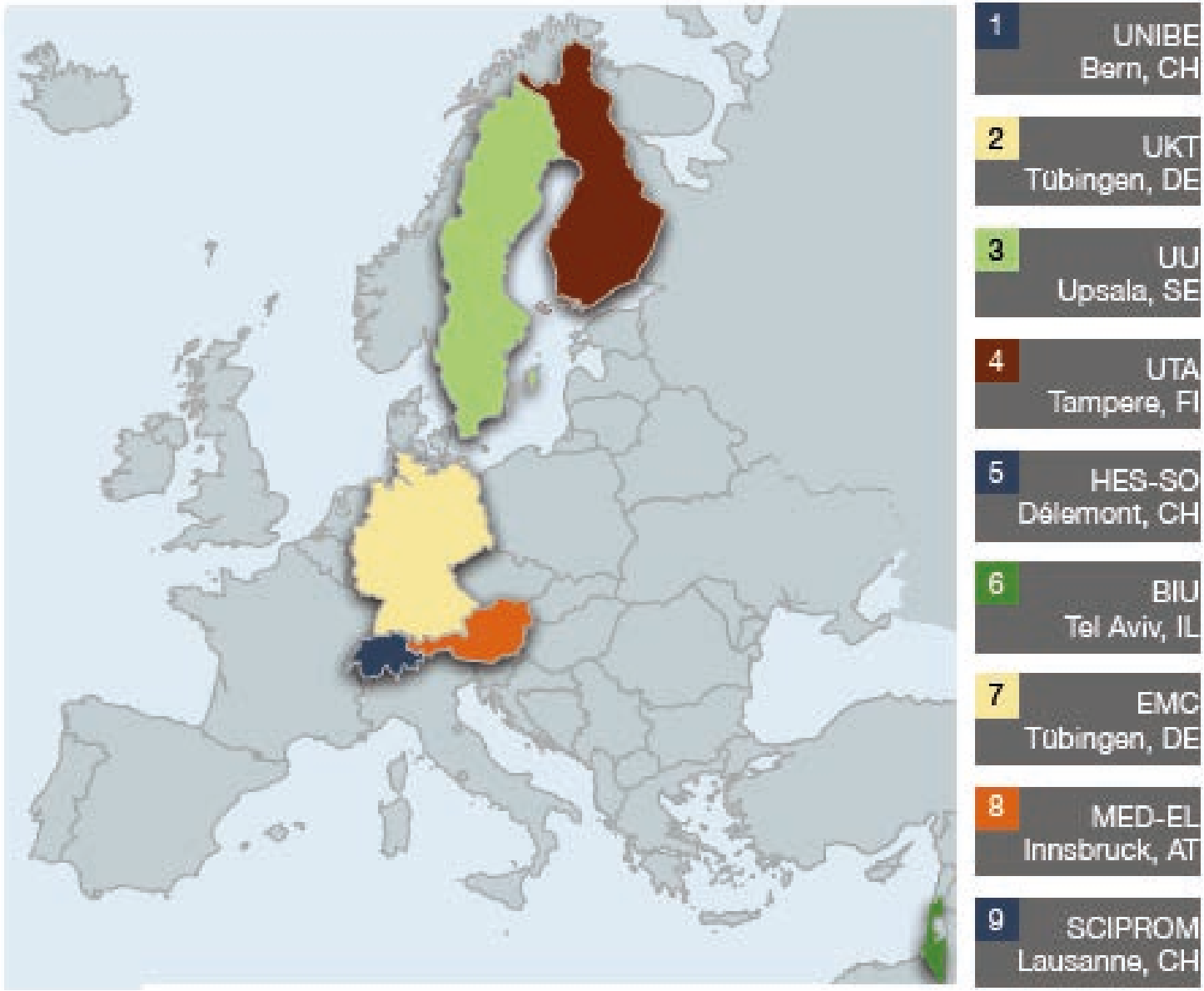
Gluckert et al, JCR 2008

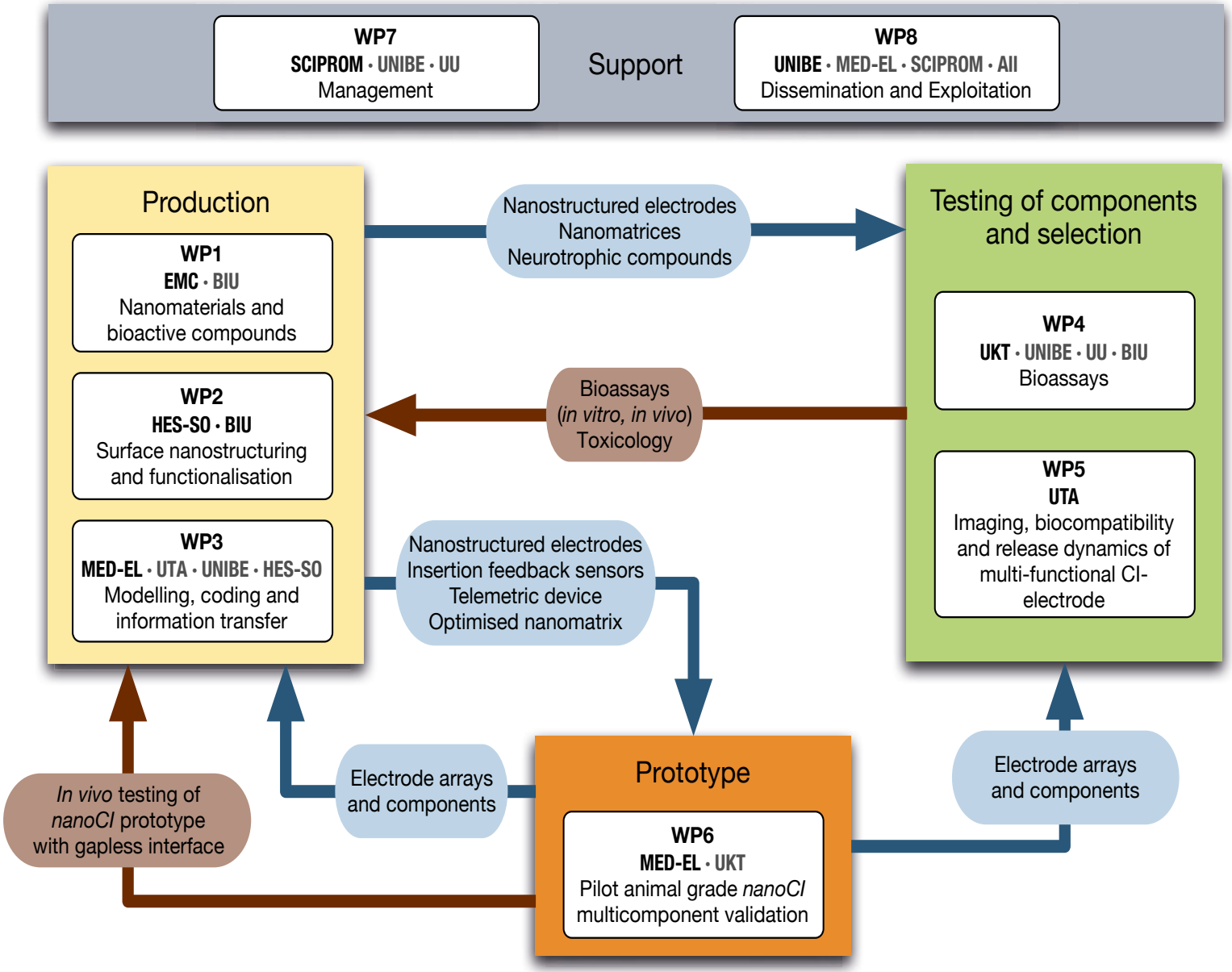


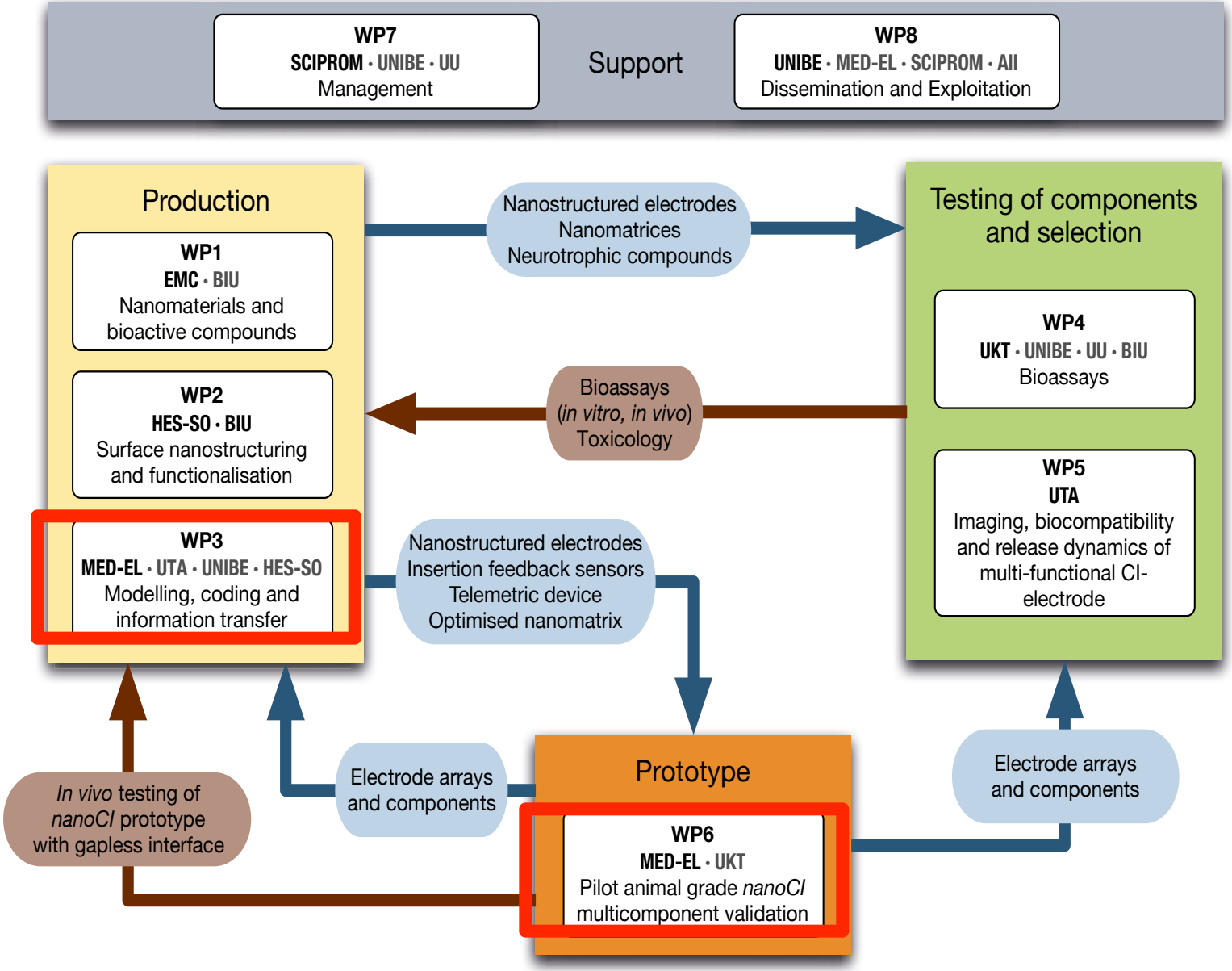

SOLID encapsulated growth factors, ionic species or drugs
Released neurotrophins, ions, etc
Antifouling agents
CPs on UV sensitive NPs grafted on parylene
Ions implanted with particle accelerator or by sonochemistry
Proteinaceous capsules implanted by sonochemistry
Parylene layer
Electrode
Electrode pad


A
B
M
C
M
D
M

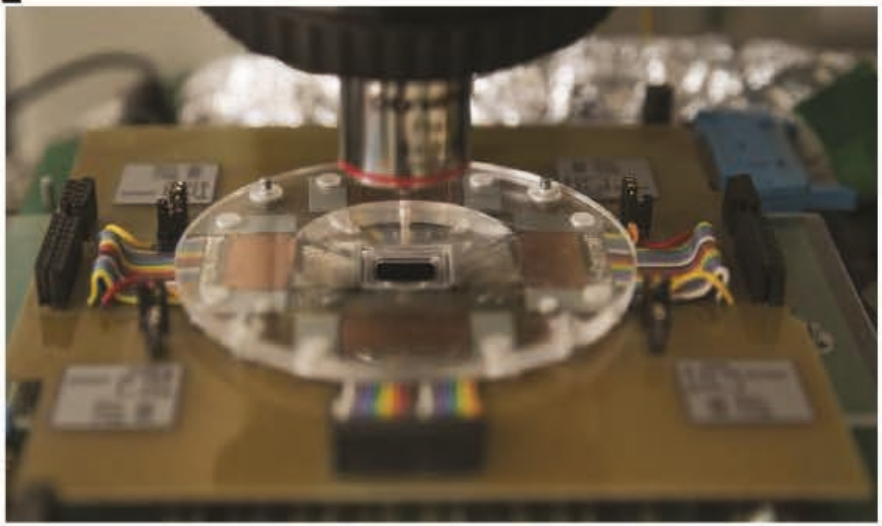

University hospitals
4
Universities
2
SMEs
2
Large industry
1

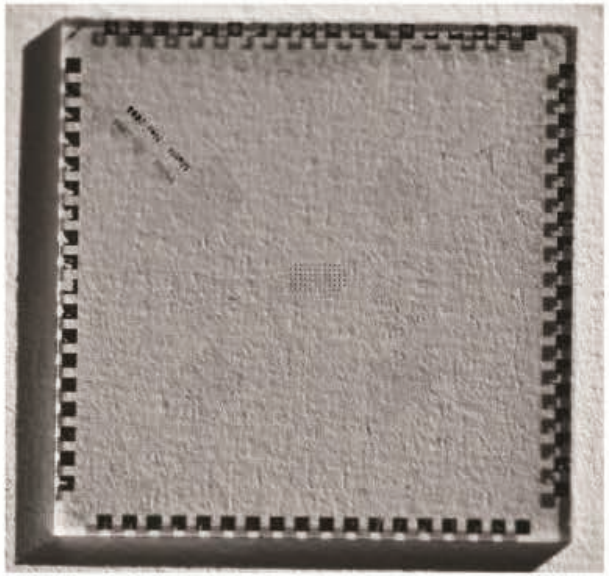

1 UNIBE Bern, CH
2 UKT Tübingen, DE
3 UU Upsala, SE
4 UTA Tampere, FI
5 HES-SO Délemont, CH
6 BIU Tel Aviv, IL
7 EMC Tübingen, DE
8 MED-EL Innsbruck, AT
9 SCIPROM Lausanne, CH

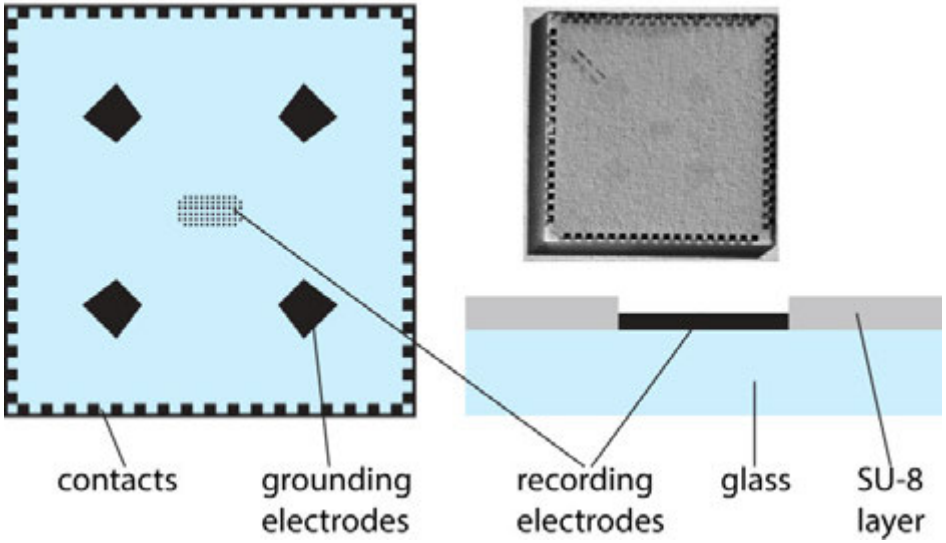

WP7
SCIPROM · UNIBE · UU
Management
Support
WP8
UNIBE · MED-EL · SCIPROM · All
Dissemination and Exploitation
Production
WP1
EMC · BIU
Nanomaterials and bioactive compounds
WP2
HES-SO · BIU
Surface nanostructuring and functionalisation
WP3
MED-EL · UTA · UNIBE · HES-SO
Modelling, coding and information transfer
Nanostructured electrodes
Nanomatrices
Neurotrophic compounds
Bioassays
(in vitro, in vivo)
Toxicology
Nanostructured electrodes
Insertion feedback sensors
Telemetric device
Optimised nanomatrix
Testing of components and selection
WP4
UKT · UNIBE · UU · BIU
Bioassays
WP5
UTA
Imaging, biocompatibility and release dynamics of multi-functional CI-electrode
Electrode arrays and components
Prototype
WP6
MED-EL · UKT
Pilot animal grade nanoCI multicomponent validation
Electrode arrays and components
In vivo testing of nanoCI prototype with gapless interface

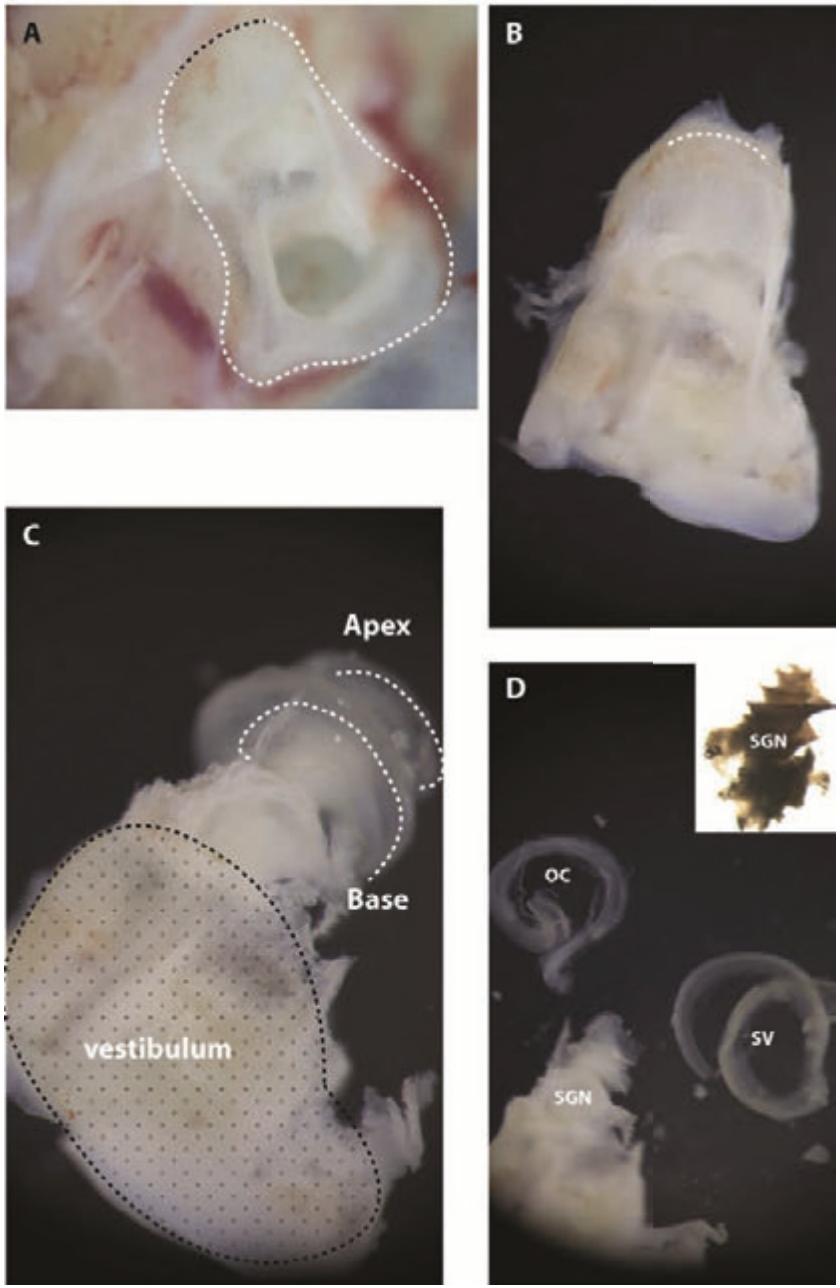

WP7
SCIPROM · UNIBE · UU
Management
Support
WP8
UNIBE · MED-EL · SCIPROM · All
Dissemination and Exploitation
Production
WP1
EMC · BIU
Nanomaterials and bioactive compounds
WP2
HES-SO · BIU
Surface nanostructuring and functionalisation
WP3
MED-EL · UTA · UNIBE · HES-SO
Modelling, coding and information transfer
Nanostructured electrodes
Nanomatrices
Neurotrophic compounds
Bioassays
(in vitro, in vivo)
Toxicology
Testing of components and selection
WP4
UKT · UNIBE · UU · BIU
Bioassays
WP5
UTA
Imaging, biocompatibility and release dynamics of multi-functional CI-electrode
Nanostructured electrodes
Insertion feedback sensors
Telemetric device
Optimised nanomatrix
In vivo testing of nanoCI prototype with gapless interface
Electrode arrays and components
Prototype
WP6
MED-EL · UKT
Pilot animal grade nanoCI multicomponent validation
Electrode arrays and components

A

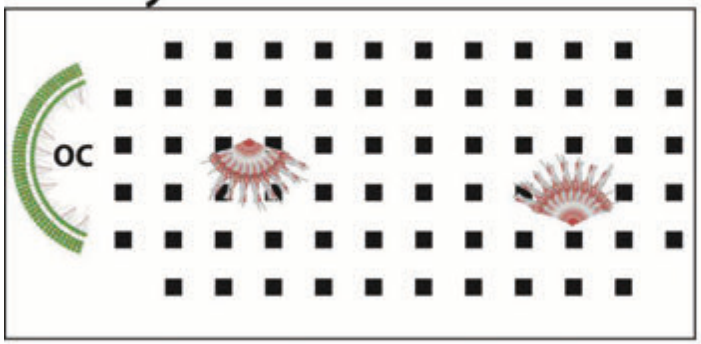


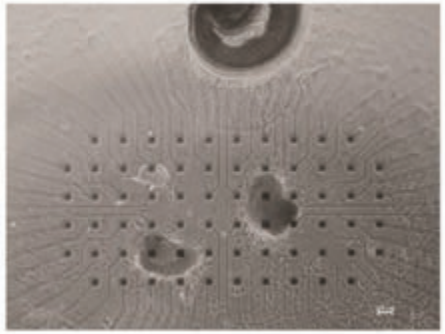



contacts
grounding electrodes
recording electrodes
glass
SU-8 layer

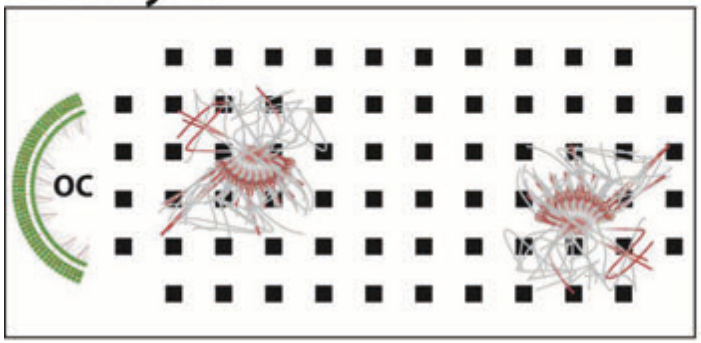

A
B
C
Apex
Base
vestibulum
D
SGN
OC
SV
SGN

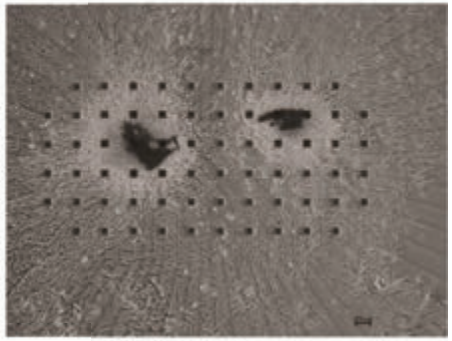
A day 1



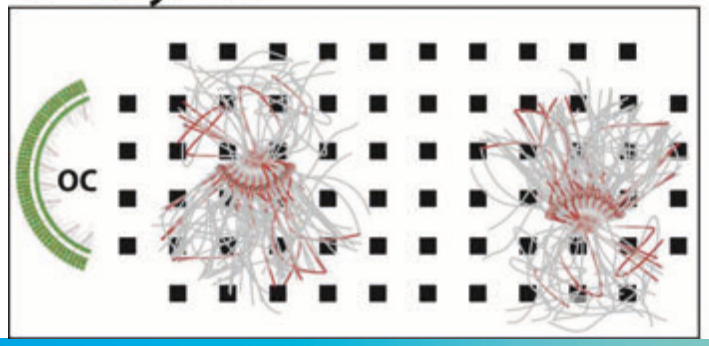


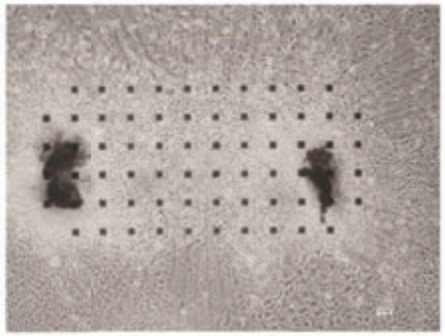
B day 6

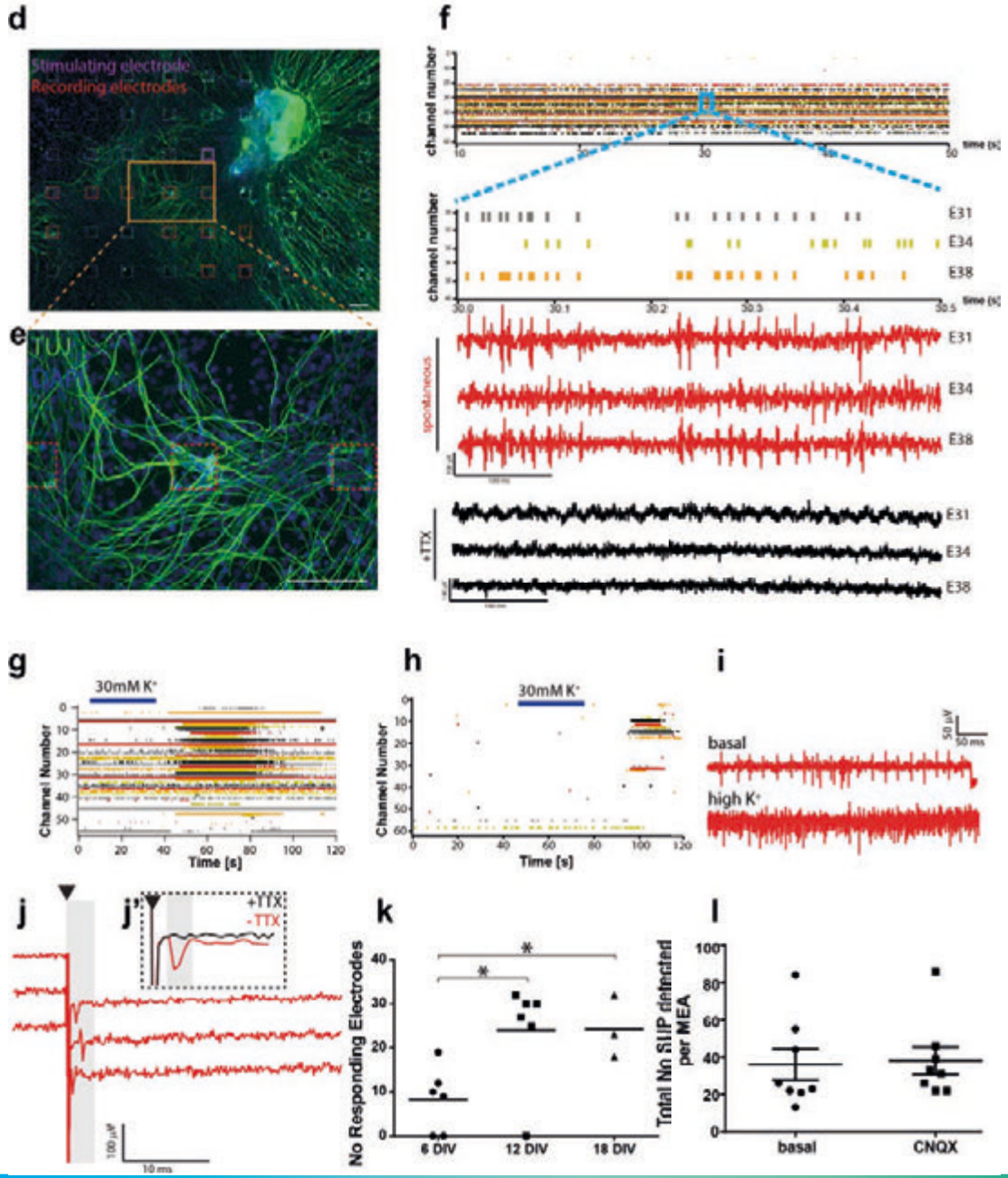


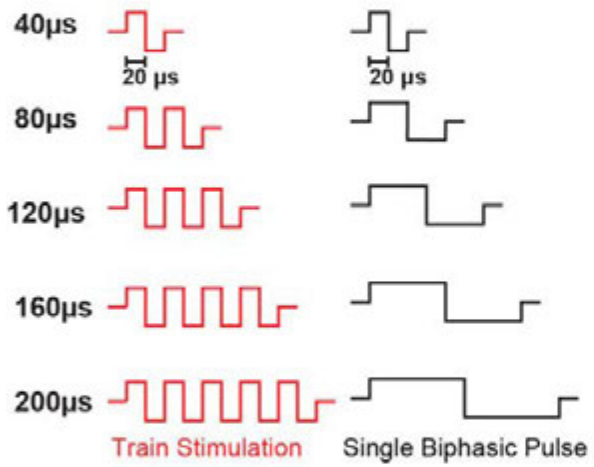


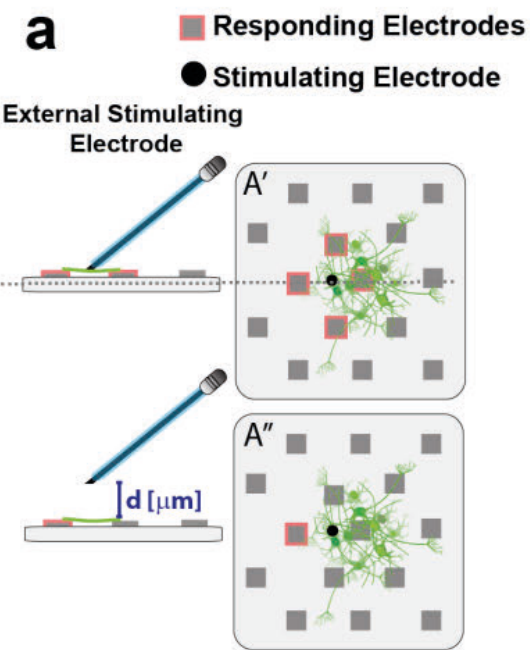
C day 18

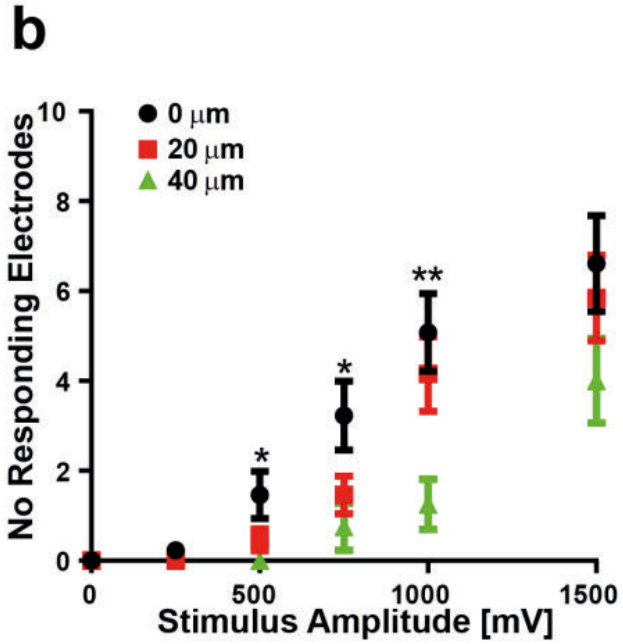


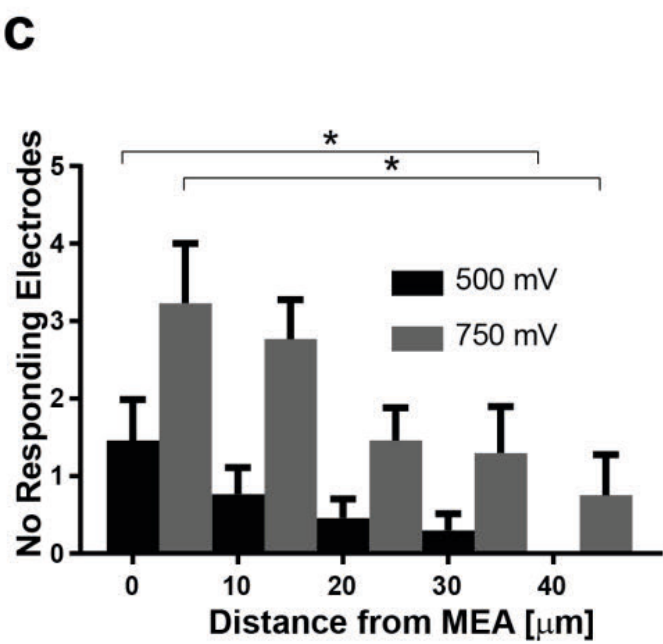


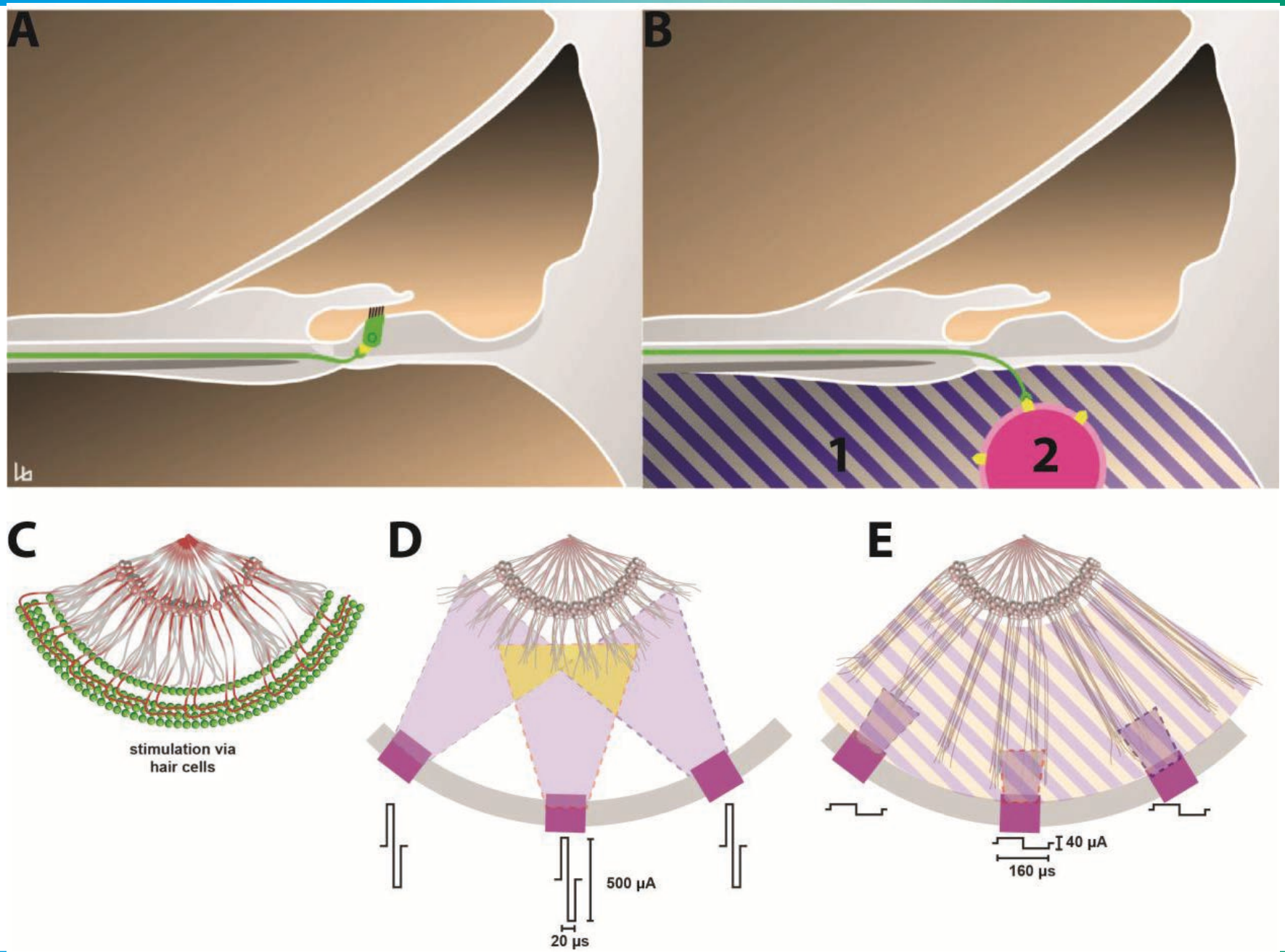

d
Stimulating electrode
Recording electrodes
e
TUJ
f
channel number
time (s)
E31
E34
E38
spontaneous
+TTX
g
30mM K+
Channel Number
Time [s]
h
30mM K+
Channel Number
Time [s]
i
basal
high K+
50 µV
50 ms
j
j'
+TTX
-TTX
100 µV
10 ms
k
No Responding Electrodes
6 DIV
12 DIV
18 DIV
l
Total No SUP detected per MEA
basal
CNQX


40µs
20 µs
20 µs
80µs
120µs
160µs
200µs
Train Stimulation
Single Biphasic Pulse


a
Responding Electrodes
Stimulating Electrode
External Stimulating Electrode
A′
A″
d [μm]


b
0 μm
20 μm
40 μm
No Responding Electrodes
Stimulus Amplitude [mV]
0
500
1000
1500
2
4
6
8
10
*
*
**


c
500 mV
750 mV
No Responding Electrodes
Distance from MEA [μm]
0
10
20
30
40
1
2
3
4
5
*
*

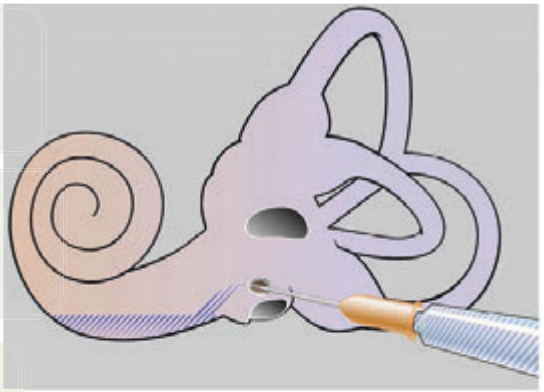

A
B
1
2
C
stimulation via
hair cells
D
500 µA
20 µs
E
40 µA
160 µs

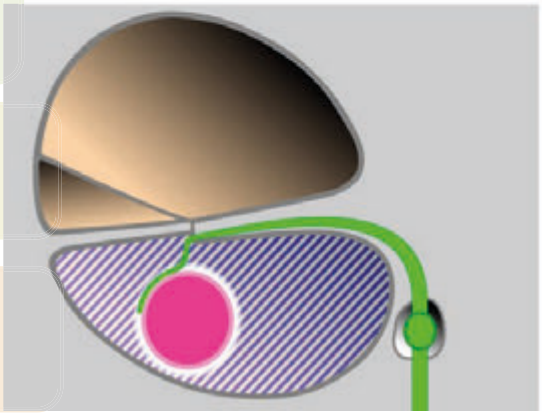
NANOCI in vivo experiments

Marcus Müller, Hubert Löwenheim
Eberhard Karls Universität Tübingen

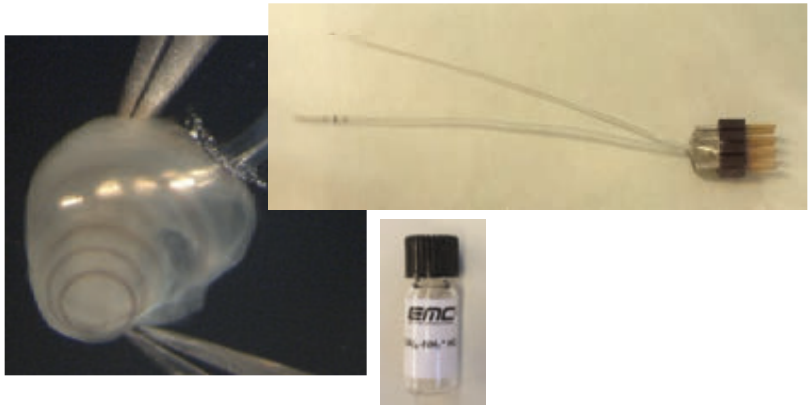
In vivo-Experiments: 10 Groups

Gel	• BDNF-Gel in scala tympani • X-Gel in scala tympani
Electrode	• cochlear implant in hearing animals • cochlear implant in deaf animals
Gel + Electrode	• BDNF-Gel + cochlear implant • X-Gel + cochlear implant
Gel + modified Electrode	• BDNF-Gel + CNT cochlear implant • Gel + THF loaded cochlear implant
modified Electrode	• Parylene coated cochlear implant • ZnCuO coated cochlear implant

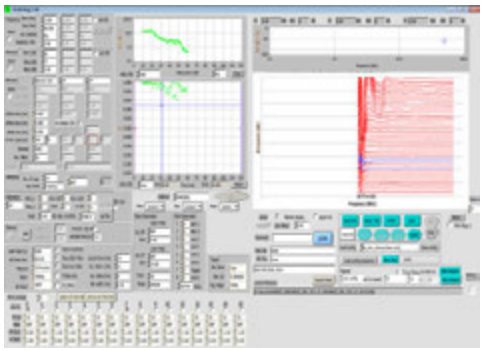




Experimental paradigm



Gel and/or cochlear implant

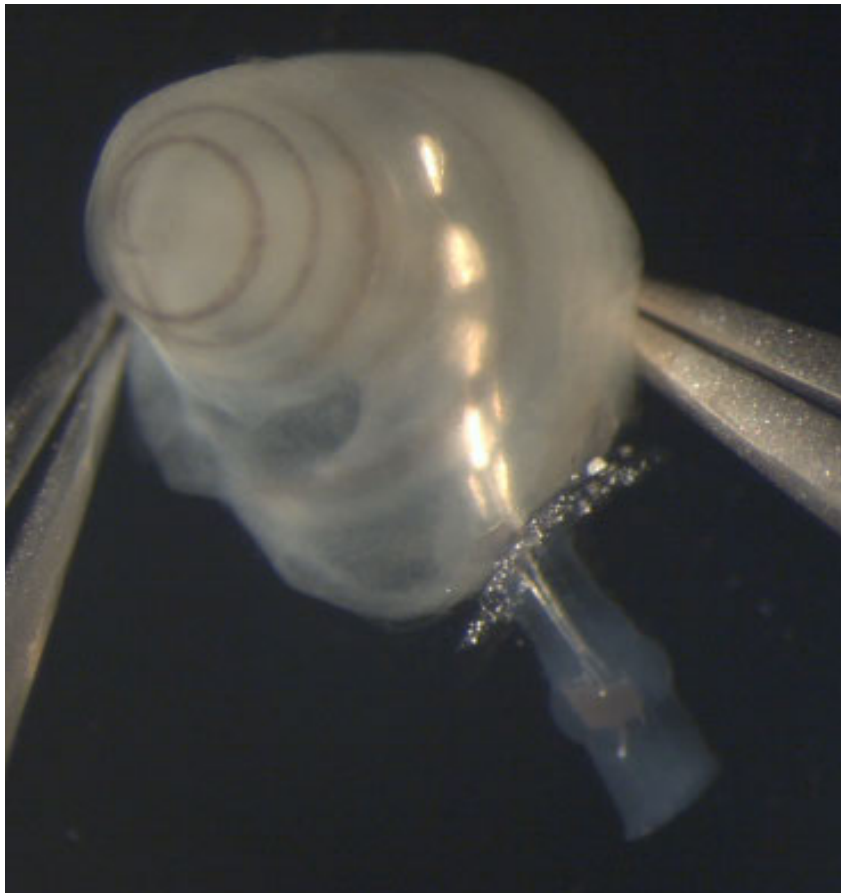


Audiology (CAP, eCAP, eABR)

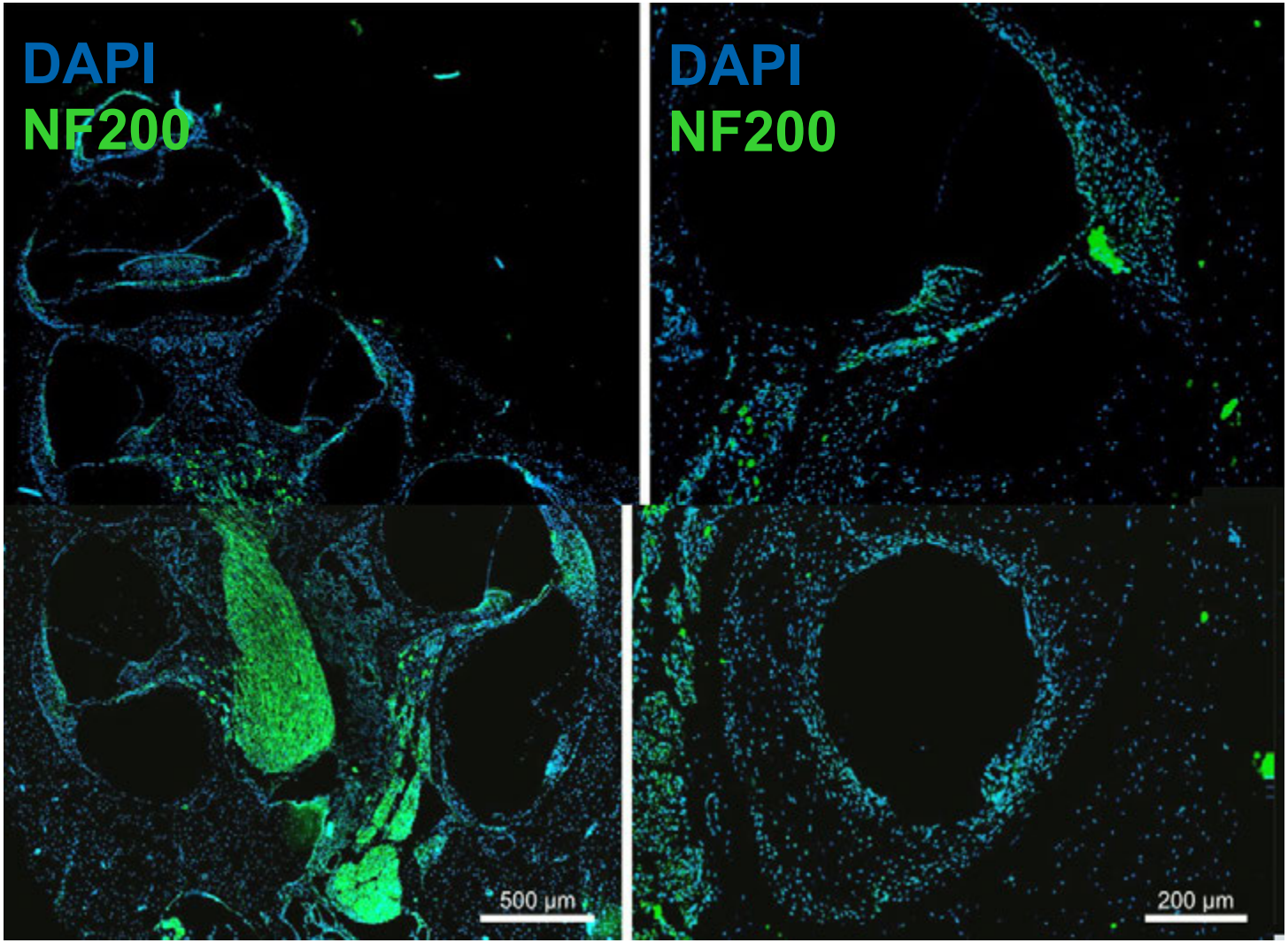
Immunohistology

Deafening

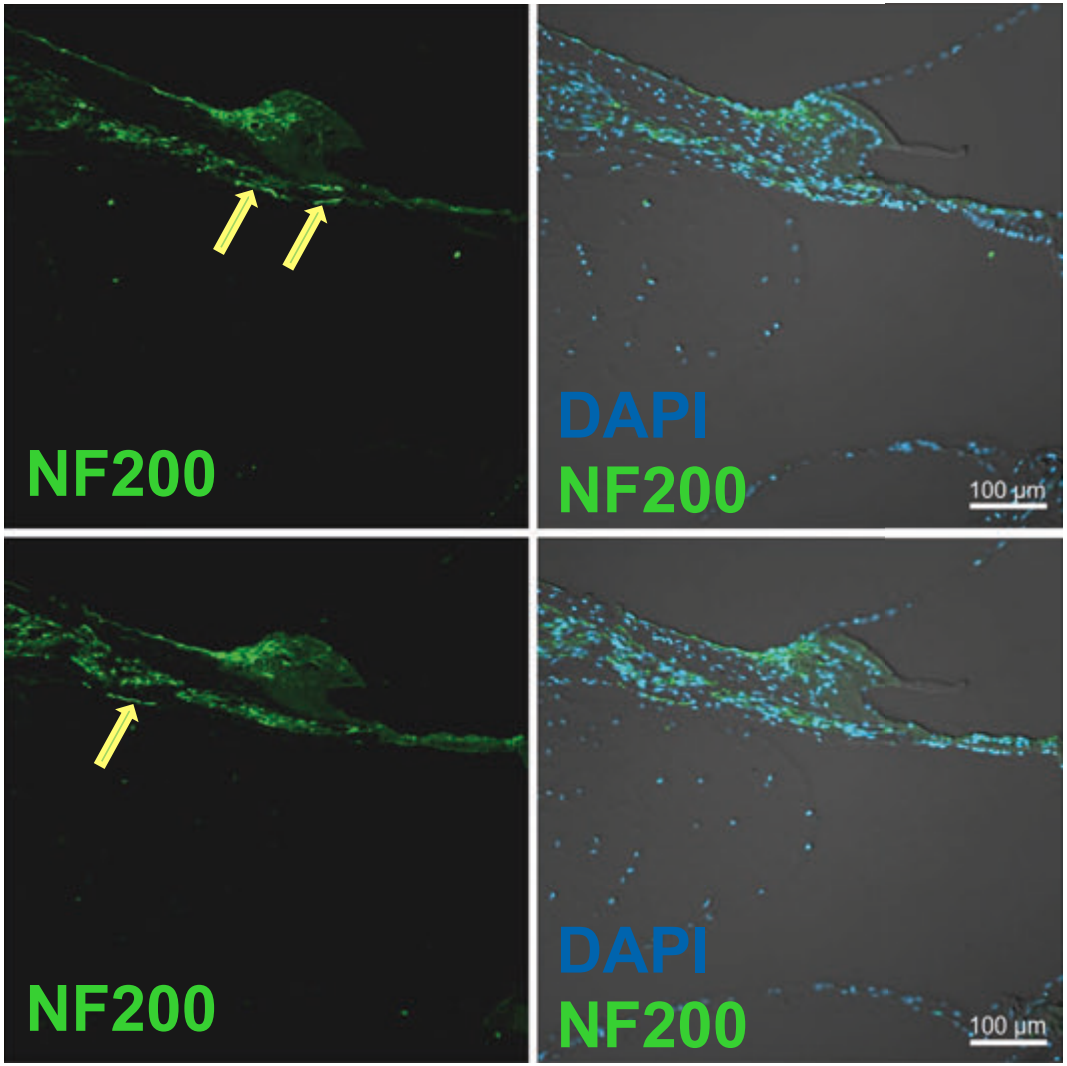
day 0 | day 7 | day 14 | day 21 | day 28 | day 35 | day 42



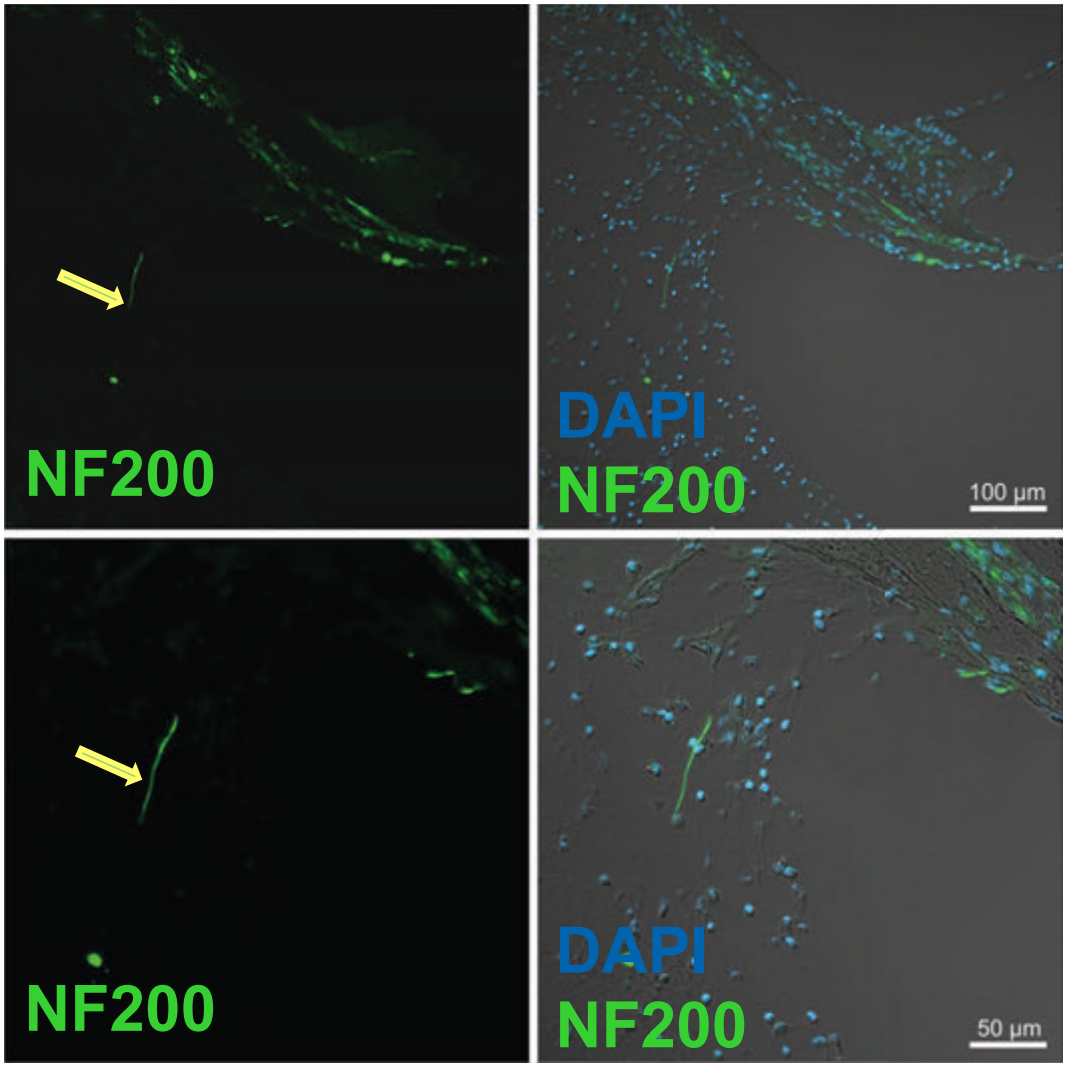
BDNF + CI



BDNF-Gel, 2 consecutive sections 35 µm



BDNF-Gel



NANOCI – project summary and conclusion

- Auditory neurons were for the first time successfully cultured and functionally analyzed on multi-electrode arrays (MEAs)
- Optimized stimulation protocols for a gapless CI were identified that should offer to reduce energy consumption of CIs in the future
- MEAs are in our view an accurate model to optimize response profiles and stimulation parameteres of auditory neurons
- The in vivo studies in Tübingen have so far yielded proof of concept that auditory neurons can be guided into the scala tympani
  - No functional results yet from these experiments

NANOCI – project summary and conclusion

- The NANOCI project proposes one concept to overcome current limitations of CIs:
  - the creation of a gapless man:machine interface in the cochlea

- Methods of regenerative medicine, nanotechnology and biomedical engineering are used in concert to achieve the ambitious approach

- If no „NANOCI“ system will be produced in the future – the whole project was still worth it!!

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Michael Perny

Laboratory for Neural Repair

Hans Ruedi Widmer

Stefano di Santo

Physiology Institute

Jürg Streit

Anne Tscherter

SEVENTH FRAMEWORK
PROGRAMME


Thank you!