Warum ist es so schwierig das Gehirn zu verstehen?

Roger D. Traub, M.D.
IBM T.J. Watson Research Center
Yorktown Heights, New York

Under the auspices of the Einstein Stiftung Berlin

Thanks also the Alexander von Humboldt Stiftung

Summary

1) We want to better treat neuropsychiatric disorders; to learn from the brain so as to imitate its functions; to understand ourselves & our origins

2) To accomplish this, we must be able to relate the physical properties of neurons and their connections to functionally meaningful circuit outputs

3) This has been possible with smaller circuits ("central pattern generators"); and in the case of highly redundant population behaviors (e.g. network oscillators, seizures)

4) For cognition, this program has proven difficult, for conceptual reasons, insufficient data, and (mostly) for lack of a suitable preparation – a preparation where both neuron/circuits and functionally relevant outputs are *simultaneously* measurable.

Die Frage

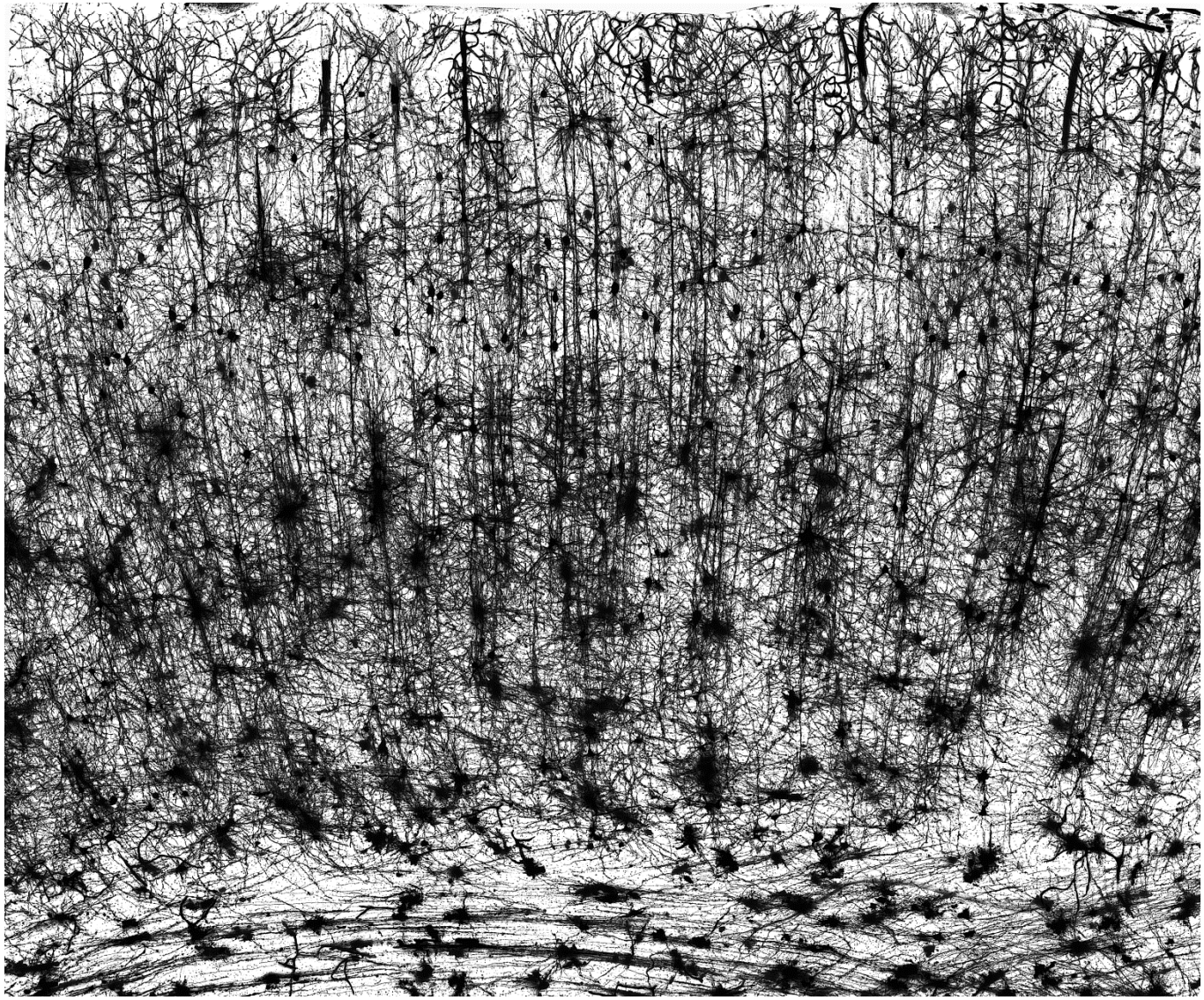
OPA: Warum hat denn jeder Mensch ein Gehirn?

ENKEL (3 Jahre): Damit wir denken können.

OPA: Ja gut, aber wie ermöglicht das Gehirn uns zu denken?

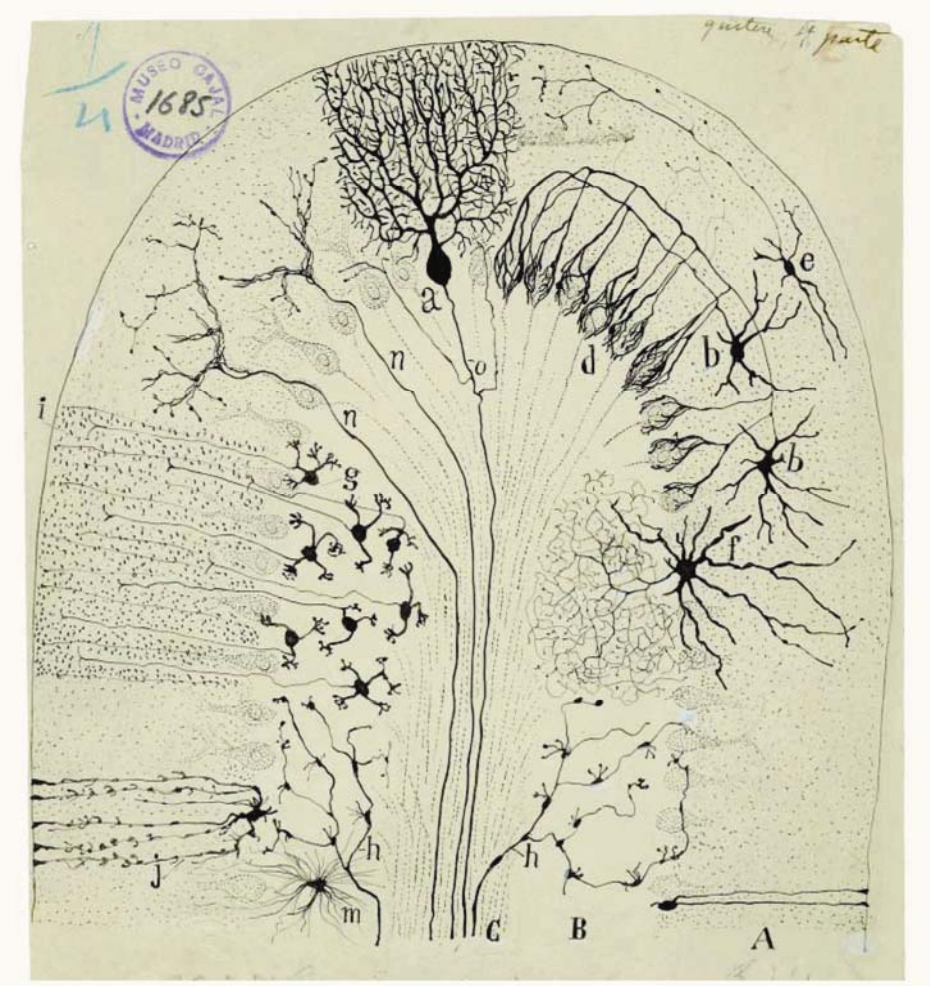
ENKEL: [Pause, tief in Gedanken] Kann ich noch einen Keks haben?

Mouse cortex (Golgi-Cox)



Dr Farid Hamzei-Sichani

Cerebellum (Ramon y Cajal)



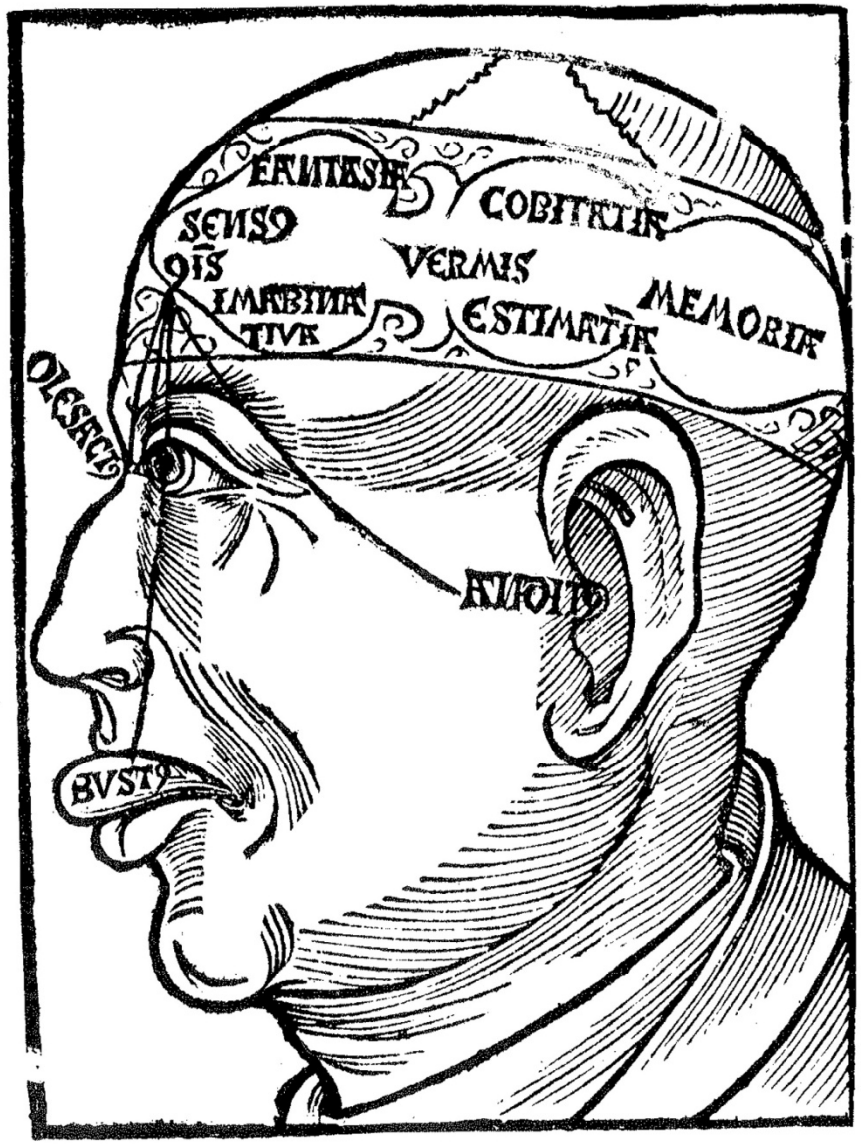


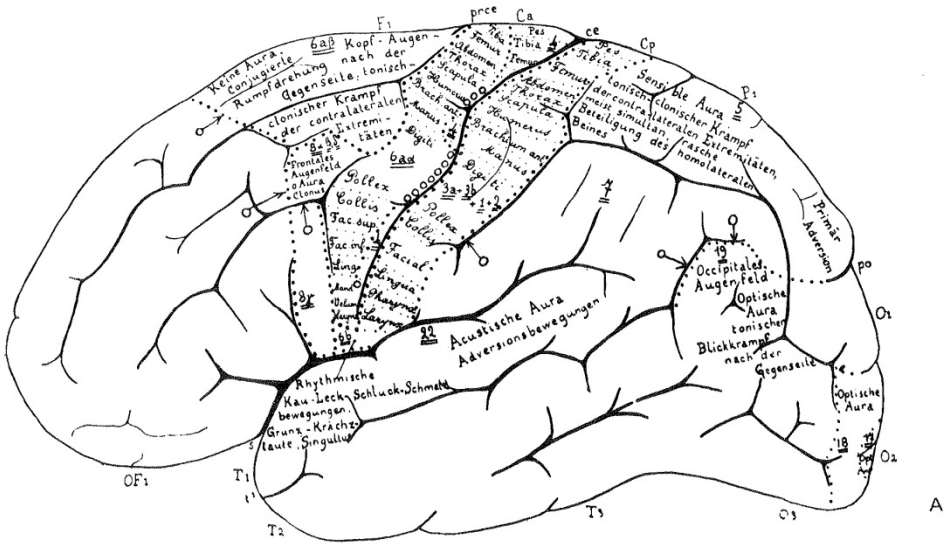
Figure 52

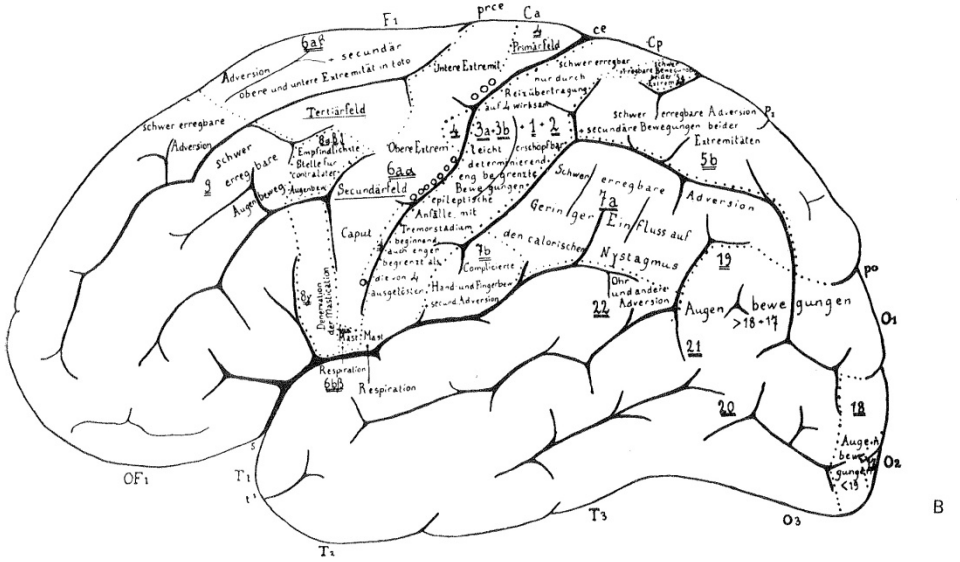
An English variant appeared in 1525 in a book on surgery by Hieronymus Brunschwig of Strassburg (1450–1512),[83] first published in German in 1497.

Clarke & Dewhurst,
An Illustrated History of Brain Function

Clarke & Dewhurst,
An Illustrated History of
Brain Function

(Oskar & Cecile Vogt worked at the Kaiser-Wilhelm-Institut fuer Hirnforschung, Berlin)





An illustration of thought disorder (McKenna, 1997):

Interviewer: **Have you been nervous or tense lately?**

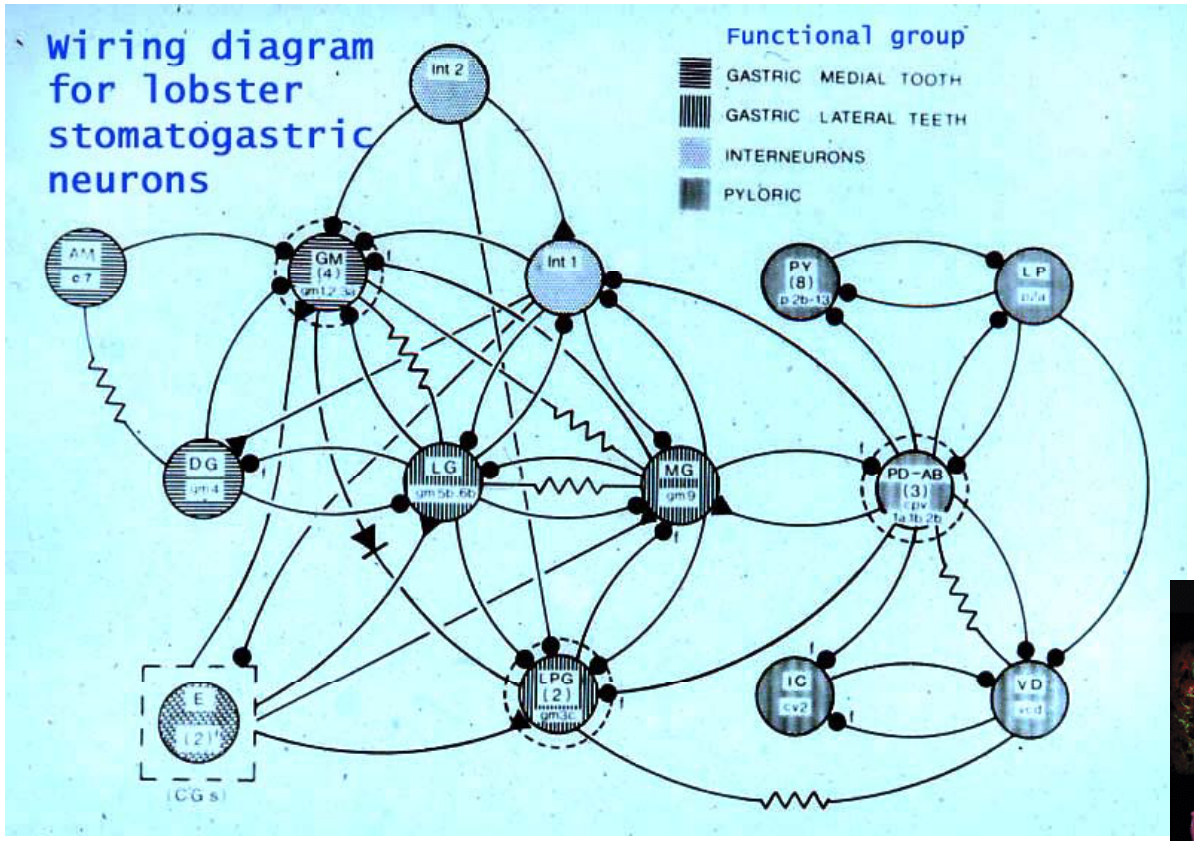
Patient: **No, I got a head of lettuce.**

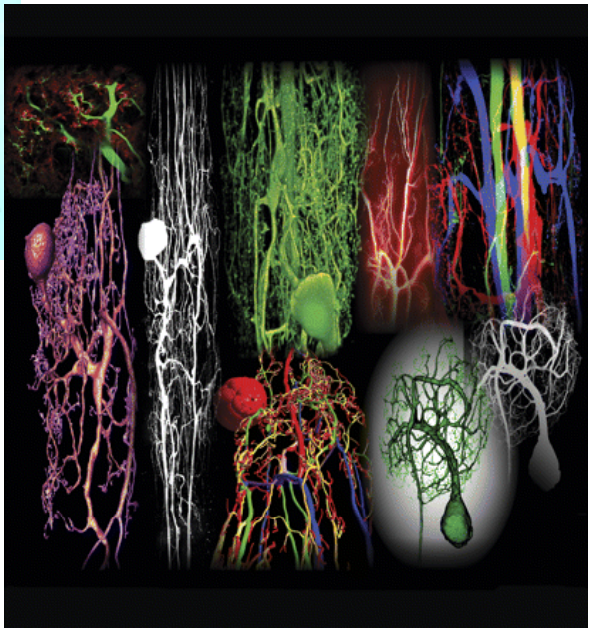
Interviewer: **You got a head of lettuce? I don't understand. Tell me about lettuce.**

Patient: **Well, lettuce is a transformation of a dead cougar**
that suffered a relapse on the lion's toe.

And he swallowed the lion and something happened.

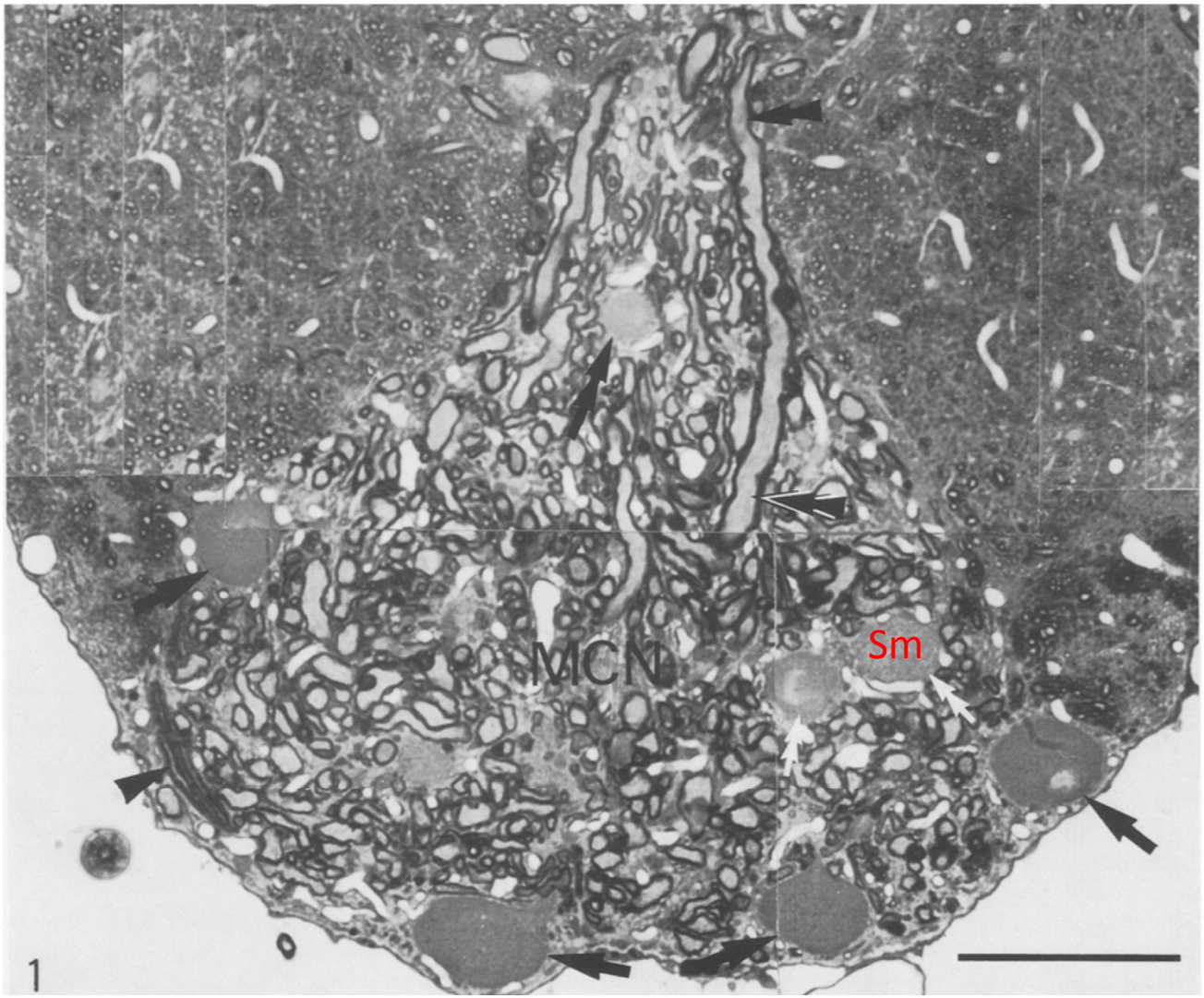
The… see, the … Gloria and Tommy, they're two heads and they're not whales.
But they escaped with herds of vomit, and things like that.





Dirk Bucher, PNAS

Medullary command nucleus, weakly electric fish

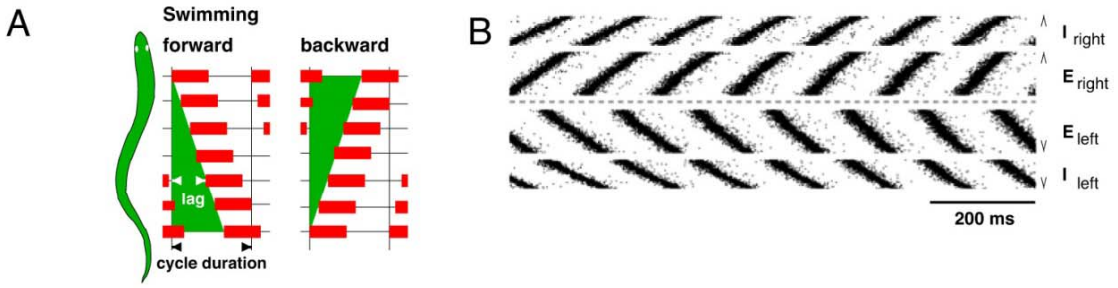


K. Elekes, T. Szabo: 1985

100 microns

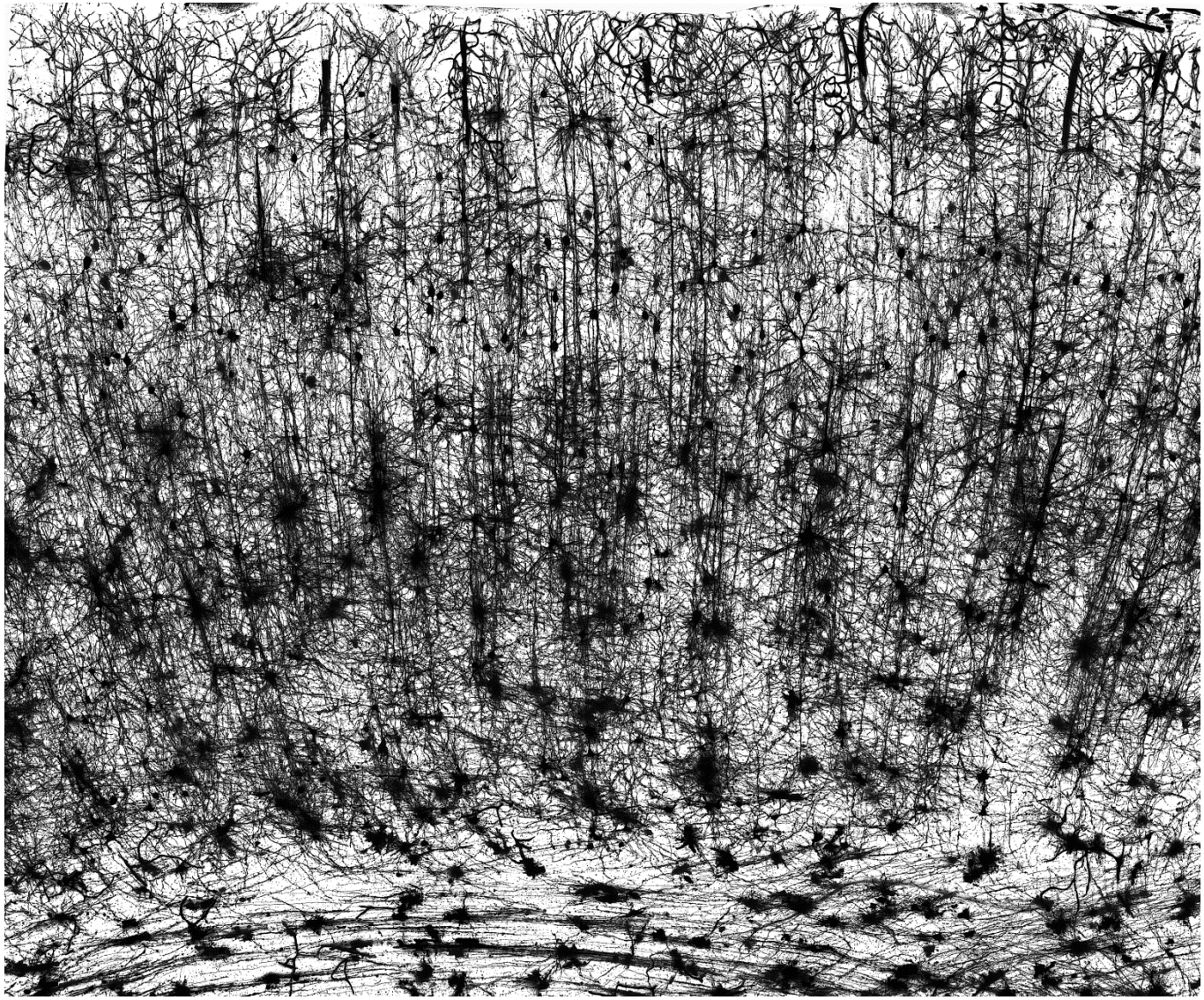
~40 large cells (arrow), 140 small cells (double white)

Lamprey spinal cord



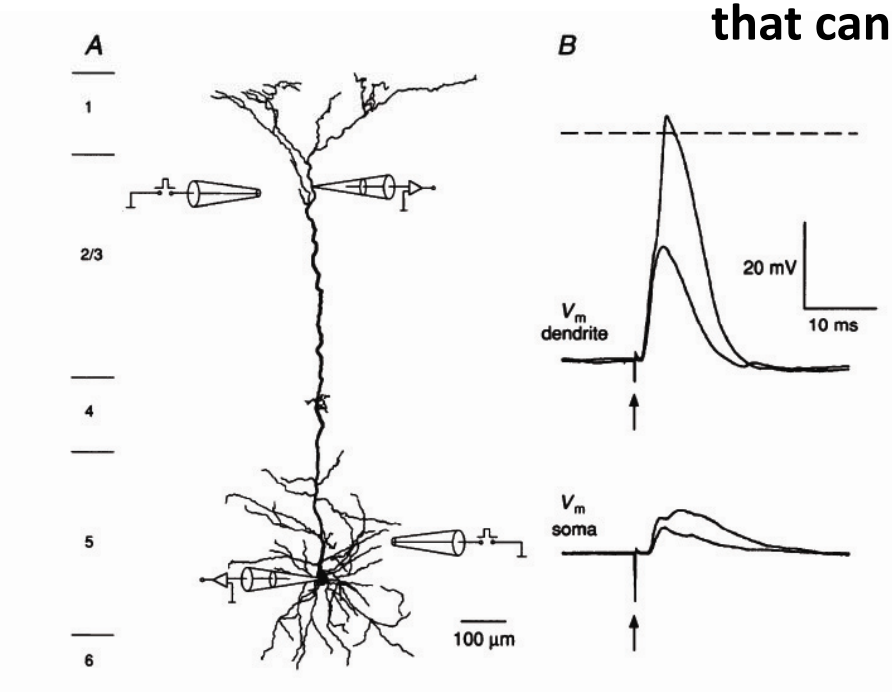
Sten Grillner & colleagues

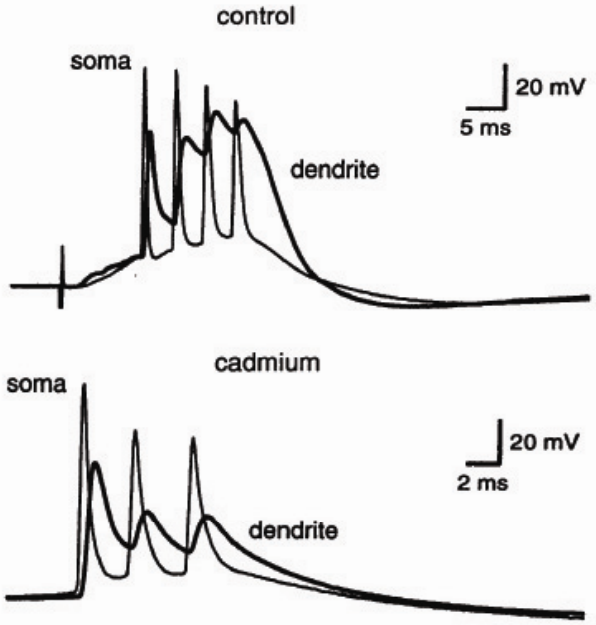
What about mammalian cortex?



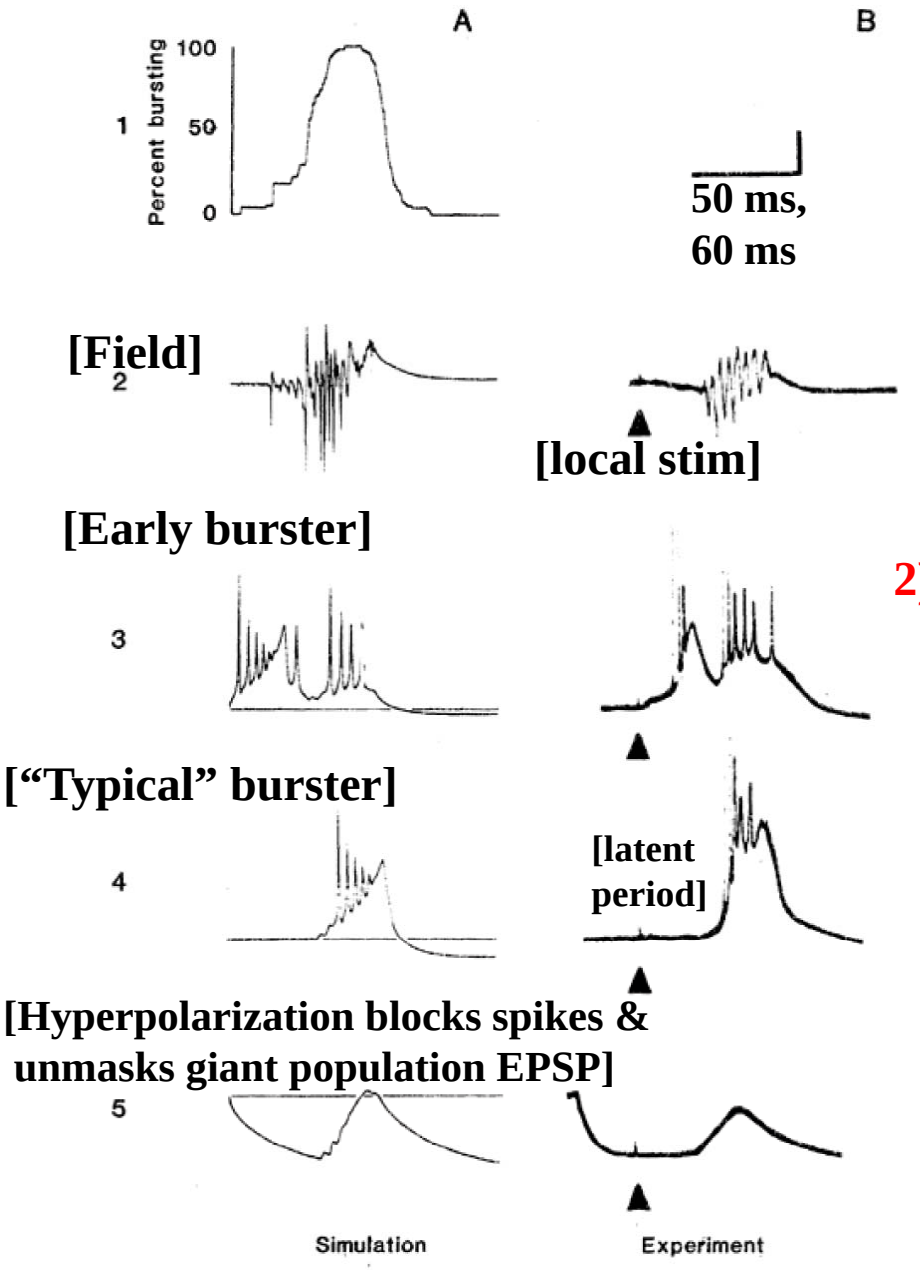
Dr Farid Hamzei-Sichani

Our neurons have complicated shapes, and complicated electrical properties – that are not even uniform from place-to-place on the same cell. Each cell also has large numbers of inputs, and large numbers of outputs, that can be distributed far and wide.





From the lab of Bert Sakmann



In vitro epileptiform synchronized burst: $GABA_A$ receptors blocked. Hippocampal CA2/CA3.

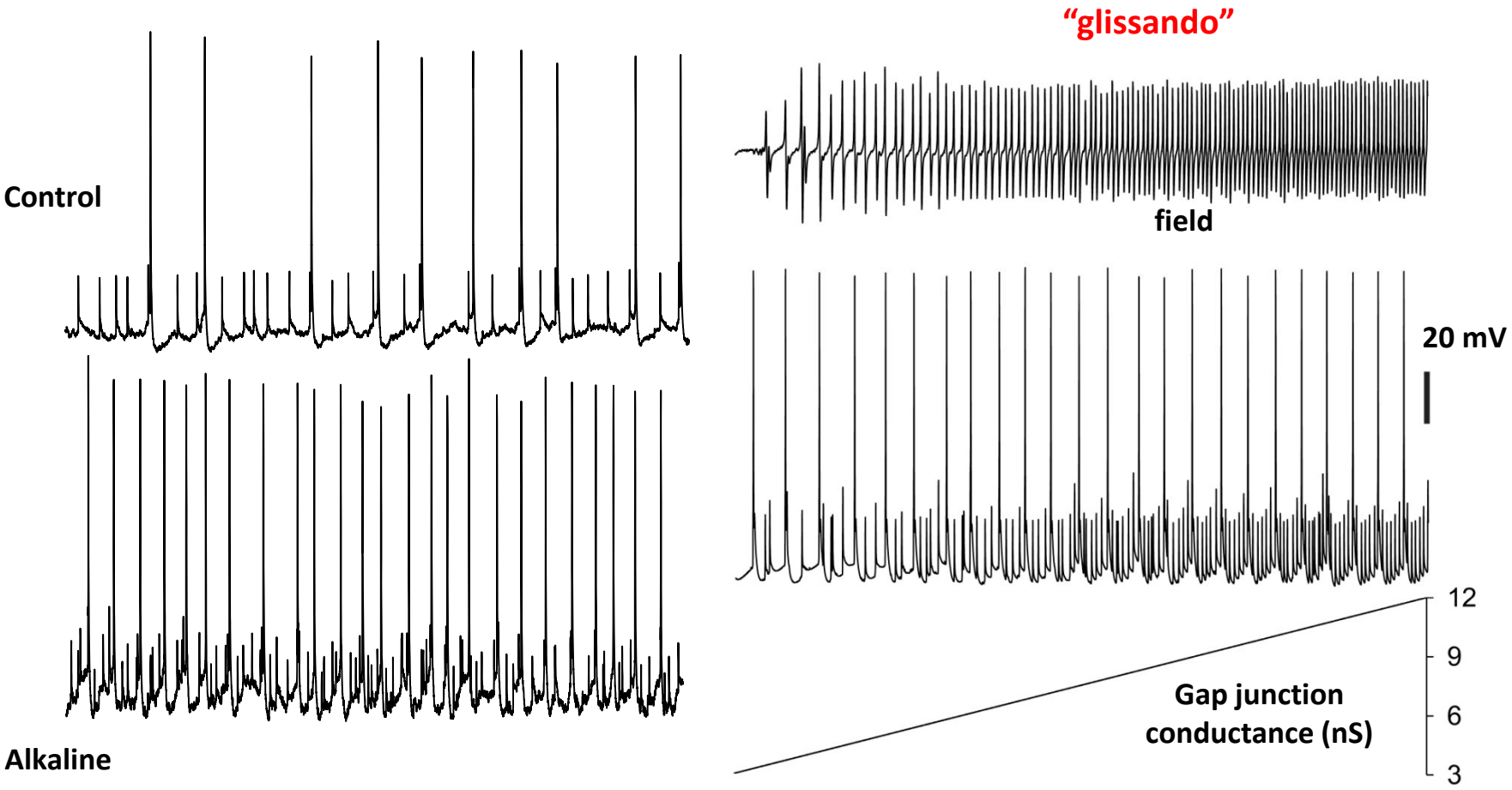
Basic model properties:

1) **Each neuron connects to >1 other;**
2) **Bursting propagates from neuron to neuron**

Traub RD, Wong RKS (1982) Cellular mechanism of neuronal synchronization in epilepsy. *Science* 216, 745-747.

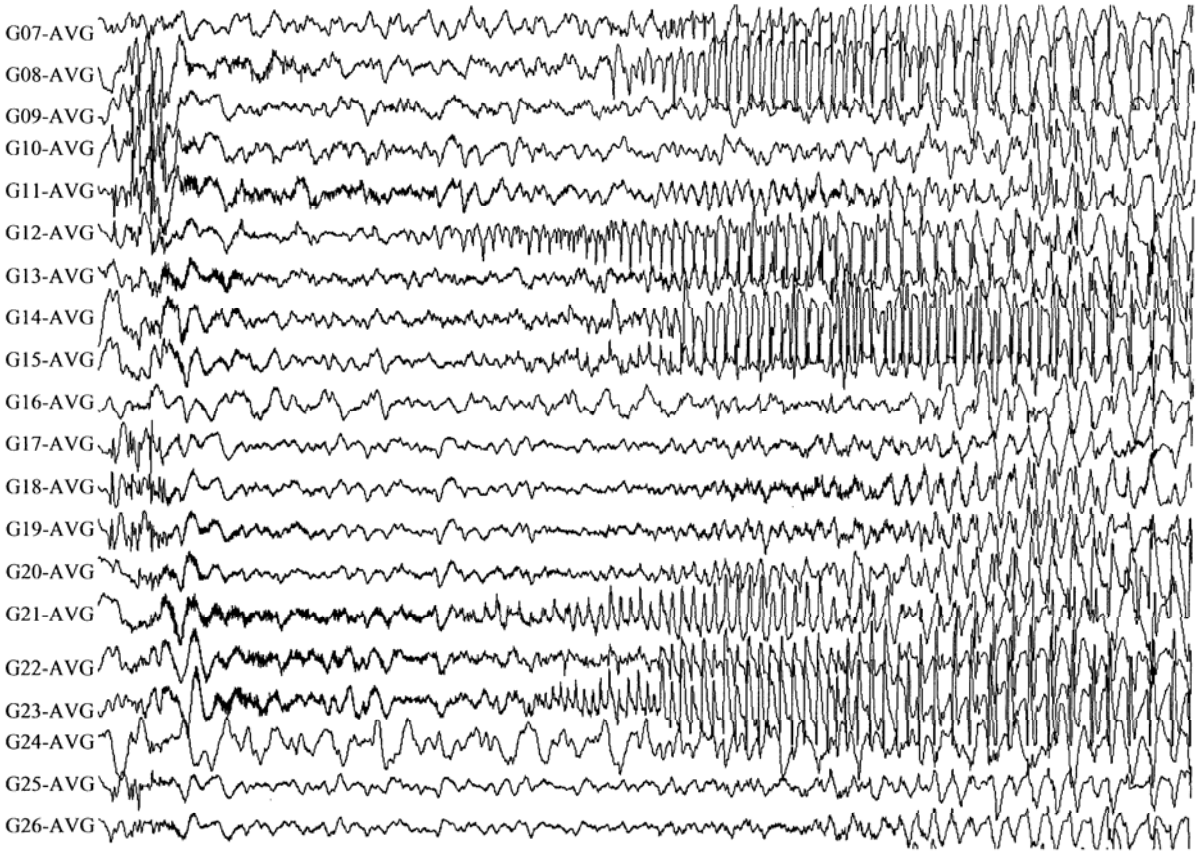
Experiment

Model



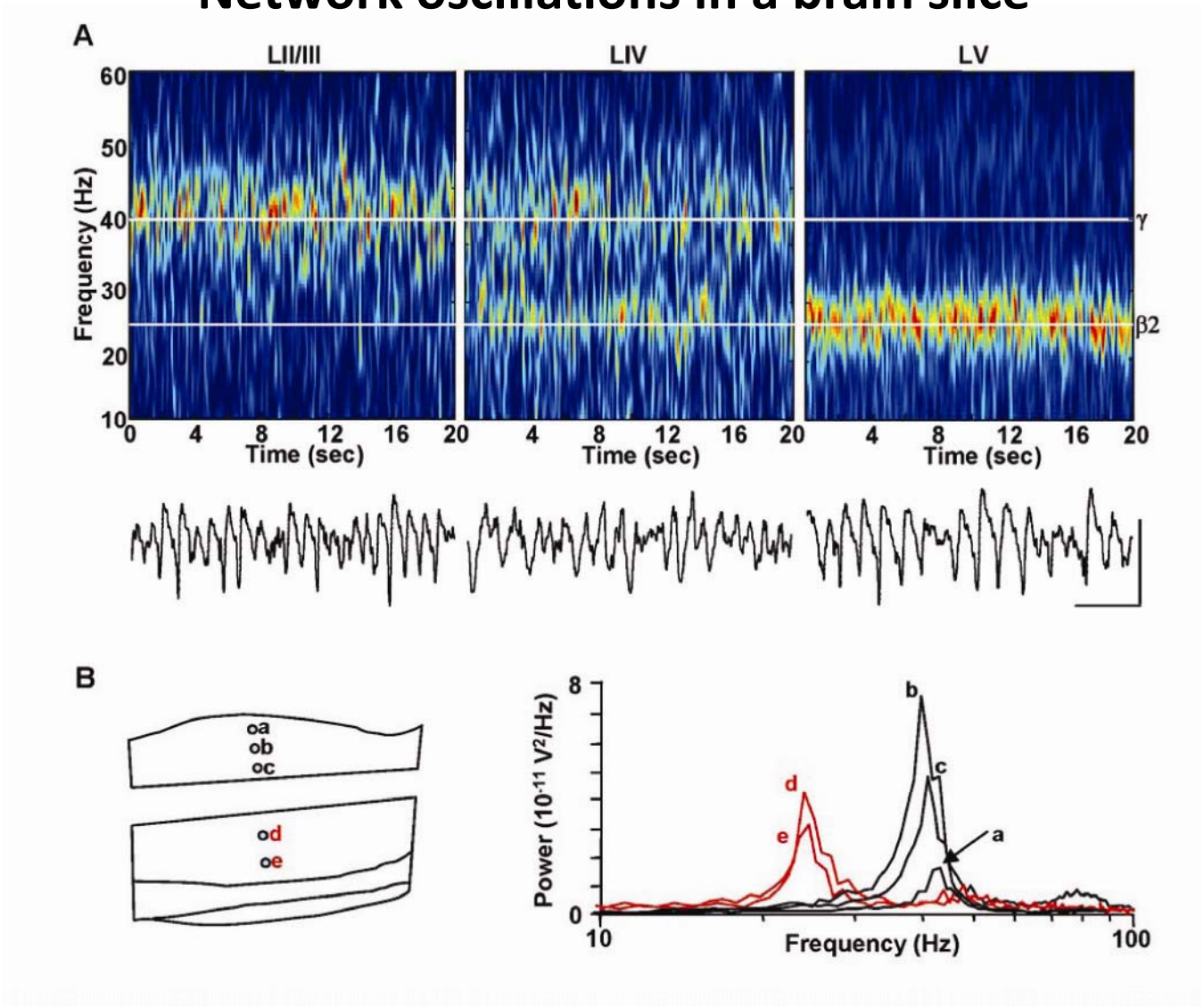
1 second traces, Layer 5 neocortex
M.A. Whittington, R.D. Traub (unpublished)

Human electrocorticography (subdural grid electrodes): very fast oscillations, followed by electrographic seizure



Traub *et al. Epilepsia*. 42: 153-170, 2001.

Network oscillations in a brain slice



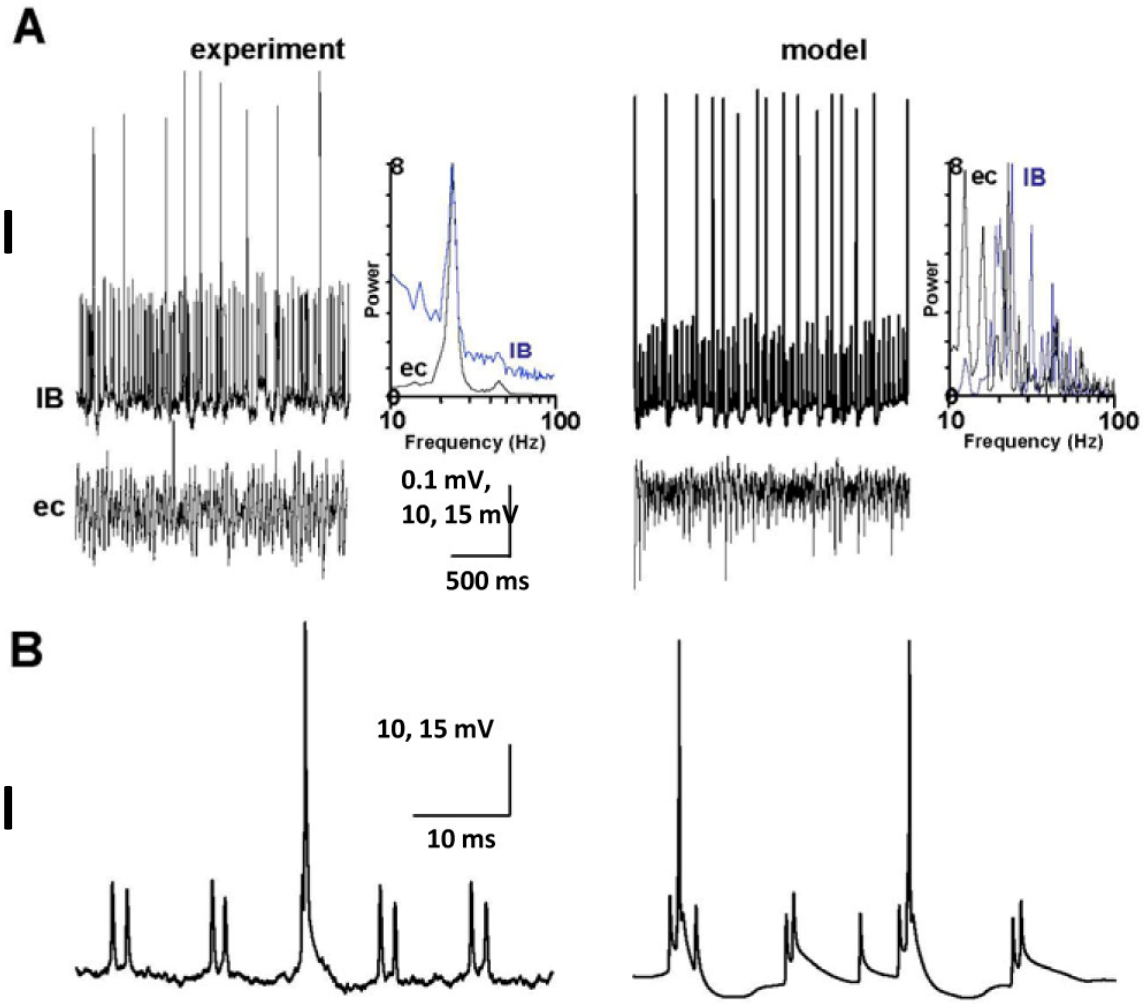
A. Roopun et al., 2006, Proc. Natl. Acad. Sci. USA

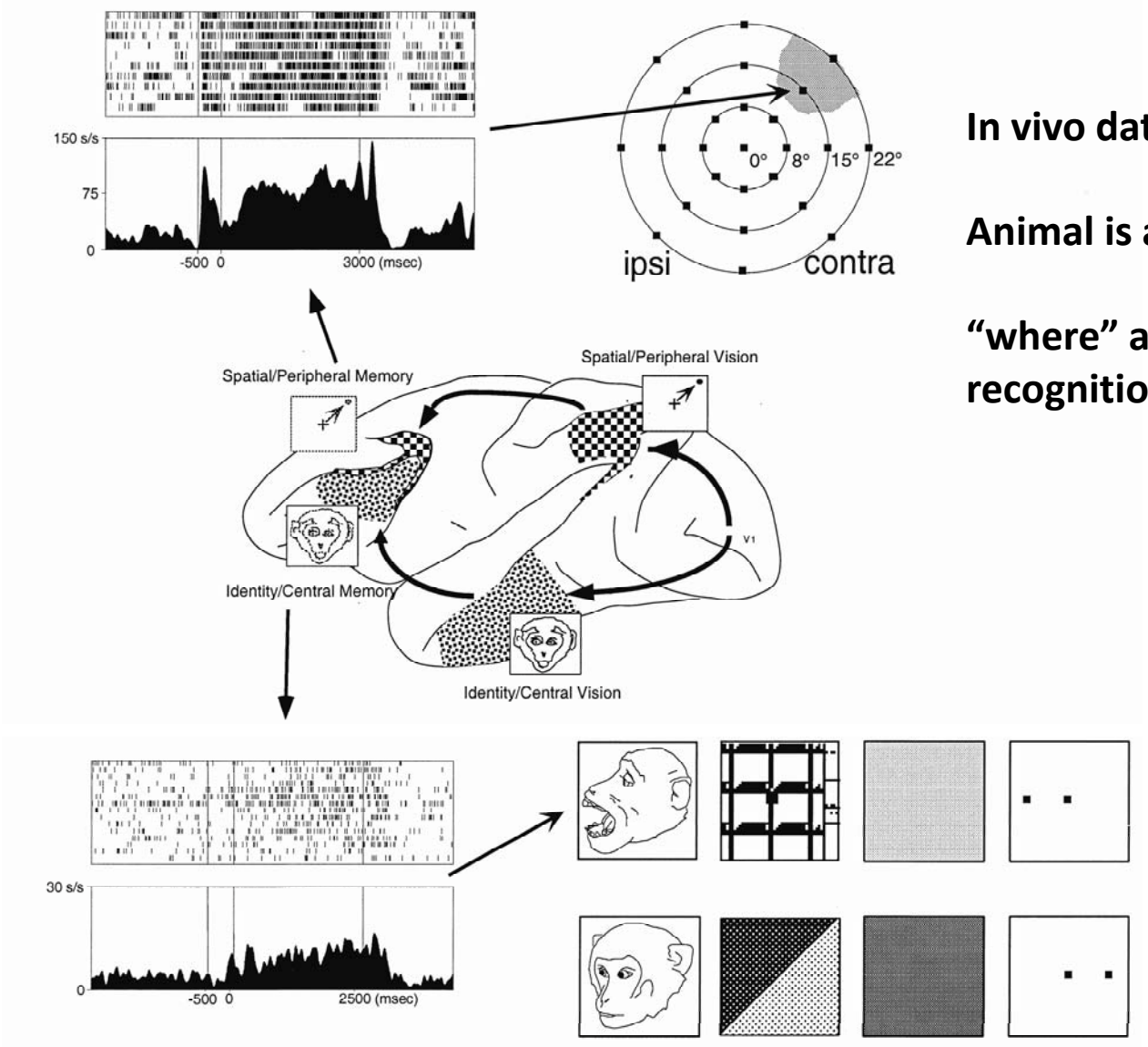
Network oscillations in a brain slice: what do cells do?

Individual cell

"EEG"

Individual cell





In vivo data, monkey cortex.

Animal is awake, cooperating.

"where" and "what" pathways: recognition & memory

Goldman-Rakic, 1999

Is there a mathematical short-cut?

(Hopfield model, in “spin-glass” form)

$$S_i = \pm 1, \quad i = 1,\ldots,N$$

Stable states: ξ^α, $\alpha = 1,\ldots,r$

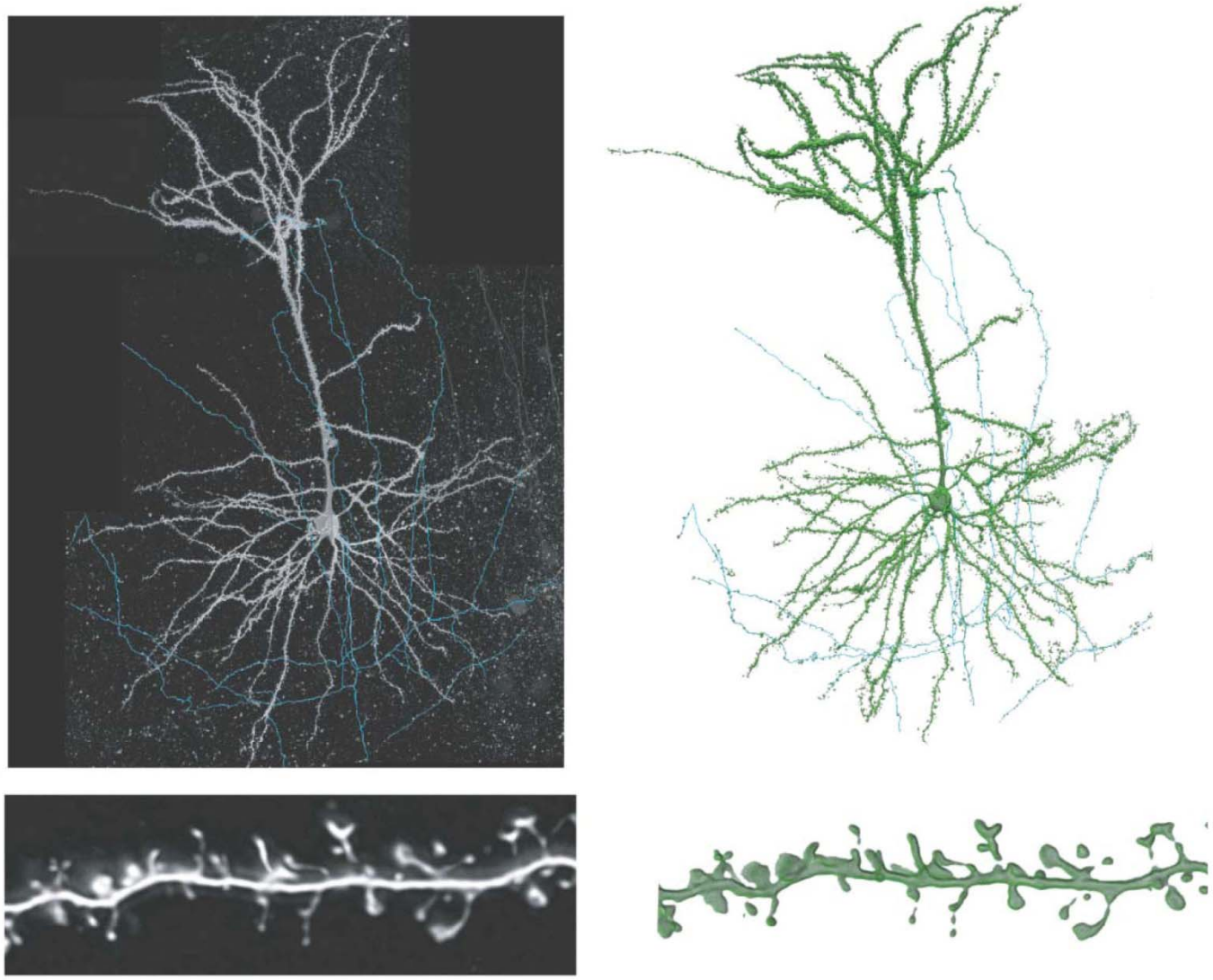
$$T_{ij} = \Sigma_{\alpha=1..r} \; \xi_i^\alpha \, \xi_j^\alpha$$

$$h_i(a) = \Sigma_{j=1\ldots N} \, T_{ij} S_j \;\; = \;\; \xi_i^a + \Sigma_{j,\, \alpha \neq a} \; \xi_i^\alpha \, \xi_j^\alpha \, \xi_j^a$$

Flip with $p = 1 / (1 + \exp(-2\beta h_i))$

$$H\,(S_1,\ldots,S_n) = - \Sigma_{i,j} \, T_{ij} S_i S_j \text{ , non-increasing when } \beta = \text{inf.}$$

(superficial) cortical pyramidal neuron



http://www.bumc.bu.edu/anatneuro/files/2011/11/Cells_JL_new.png 1/27/2012

Summary

1) We want to better treat neuropsychiatric disorders; to learn from the brain so as to imitate its functions; to understand ourselves & our origins

2) To accomplish this, we must be able to relate the physical properties of neurons and their connections to functionally meaningful circuit outputs

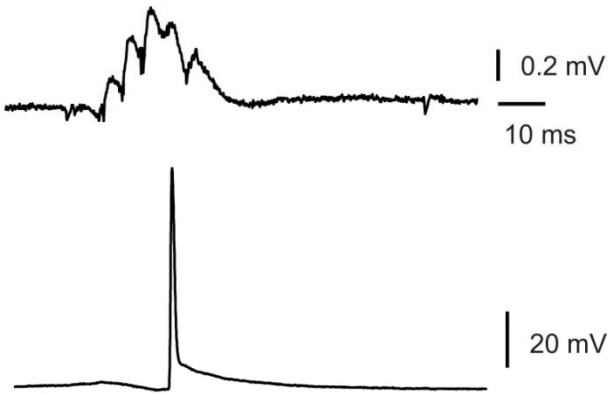
3) This has been possible with smaller circuits ("central pattern generators"); and in the case of highly redundant population behaviors (e.g. network oscillators, seizures)

4) For cognition, this program has proven difficult, for conceptual reasons, insufficient data, and (mostly) for lack of a suitable preparation – a preparation where both neuron/circuits and functionally relevant outputs are *simultaneously* measurable.

What distinguishes normal from pathological oscillations?

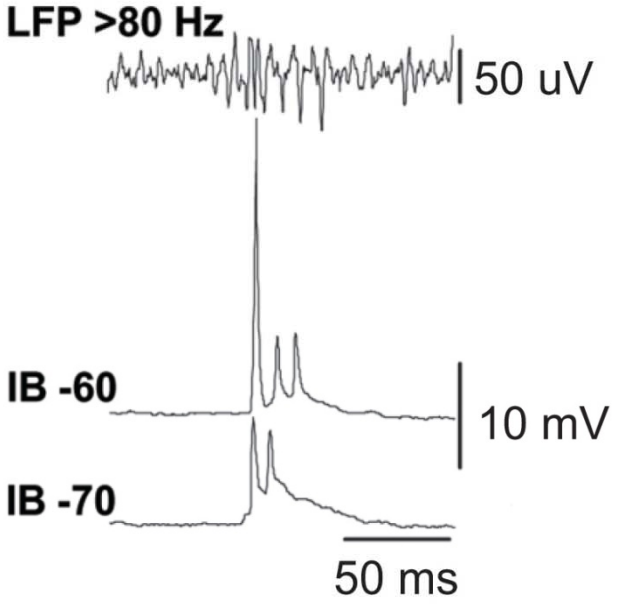
Normal

SPW/R
mouse hippocampus,
in vitro



Pathological

Human
epileptic neocortex,
in vitro

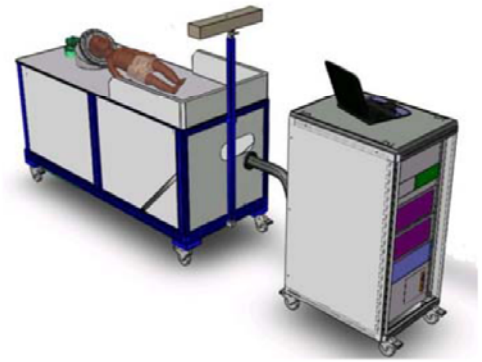


TECHNOLOGY – BRAIN/COMPUTER INTERFACE
Magnetoencephalography – portable?

TRISTAN TECHNOLOGIES

babySQUID® *Neonatal Biomagnetometer*

A new, noninvasive investigational tool for pre- and full-term infants



Mapping brain function and detection of neurological abnormalities in infants

Detection of cortical function in newborns is needed for clinical intervention in the early stages of neurological disorders, before external signs appear and the conditions develop and worsen. Areas where babySQUID® could be used for neonatal neurological assessment include:

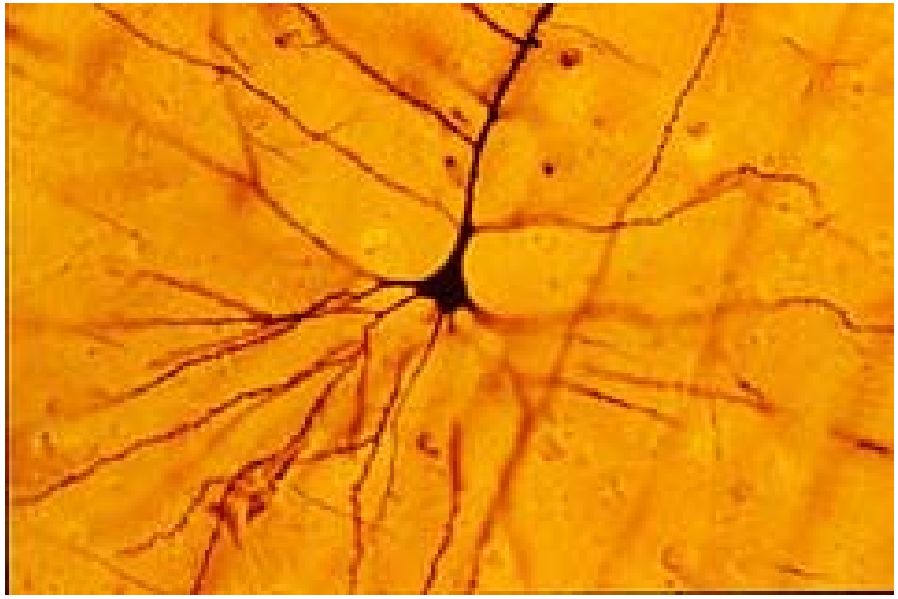
- Epilepsy
- Cerebral palsy
- Perinatal asphyxia
- Hypoxemic-ischemic encephalopathy
- Periventricular white matter injury
- Monitoring recovery from trauma

Unique Features of babySQUID®

Superior spatial resolution and sensitivity

- babySQUID® is significantly more sensitive to neuronal sources than conventional whole-head MEG systems
- Spatial resolution is four times better than existing whole-head MEG sensors
- Better spatial resolution than EEG (EEG signals are distorted by skull defects (fontanels and sutures), making it difficult localize epileptiform tissue
- No need for gluing and attaching any EEG leads
- Rapid scanning: A typical clinical scan can be completed within thirty minutes
- Anti-vibration construction; infant motion will not cause vibrational artifacts
- Sensor noise < 20 fT/√Hz

WHAT MAKES US HUMAN?



Human pyramidal neuron (Golgi)

Jetzt wohin?

“Wovon man nicht sprechen kann, darüber muss man schweigen” –

Ludwig Wittgenstein, *Logisch-Philosophische Abhandlung*

Special thanks to Miles Whittington, Dietmar Schmitz, Andreas Draguhn, Hannah Monyer