Why Study Neural Development:

- The adult brain is arguably the most complex object in our known universe – quite a challenge to study it
- Santiago Ramon y Cajal chose to study "the young wood, in the nursery stage … rather than the … impenetrable … full grown forest."
- Brain development during embryogenesis continues in the mature brain and changes during embryonic development and during adult plasticity are fundamentally similar (permanent development)
- Abnormalities in developmental mechanisms lead to brain disorders that only become manifest in adulthood – thus understanding development may help to develop therapeutic approaches

Construct an Organ:

- Surface of a gigantic wallnut „creme-coloured and wrinkled“
- Consistency of a ripe avocado „gelly-like or buttery“
- Electrode in the brain is like a „saber in yoghurt“
- The best-protected organ (cerebrospinal fluid, bones)
- represents ~3 % of body weight, consumes at rest ~20% of the oxygen/glucose (120 g/d) – quite luxurious
- Energy would be sufficient for a 15 W light bulb
- However: brain is cheap: 1 kg calf brain costs € 14, calf meat/ -filet is twice as expensive! Calf liver as well!

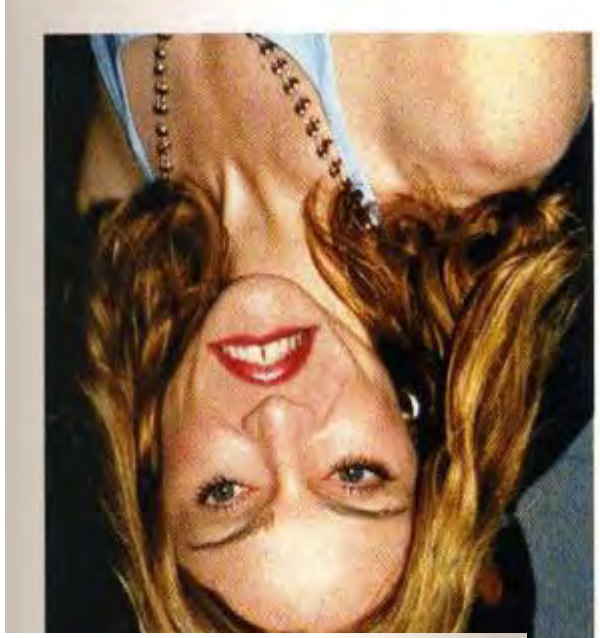
Construct a Machine:

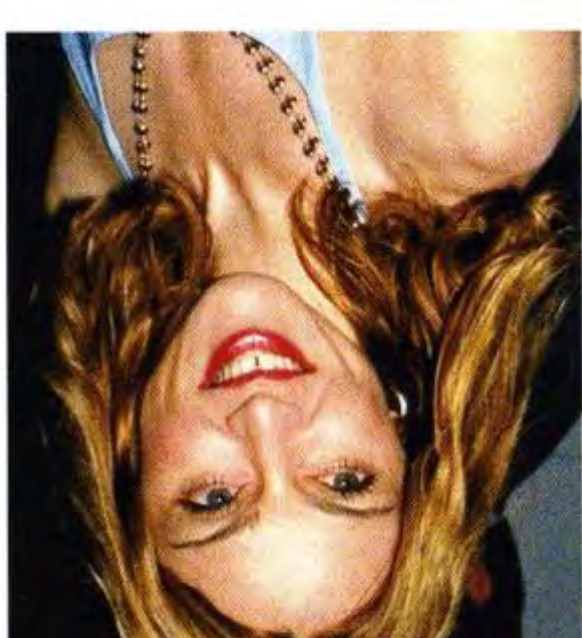
- Consisting of 100 billion individual parts with each component communicating with to approximately 1.000 other parts
- The communication is flexible and dynamic and use of each individual part will change the efficacy of communication (the brain is a “moving target”)
- Every part is connected to other parts via cables with a total length of ~500.000 km (earth-moon: 380.000 km)
- Information transport has a frequency of 100 – 1000 Hz
- Maximal energy consumption is ~15 watt
- For the construction of this machine you have only about 25.000 information units available (which must also suffice for a lot of other machines)
- The machine should have a weight of ~1,4 kg and has to function more than 90 years without major failure

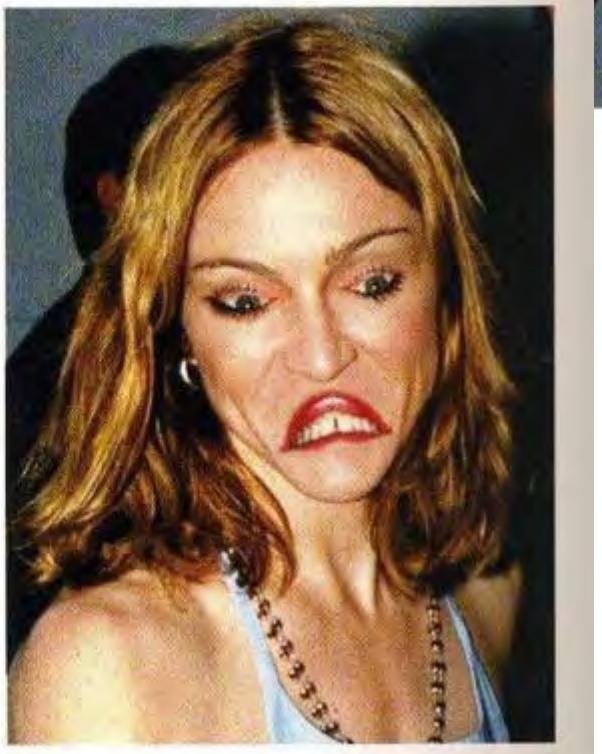
Questions:

- How can we organize such an extremely complex system of 100 billion cells with about ~5.000 synapses per cell, if we only have about 25.000 genes?
- How can we generated an ~1,5 kg organ, that is more complex than anything else that we know in nature, from a single fertilized egg?
- Don’t intend to construct it – let it construct itself and optimize it by evolution

Welches dieser beiden Portraits könnte Madonnas Gefühle ausdrücken, nachdem MTV ihr neuestes Video abgelehnt hat?





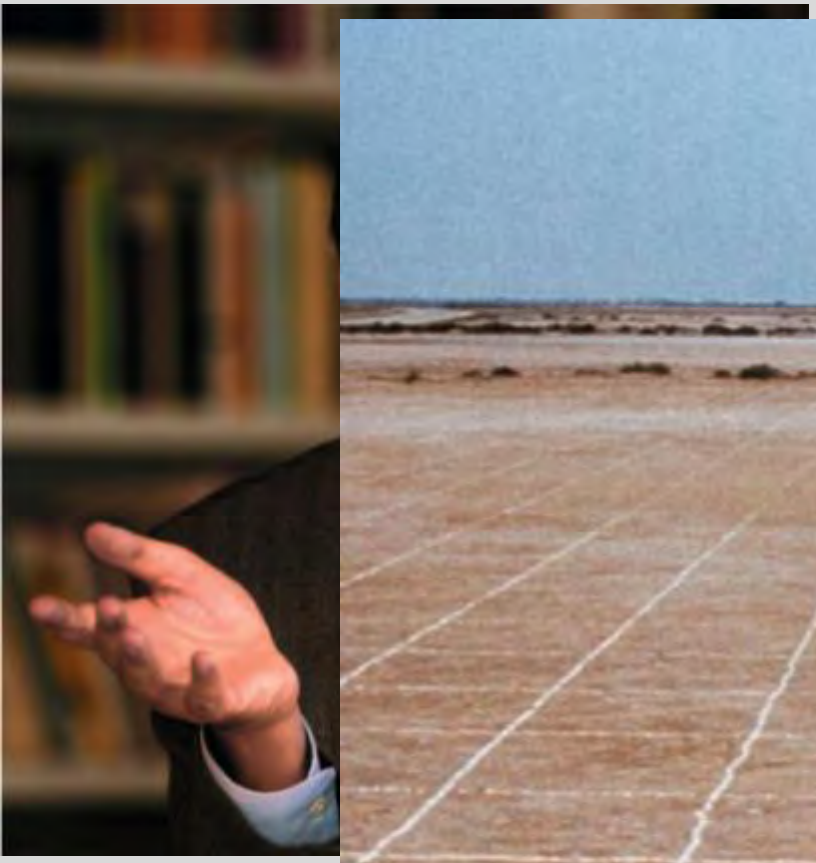


Zimbardo (2004)
Psychologie
Pearson Press

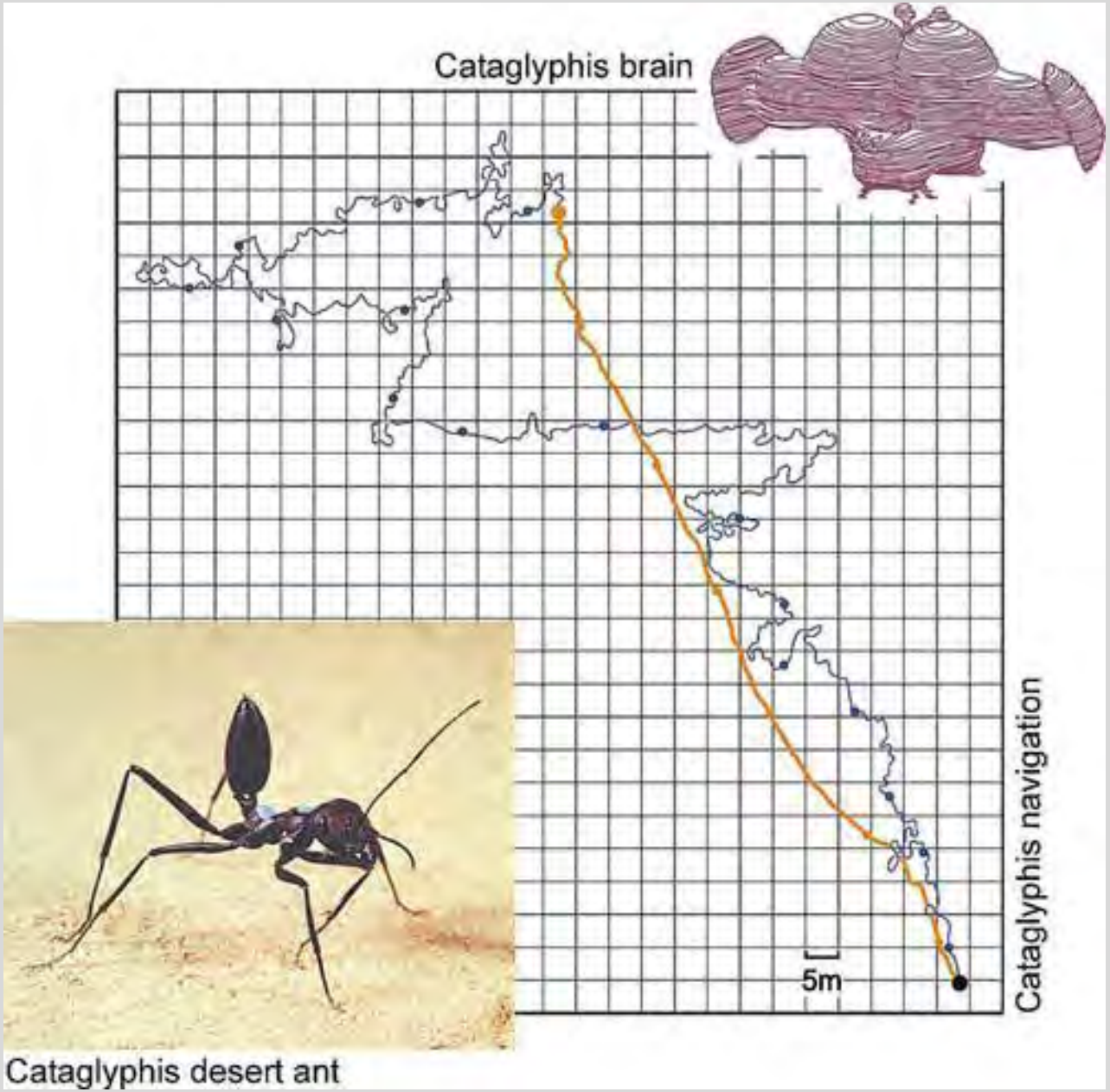
The Binding Problem

The Binding Problem

Construct a Machine:



Behavior of *Cataglyphis*:



Sahabot2:

- What a few hundred neurons do in a tiny ant, needs a big machine, when reproduced
- Möller et al., (2001) Biorobotics - Methods and Applications (B. Webb. T. Consi, eds.), pp. 37-66, AAAI Press / MIT Press
- http://www.ti.uni-bielefeld.de/html/research/sahabot/

Answers:

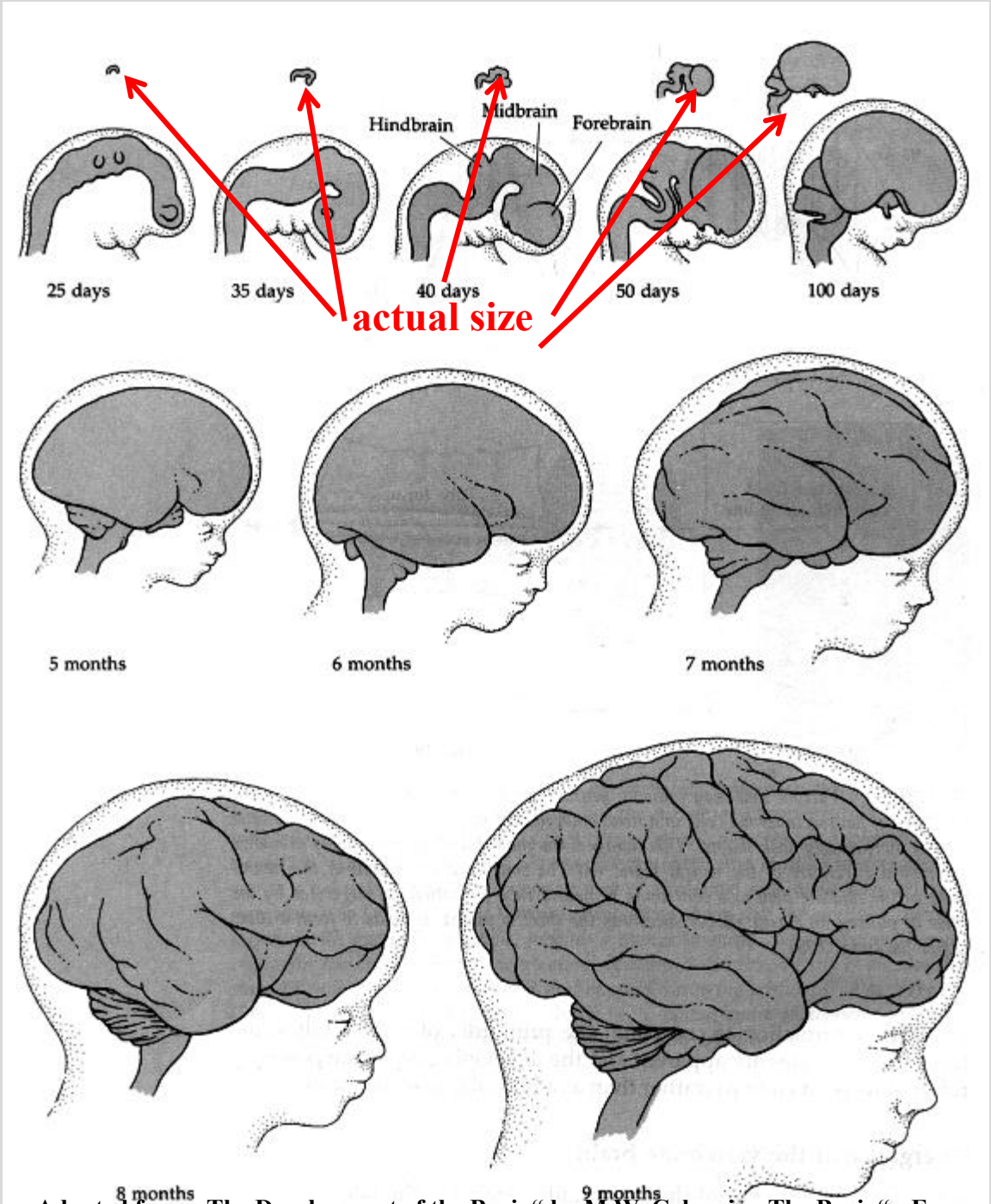
- The most important point of todays lecture: don't expect an answer to these questions. There are many more open questions than answers available in the area of Developmental Neuroscience.
- It appears, that the development of the brain is a relatively plastic process, and that the precise regulation is via a hierarchy of events
- Only few possibilities of the development are „hard-wired" – most depend on the exchange of signals.
- This allows the large degree of flexibility required for the nervous system development.
- Development of the brain has evolved but the mechanisms are conserved – thus mechanisms exist
- There similar rules govern development in vertebrates and invertebrates

Brain Development Proceeds According to Rules:

- Brain development is a hierarchical process: simple/coarse processes first, complex fine processes later
- Flexibility is high at the beginning, and lower at later stages
- Regionalization in body plan: anterior before posterior, inside before outside; polarity and segmentation
- First determined mostly by genetic, later by self – organization through experience/environment – both depend on each other
- First excess (overproduction), then elimination/pruning
- First suboptimal function, then improvement of efficacy.

Brain Development Proceeds According to Rules:

- Brain development is a very complex process
- Therefore: breakdown of processes into specific parts.
- In every part only a very small number of instructions is executed so that the development appears as a continuous process
- However, with respect to the mechanisms involved, it's a succession of small events with each regulating only a few steps



In addition to the increasing mass, a very complex cellular architecture is generated with specific cell types being generated only in particular parts of the CNS

General mechanisms are necessary to specify the 10^{11} neurons and 10^{12} glial cells

What are the individual steps?

Adapted from „The Development of the Brain“ by M.W. Cohen in „The Brain“ ; Freeman, San Francisco

Stages of Brain Development

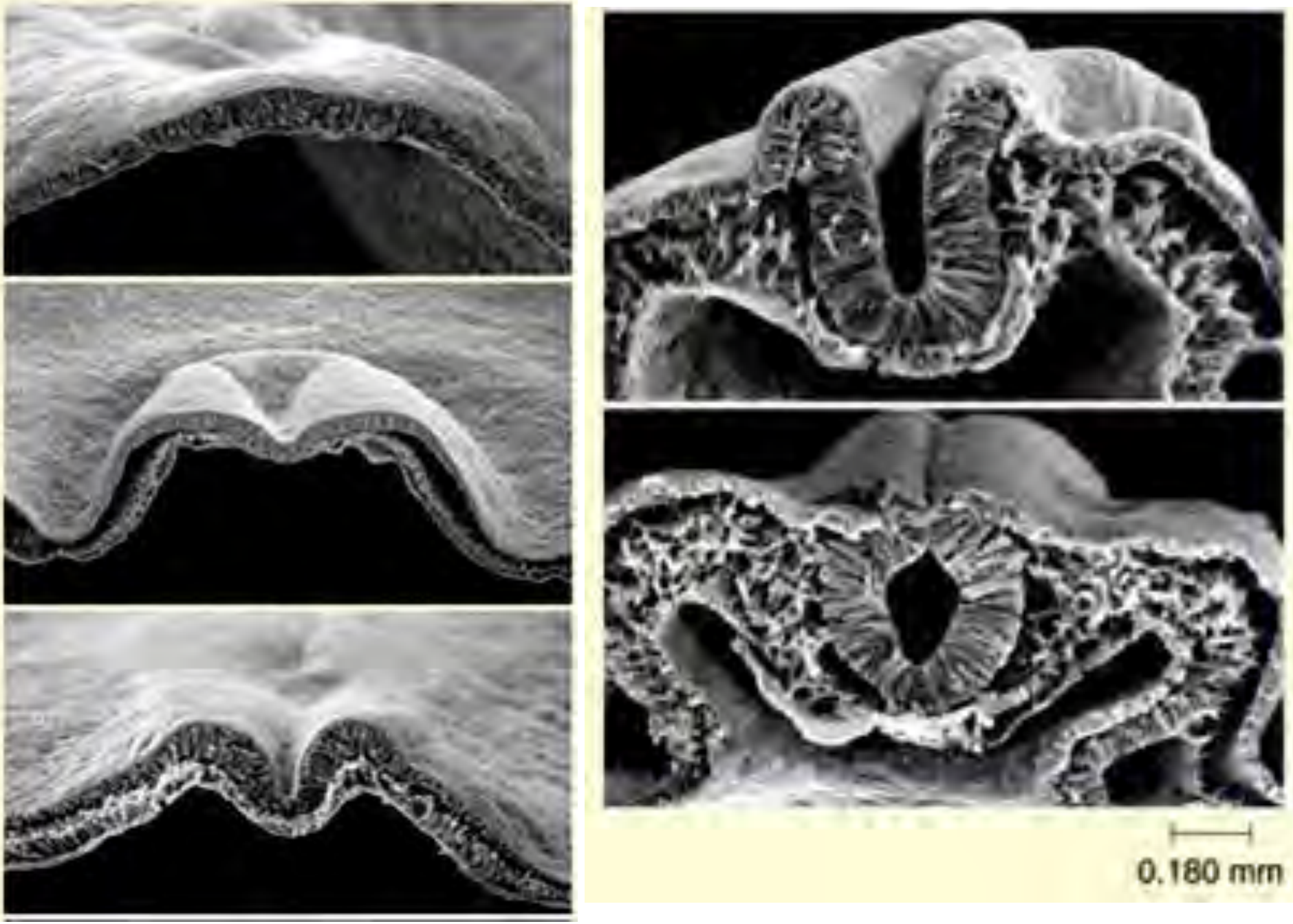
- **Before synaptogenesis – mostly genetically encoded:**
- Neuronal induction (neurulation, formation of neural tube)
- Neuronal differentiation (formation of nerve cells)
- Neuronal migration
- Axonal and dendritic growth and pathfinding
- Synapse formation
- These processes establish functional circuits – and the use of these circuits will then drive its maturation and its adult properties
- **After synaptogenesis – mostly experience-dependent:**
- Neuronal cell death
- Use-dependent modulation of connections
- Myelination

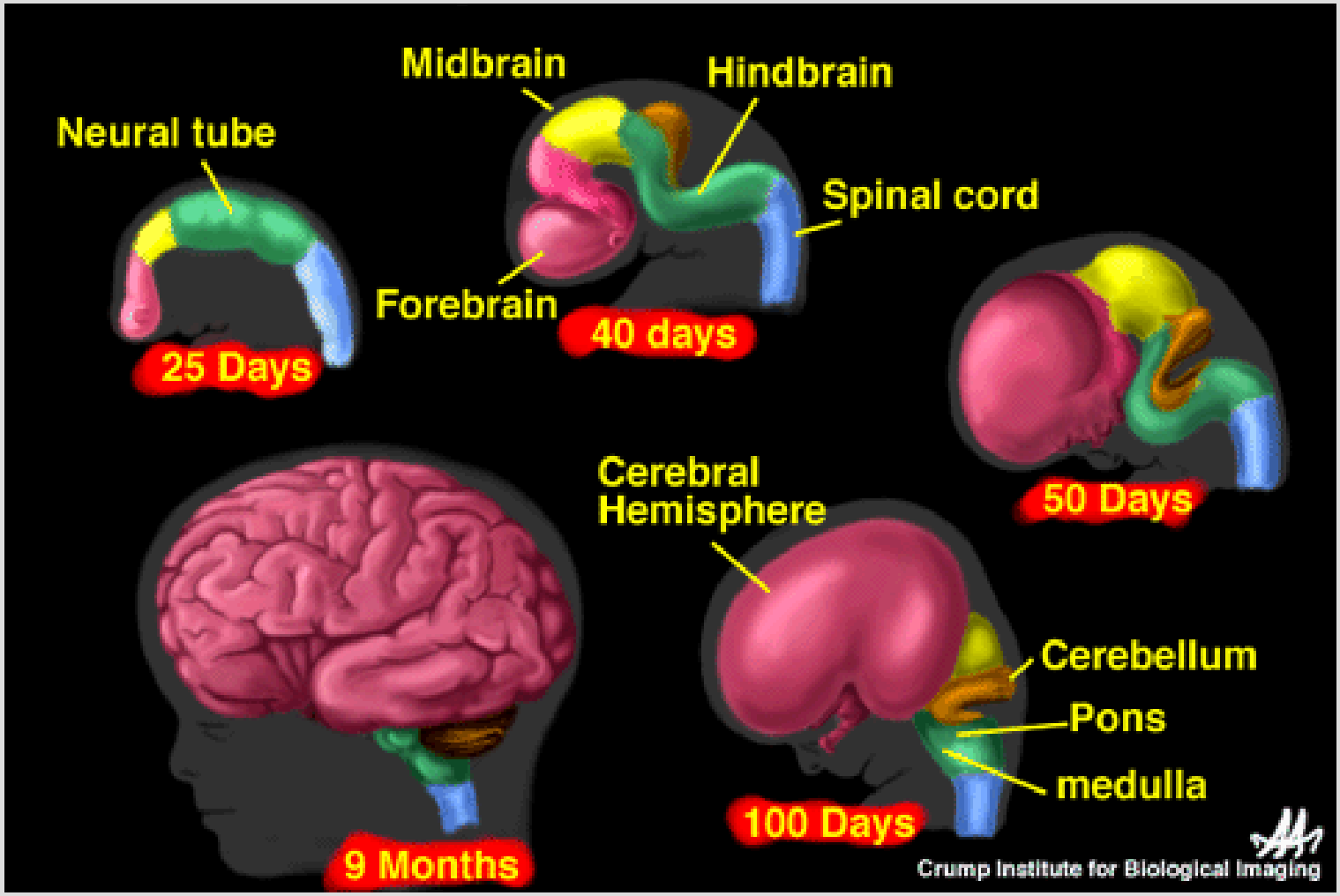
Stages of Brain Development

- The different stages are sequential for a particular neuron, but occur simultaneously (overlapping) within the developing brain
- The stages are severely overlapping depending on the brain region analyzed
- The stages are of different length – some short, some very long
- Some stages are only found primarily in males and only during some particular periods:::

Stages of Brain Development

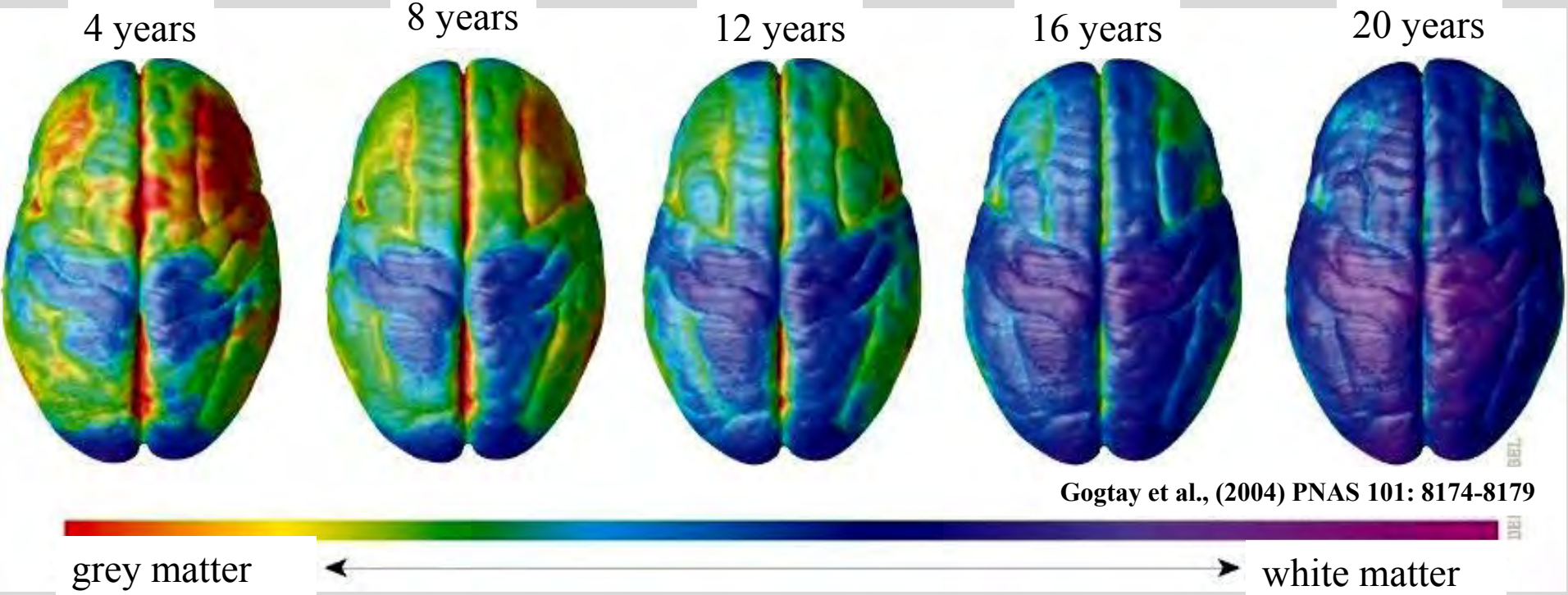
- **Before synaptogenesis – mostly genetically encoded:**
- **Neuronal induction (neurulation, formation of neural tube)**
- Neuronal differentiation (formation of nerve cells)
- Neuronal migration
- Axonal and dendritic growth and pathfinding
- Synapse formation
- These processes establish functional circuits – and the use of these circuits will then drive its maturation and its adult properties
- **After synaptogenesis – mostly experience-dependent:**
- Neuronal cell death
- Use-dependent modulation of connections
- Myelination


0.180 mm



- Already very early – before the differentiation of the first nerve cells in the neural tube, a local specialization of brain regions can be detected.
- Segmentation or regionalization – the neural tube is not identical along its length
- Different brain regions grow with different speeds
- In addition to the overall growth: morphological changes, including folding and curving

Brain Development is NOT over at Birth



- Gray matter decreases, white matter increases – myelination
- Frontal cortex ceases development last – responsible for „self-control“ and other high order executive functions, including selective attention, decision- and problem solving competence and ability to suppress emotional reactions
- Development of the brain is finished only years after puberty!
- Then the brain starts to loose neurons – about 1 per sec
- Flexibility of the brain remains high throughout life