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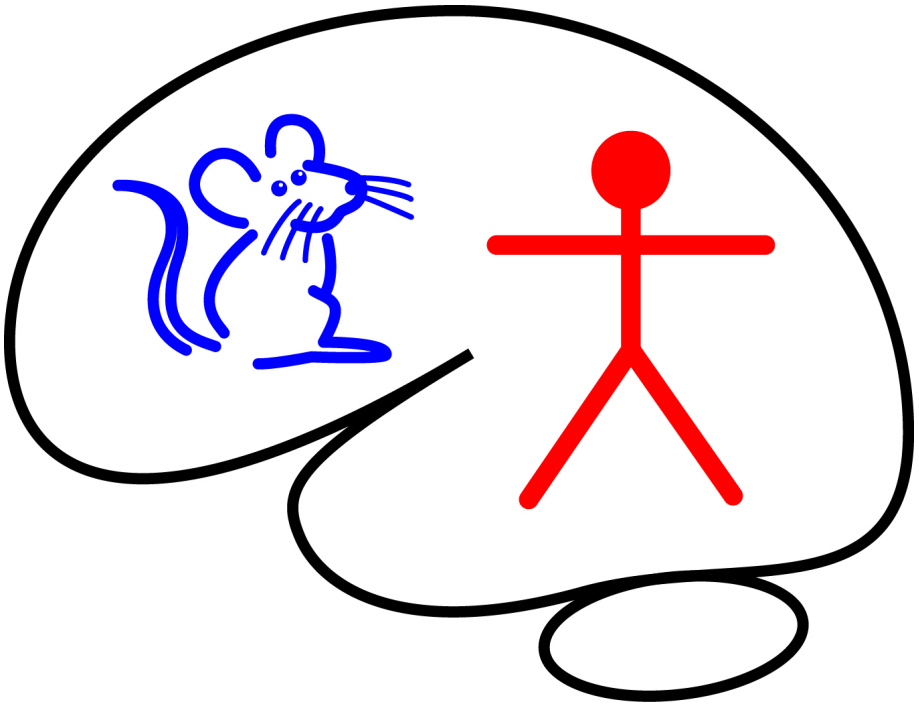


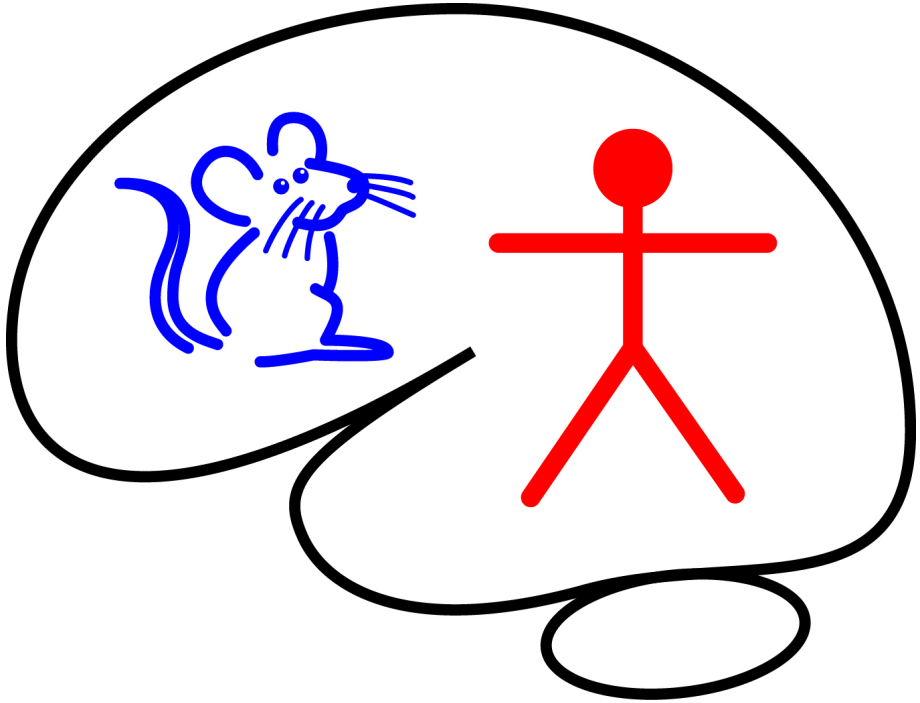
6.2 Man and mouse

Cellular Mechanisms of Brain Function

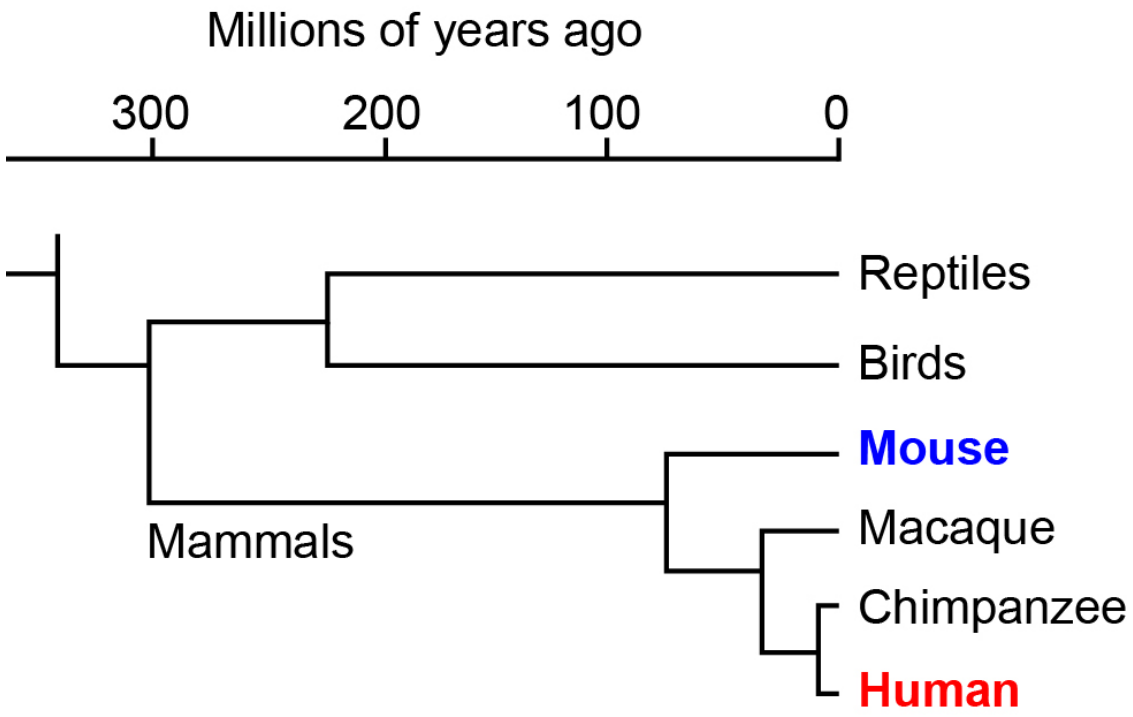
Prof. Carl Petersen

The mammalian brain

Man and mouse



Evolution



The closest common ancestor between man and mouse is thought to have lived ~80 million years ago.

~99 % of genes coding for proteins have homologs comparing man and mouse.

Mammalian brain size

Mouse

~1 g
~10^8 neurons

5 cm

Macaque

~100 g
~5×10^9 neurons

Human

~1500 g
~10^{11} neurons

There are big differences in brain size and neuron numbers.
However, many of the organising principles are very similar.

Organisation of the mammalian brain

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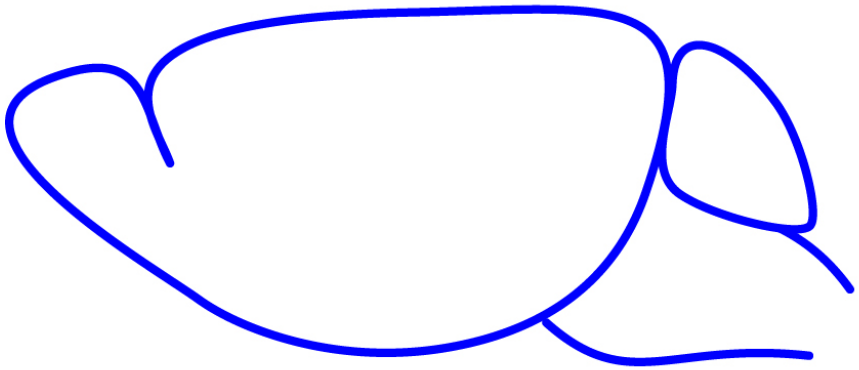
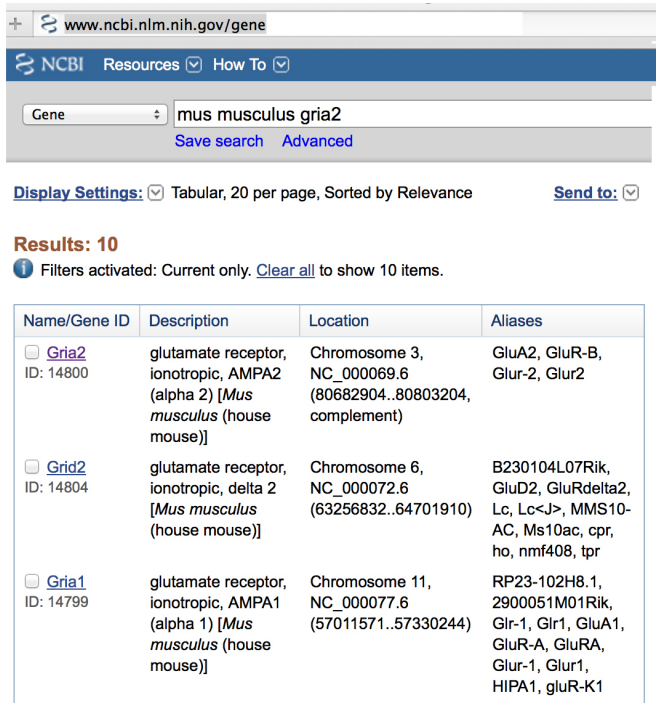
Mouse



Human

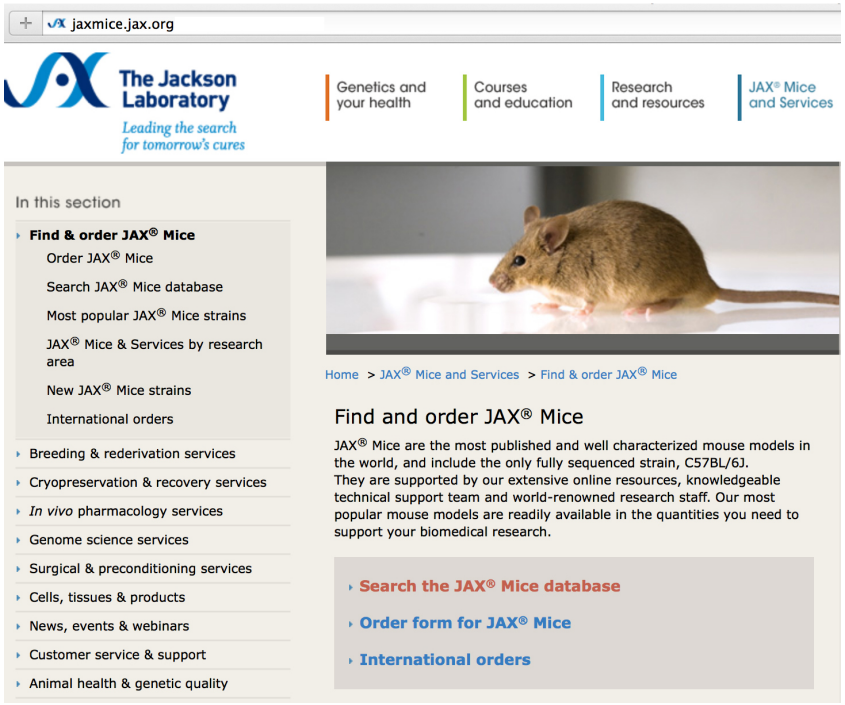
Mouse genetics

www.ncbi.nlm.nih.gov

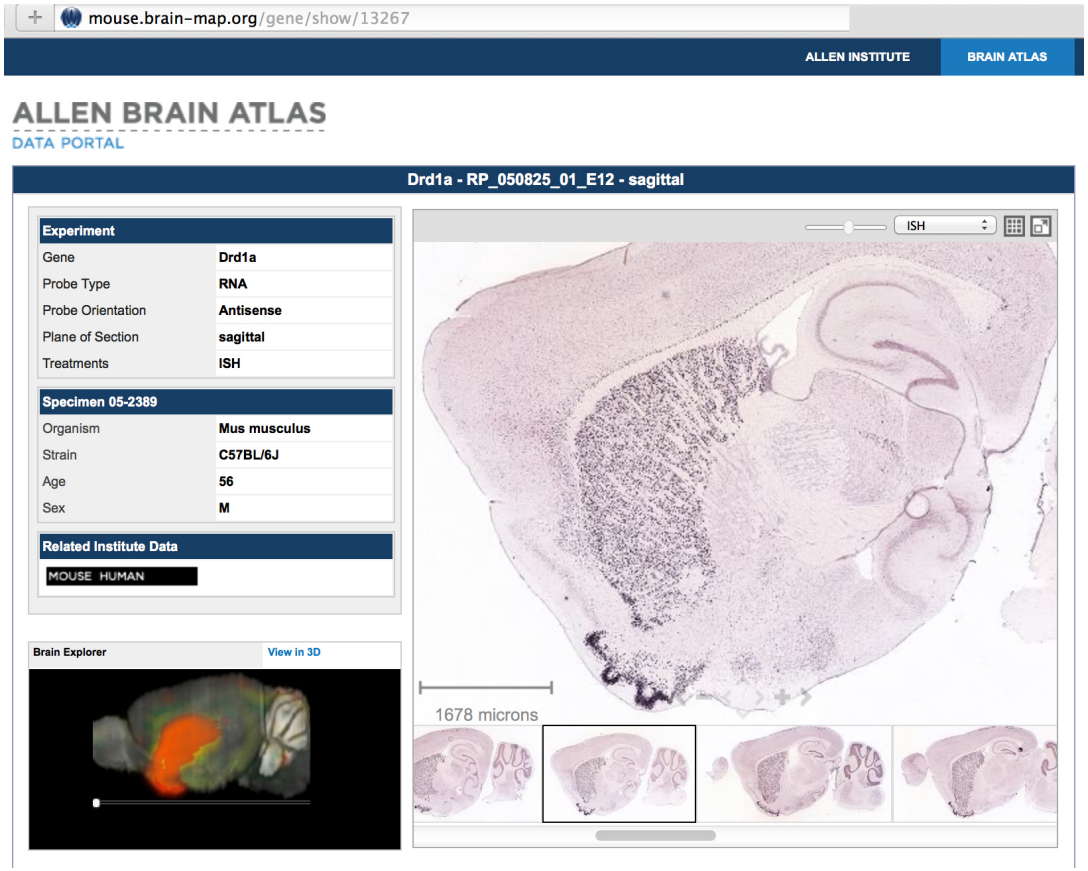


NCBI - National Center for Biotechnology Information

www.jax.org



Gene-expression maps of the mouse brain



www.brain-map.org

Allen Brain Atlas

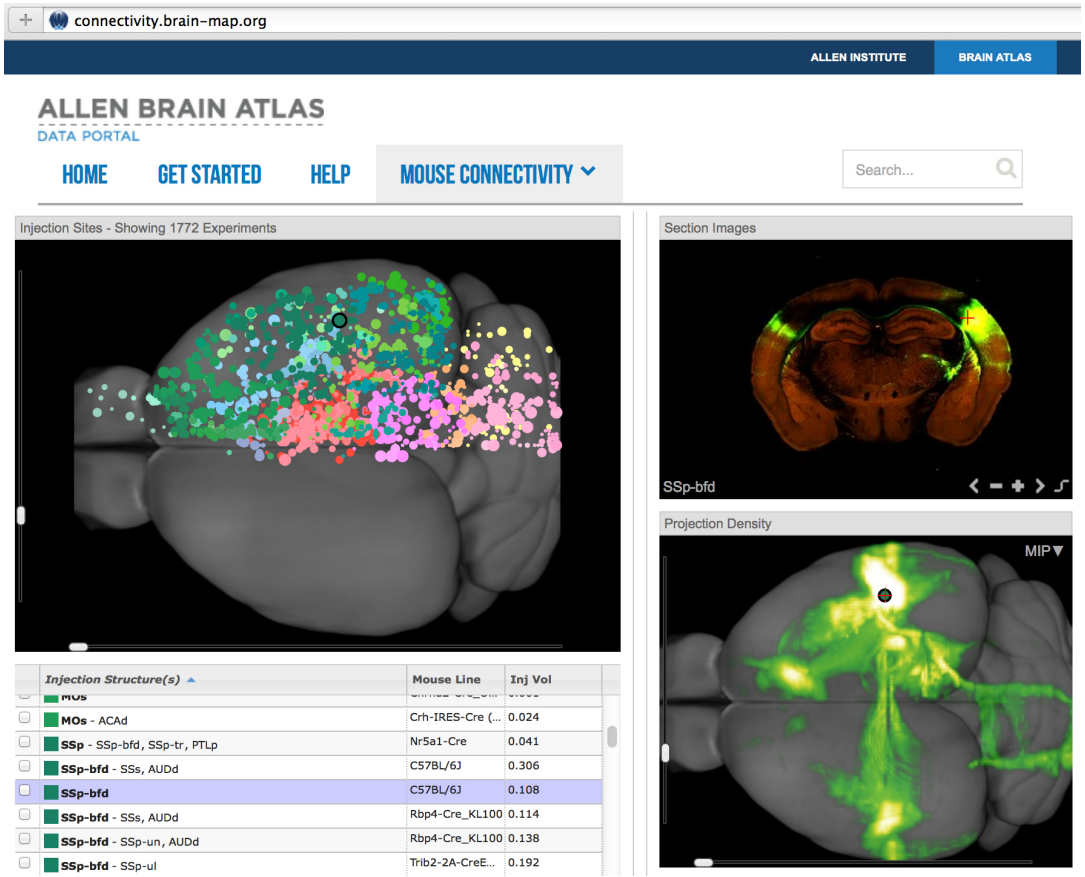
Complete gene expression atlas of the mouse brain.

Genetically-defined cell-types

Transgenic or knock-in of GFP, Cre-recombinase, …
Cre-LoxP system for precise genetic manipulation
LoxP = **ATAACTTCGTATA**GCA**TA**CAT**TATACGAAGTTAT**

Highly-specific genetic manipulation in well-defined cell-types.
Essential for causal and mechanistic understanding of brain function.
Cre-LoxP system is part of a family of recombinases e.g. Flp-FRT

Projection maps of the mouse brain



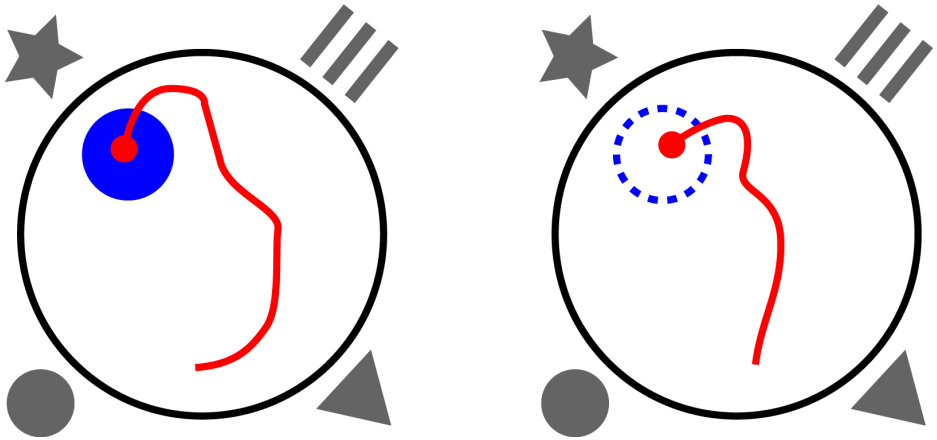
www.brain-map.org

Allen Brain Atlas

Long-range connectivity map of the mouse brain.

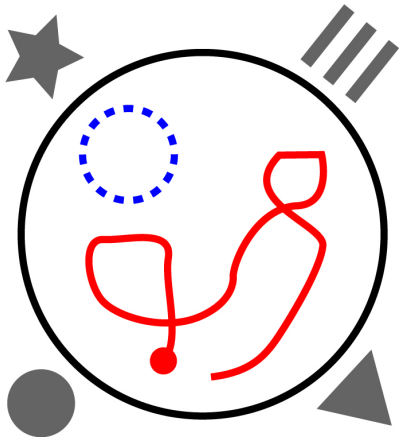
Mouse behavior

Morris water maze

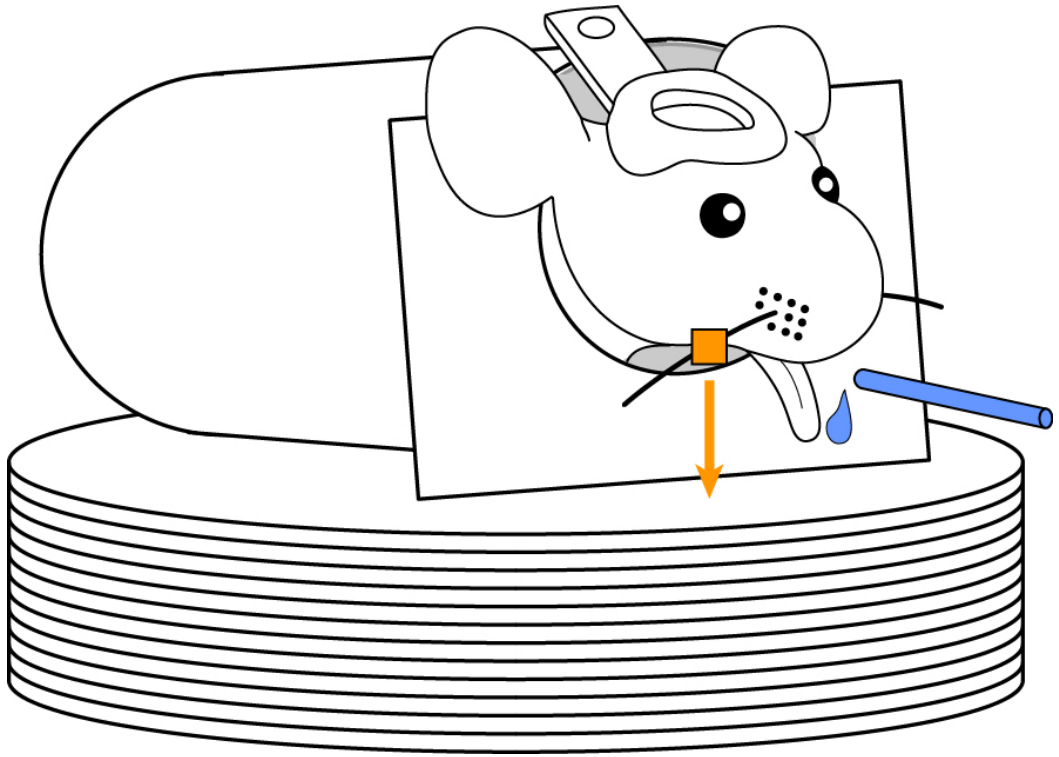


CA1 knockout of NMDA receptors

CA1-Cre
x
Flox-NR1



Head-restrained mouse behavior



Sachidhanandam, Sreenivasan, Kyriakatos, Kremer & Petersen, 2013

Brain dysfunction

Brain diseases make a big impact upon the world,
both at the level of individuals and for society as a whole.

A key goal for neuroscience is therefore to develop better treatments for brain diseases. In order to improve our ability to repair the brain it would be helpful to understand more about it.

Challenge: can we develop *rational* therapies for brain diseases?
Translational neuroscience research: mouse ➔ monkey ➔ man

Cellular mechanisms of mouse brain function

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- Understanding the mouse brain will likely provide clues about the workings of the human brain.
- Large-scale efforts in mouse genetics and brain mapping are helping to accelerate research.
- The mouse is well-suited for detailed causal and mechanistic study of brain function during simple behaviors.