Simon Sprecher in his laboratory in the Department of Biology at the University of Fribourg.

The SynaptiX RTD Project

# Looking into the mechanisms of forgetting

**Within the scope of the SynaptiX RTD Project, scientists are investigating the process of forgetting on the neuronal, genetic and molecular levels. Experiments using fruit flies are to elucidate the function of individual neurons and substances. In the future, the results may form the basis for the development of drugs for ailments such as Alzheimer's disease.**

Strawberries or bananas? The fruit fly has no trouble deciding which odor it prefers. Having learned that following the smell of bananas results in a light electric shock, the fly settles for strawberries.

This olfactory conditioning experiment is part of a first series of experiments performed within the scope of the SynaptiX RTD Project, headed by Simon Sprecher. This biology professor, working at the University of Fribourg, as well as four additional scientists and their teams are investigating the process of forgetting on the genetic, molecular and neuronal levels since May 2013.

## Forgetting so as to learn something new

Simon Sprecher describes the initial situation: "We know where and how information is inscribed in the brain. However, we do not know how this information is stored or how it degrades." In order to be able to investigate the actual research subject, forgetting, the team is first looking into learning processes in fruit flies. At first glance, this might seem paradoxical. But learning and forgetting are tightly linked. "The capacity of the brain is limited. Forgetting helps make room for newly acquired knowledge", explains Sprecher. The areas of the brain responsible for learning processes are therefore most probably also involved in the process of forgetting.

## Fruit flies as model organisms

The current conditioning experiments serve the purpose of understanding changes in the olfactory memory of animals. The fruit fly *(Drosophila melanogaster)* is well suited for these experiments for two reasons. On the one hand, this insect's brain has been extensively studied. On the other hand, its brain resembles that of humans in many respects. "On the molecular level, the ageing process in fruit flies, for instance, is the same as in humans", clarifies Sprecher. "An older fly learns more slowly than a younger one."

In order to be able to learn as much as possible about memory processes, Sprecher and his team vary the experiments. For example, fruit flies are trained to avoid the odor of bananas in a first step, then conditioned to differentiate between the smell of lemons and marzipan. The aim of this experimental setup is to determine the extent to which new knowledge erases previous experiences: will fruit flies still remember that they should avoid the banana odor? Or have they already forgotten what they learned earlier?

Inken Heeb

## A microscope reveals modifications in the brain

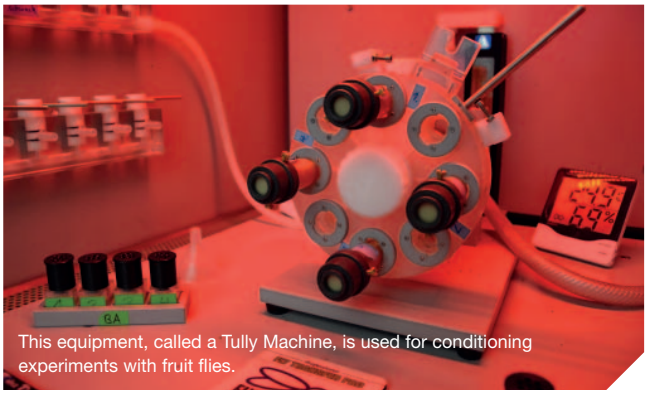
The scientists are most interested in the events taking place in the brain at the molecular level, rather than the behavior of the flies. In order to visualize these processes, Frank Scheffold, a physics professor at the University of Fribourg, has refined a high-resolution light microscope especially for this project. Now, it is even possible to observe processes taking place in the synapses, the links between neurons in the fly's brain.

The experiments using odorants cause alterations in Drosophila's so-called mushroom bodies, important in olfactory memory. Each fruit fly has two such mushroom bodies. They contain 2000 neurons and approximately 13,600 genes each. Only a fraction of these genes are involved in the learning process.

In order to determine which genes are important for learning, the scientists extract various neurons and perform further analysis using transcriptomics. This technique is used to measure which genes are switched on or off during a given process. A database of the presumably essential genes involved in the processes of learning and forgetting is thus generated during the course of the various experiments.

## Tests using genetically modified fruit flies

As the project continues, the scientists will manipulate the genome of the fruit fly by switching certain genes on or off. "By modifying the genes, we want to find out where and how learning and forgetting occurs, and to identify the changes that take place when information is actively substituted", explains Sprecher. These experiments are planned for the next phases of the project which runs until 2017.



This equipment, called a Tully Machine, is used for conditioning experiments with fruit flies.

Providing the scientists can unravel the process of forgetting and can determine which substances in the brain are involved, this knowledge could form the basis for medical research and the development of drugs for ailments such as Alzheimer's disease, an increasingly relevant topic in an ageing society.

### SynaptiX at a glance

Principal investigator: Prof. Simon Sprecher

Research groups:

- Prof. Simon Sprecher, Department of Biology, University of Fribourg – Quantitative behavioral experiments
- Prof. Alex Keene, Department of Biology, University of Nevada, Reno – Quantitative behavioral experiments
- Prof. Walter Senn, Computational Neuroscience, Department of Physiology, University of Bern – Theory of remembering and forgetting
- Dr. Rémy Bruggmann, Bioinformatics and Computational Biology, University of Bern – Transcriptomics
- Prof. Frank Scheffold, Department of Physics, University of Fribourg – Advancement of high resolution STORM microscopy

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Project type: Research, Technology and Development (RTD) Project

**SynaptiX**
Systems Biology of Forgetting