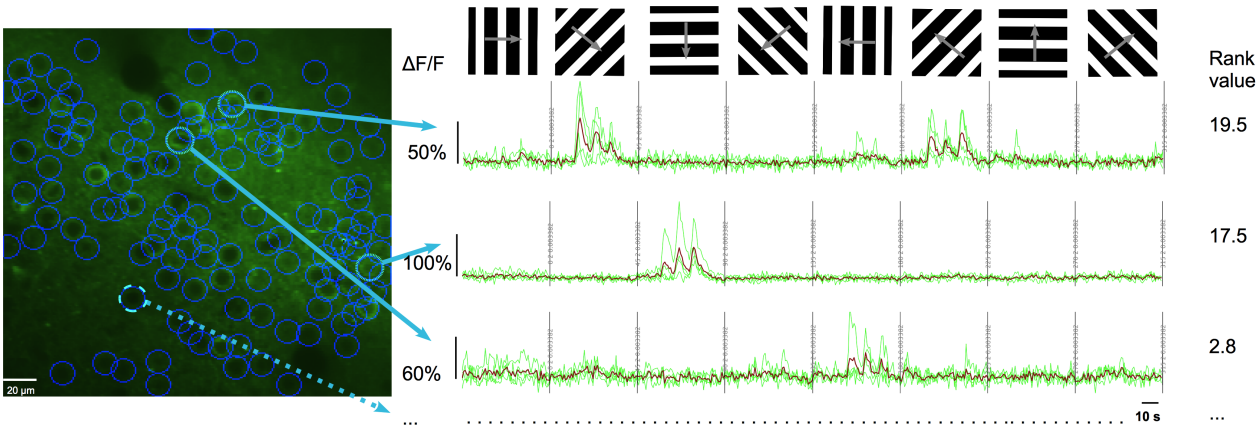
Retinal processing changes at different ambient light levels: rods at low light levels drive different responses than cones which are active at high light levels. Therefore the message sent to the cortex is substantially different at light levels that activate rods versus cones. I worked to find out if cortical circuits compensate or augment these differences resulting in similar or different perception of the same objects at low and high light levels.
The two years of Marie Curie support yielded two main results:

1. I have built a measurement and analysis system that is a prerequisite for recording stimulus evoked calcium dynamics dependent fluorescence change simultaneously from many cells in-vivo.
2. I performed experiments to reveal the differences in cortical processing between dark and light adapted states of the mouse.

The first part of the system I have built solves the problem of presenting complex visual patterns to the animal and perform two-photon imaging at the same time. Based on a commercial two-photon setup I developed the experimental setup and the underlying hardware-software environment.
The second part of the development work was to design and implement the framework and the particular algorithms to automatically analyze the recorded data. Conventional image and signal processing tools could not be directly applied for 4D experiments. To be able to perform experiments I created a completely new algorithm development framework, the structure and the interface of a database in which I store the raw recordings and various display methods to assess the results of the experiments.
I contributed to the development of a new 4D microscope in collaboration with Balázs Rózsa's group in Budapest. The few currently available two-photon microscope designs can scan only images in 2D. However the tissue being imaged contains a 3D network of neurons that process the visual stimulus. The new microscope built within the collaboration will be used to measure activity from thousands of points in space and time (4D) from the cortex.

In parallel to the development of the system, I received the necessary training in biology and attended courses and conferences where I gained an overview of the field and established new contacts. I started to perform experiments that will reveal fundamental properties of how visual information is processed by neuron populations in the primary visual cortex. I worked out the methodology to perform chronic experiments and record activity of neural networks with the genetically encoded calcium sensor GCaMP3.
I imaged in-vivo the calcium signals of many cells using organic Ca indicators or virally delivered genetically encoded Ca sensors in cell populations in layer 2/3 of the visual cortex while stimulating the recorded mouse with moving patterns. My preliminary results show that in cone driven visual conditions the neurons in layer 2/3 are highly specialized and tuned to relevant visual features.



The figure shows one of the experiments I performed. On the left, a section in layer 2/3 of the primary visual cortex is shown. GCaMP3 labeled cells show up in green. The blue circles show cells automatically extracted by my automatic analysis algorithm. Average value of the pixels assigned to individual soma are calculated at each recorded time instance. From the resulting

vectors of averaged responses, repeated blocks for each stimulus direction are grouped together. A rank value is calculated for each cell's fluorescence time course. Cells are sorted along their rank value so that only responsive cells are analyzed further.
Previous studies indicated that the moving bar stimulus is effective in activating cells. Direction selective cells respond only to one particular direction of moving bars, orientation selective cells respond to a given orientation and to the opposite orientation. On the right side of the figure the upper trace shows GCaMP3 responses in a direction selective cell. The middle trace shows responses in an orientation selective cell. The lowest trace shows again a direction selective cell.
Repetitions are superimposed, the mean of the repetitions is shown in dark red. The orientation of the moving stimulus bars are shown at the top.

I facilitated the socio-economic use of the project by publishing the system I have built as an open source project. The insights gained by my experiments can be of potential use to assess visual function in the vision restoration project running in the host laboratory. On the longer term, investigations of the rules of activity in the primary visual cortex might teach us common computational rules in the nervous system.

In conclusion, the project enabled me to learn and deploy a new method that opens a new front in the host laboratory's research and will provide answers to fundamental principles in processing visual information by cortical neural circuits.