**Master's thesis: Robust registration to a template brain for the Drosophila larva**

The Drosophila larva is a model organism for neurobiological research, and registration of light microscopical image stacks of individual brains to an average or typical template brain is an important computational tool for neurobiological data analysis.

Muenzing et al. (Neuroinformatics, 2018) have created a template brain for the Drosophila larva, along with developing a method, "larvalign", for registration to the template. Fully automated high-throughput applications are currently limited by the need for manual, landmark-based corrections of the registration results, and computation time for a single registration is still relatively high.

Fast and robust registration to the light microscopy template brain is thus highly desirable, and the goal of this thesis is to analyze whether learning-based registration strategies can be more robust than larvalign that is not learning-based. Where the latter computes a new deformation field for every image pair to be registered, learning-based strategies, e.g. VoxelMorph (Balakrishnan et al., IEEE TMI, 2019) rely on training examples to learn a function that maps an image pair to a deformation field, and this function improves during training.

While there is often no qualitative advantage with respect to a single registration task, a learning-based approach can gain experience through registration of many variable brains to the same template. This alone can help to regularize the deformation field, in the sense that also outlier brains will be deformed correctly, and we will analyze which registration network (with which parameter settings) is best suited for registration to the Drosophila brain template.

In addition, we will investigate how auxiliary information in the form of landmarked-based corrections (as in Muenzing et al., 2018) can be inserted into the training process. This may be achieved by adding a term involving point correspondences or corresponding segmentation masks to the loss function to be optimized during training. Including such corrections at training time can improve the learning process and it can help to avoid that the same type of registration mistake will be made over and over again, as it is currently the case for larvalign.

Annotated light microscopy data sets are already available from a previous collaboration with Andreas Thum’s group, and further unannotated (the method is self-supervised and does not need annotations) image stacks could be easily provided. At the end of a successful thesis, we will ideally have larvalign 2.0 that could be faster (at run-time, i.e. when fully trained) and more robust than the original larvalign.