1/ Project supervisor:

Name: Maria Alieva

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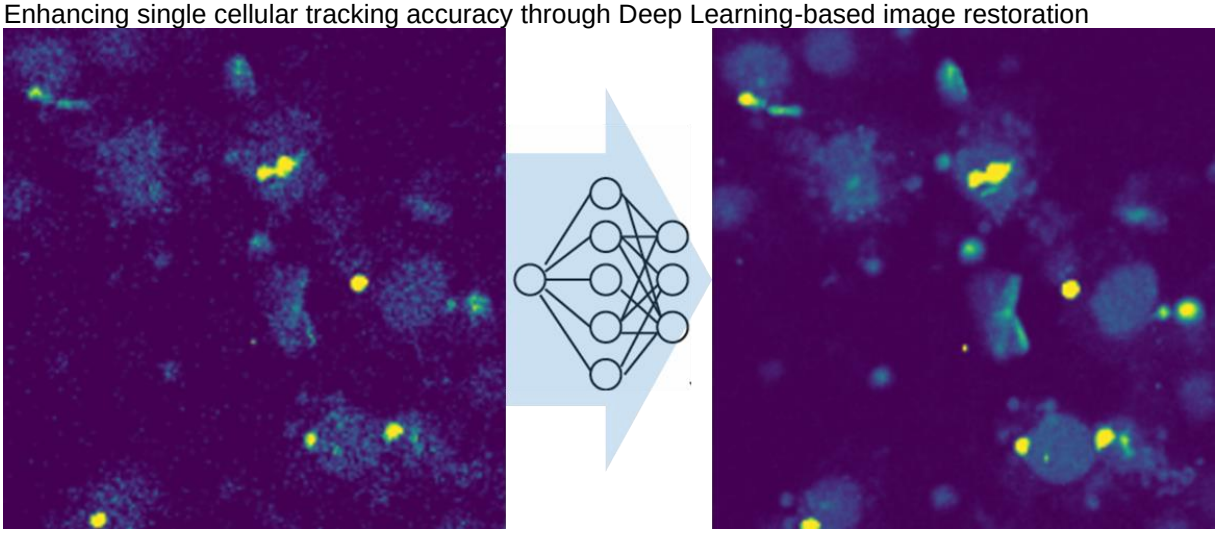
2/ Project title:
Enhancing single cellular tracking accuracy through Deep Learning-based image restoration



3/ Summary:
Live-cell imaging, a crucial tool in understanding dynamic processes within living tissues, utilizes fluorescence microscopy to observe labeled cellular components while preserving viability and function. In oncology research, it proves invaluable for comprehending cancer responses and enhancing treatment outcomes. Our previous work introduced BEHAV3D, a 3D imaging and analysis platform for monitoring engineered T cells targeting cancer. Despite its effectiveness, analyzing live-cell imaging data, especially regarding cellular tracking for parameters like motion, morphological changes, or division, presents considerable challenges. This challenge intensifies in complex scenarios involving modern data, such as organoids, co-culture assays, or tissue imaging, which encompass diverse cell types with varied behaviors and morphologies, exacerbating tracking difficulties. One central issue arises from the trade-off between resolution and tracking precision inherent in live-cell imaging. Capturing sequential images at brief intervals, while necessary for monitoring individual cells over time, compromises image resolution, resulting in diminished quality. Consequently, lower-resolution images pose challenges in segmentation and tracking.

To address these issues, our goal is to develop a user-friendly framework integrated with BEHAV3D that enables training a model to enhance low-resolution images. By implementing a 3D restoration Unet neural network, named CARE3D, in the Google Colab environment, we not only simplify the solution's implementation but also make it accessible to non-coding biologists involved in data analysis. Our internship aims include CARE3D training and model optimization, implementing user-friendly code in Google Colab, and quantifying tracking accuracy with the improved model. We anticipate that these efforts will enhance tracking efficacy, providing deeper biological insights.

4/ References:

- Dekkers, J.F., Alieva, M., Cleven, A. *et al.* Uncovering the mode of action of engineered T cells in patient cancer organoids. *Nat Biotechnol* **41**, 60–69 (2023). https://doi.org/10.1038/s41587-022-01397-w
- Weigert, M., Schmidt, U., Boothe, T. et al. Content-aware image restoration: pushing the limits of fluorescence microscopy. Nat Methods 15, 1090–1097 (2018). https://doi.org/10.1038/s41592-018-0216-7
- von Chamier, L., Laine, R.F., Jukkala, J. *et al.* Democratising deep learning for microscopy with ZeroCostDL4Mic. *Nat Commun* **12**, 2276 (2021). https://doi.org/10.1038/s41467-021-22518-0
- https://github.com/HenriquesLab/ZeroCostDL4Mic

5/ Expected skills:

The successful applicant will get the chance of getting to grips with increasingly essential machine learning methods (deep-learning), but more general skills in 3D image analysis (e.g., image processing, resolution conversion, segmentation, tracking). He/she/they will learn to work with distinct types of data: video data and fixed imaging data. To be successful in this challenging assignment, technical curiosity, persistence and (Python/R) coding skills are indispensable, massive motivation for image analysis even more so.

6/ Bioinformatics human resources (for guiding the computational work):
Dr. Maria Alieva will be the daily the daily supervisor of the student for computational work. Two other computational members of Dr Alieva team guide and support the student. Additionally, the student will be integrated in the computational team of the Rios group and the Prinses Maxima Center (Netherlands), with whom we collaborate on this project and others. We have shared lab and computational meetings (in English), with two-three other computational scientists providing guidance and feedback on the project and a unique opportunity to get integrated into an international scientific environment.

7/ Computational infrastructure:

Most part of the project is expected to be carried on the personal laptop of the student, with remote connection to HPC, Google Colab Pro account (with more potent GPUs available) or 2-3 high-end workstations (shared resources of the team).

8/ Possibility of funding:

Although funding is not anticipated for this TFM, there is potential for further opportunities, such as pursuing a Ph.D. or securing a research assistant position in the group.