COncISE
COmputatioNal Imaging as a training network for Smart biomedical dEvices

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**Issue 1**
*August 2024*


# DC NEWSLETTER



Funded by the European Union

Engineering and Physical Sciences Research Council

Funded by the European Union (GA 101072354). Views and opinions expressed are however those of the author(s) only and do not necessarily reflect those of the European Union or the European Research Executive Agency. Neither the European Union nor the granting authority can be held responsible for them.
UK participants are funded by UK Research and Innovation (UKRI) under the UK government's Horizon Europe funding guarantee grant number EP/X030733/1).

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# OVERVIEW

The primary purpose of this newsletter is to share information about ongoing research, project objectives, and the daily experiences of PhD students, as well as to provide updates on their participation in conferences and events!

If you are not yet familiar with the CONcISE Project, the first article of this newsletter provides an overview of its rationale and objectives. It provides a straightforward explanation of the scientific background of the project, along with details about its funding, collaborations, and participants.

In the second article, John shares his personal experience of pursuing a PhD within a high-tech company. He offers a view of the blend of academic rigour and industrial dynamics, of his daily work routine, and the challenges and rewards of this dual environment.
Next featured are insights from our dedicated PhD student Shiva who shares updates on their research progress. Shiva provides updates on advancements in the Single-pixel microscope.

Following the research update, we present the recent participation of Samuel and Heberley at the Adaptive Optics for Industry and Medicine XIII (AOIM) conference, which took place in Padua, Italy, from March 11 to 15, 2024. This article shows that scientific conferences offer more than just opportunities for knowledge exchange and professional networking. They also provide chances to travel, explore “locales molto belos” and meet friends!

In the penultimate Lindsey shares updates about a SMART-2PM paper Heberley, Samuel, and herself have been working on. To conclude the first issue of the newsletter, Aapo approaches the field of biomedical imaging and its role in medical diagnostics and research. He presents a discussion about the technique of semantic segmentation and how convolutional neural networks, such as U-Net, are revolutionising this field. He also introduces nnU-Net, an innovative method of automating the image segmentation process, making it more accessible and efficient. In this article, you will discover what these technologies are and how they are shaping the future of biomedical image analysis!

We hope that you have a great time reading our newsletter and that it can provide you with new insights into a researcher's life, career perspectives and lots of scientific learning!

The CONcISE DCs

# THE CONCISE WAY OF IMAGING

The extensive use of imaging techniques, which are used to extract information from objects of interest such as the human body, microorganisms, or black holes, has been instrumental in addressing challenges in various fields including medicine, biology, and astronomy. Under certain principles, each of these evolving fields has developed its own set of tools to achieve goals, and even within the same one, methodologies are often difficult to relate. The available data, massive in most cases, eventually leads to a problem in its usage, due to its collection regardless of the quality, making it difficult to manage, transfer and analyse.

In biomedical imaging, translating research developments in image processing and analysis to healthcare devices often raises important questions. These include whether changes to current technology should be implemented, considering the potential benefits to both the patient and the provider. Concerns can be addressed when a proper back-and-forth relation between computational experiments and real data from an experimental setup exists.

The CONcISE network aims at reconciling the usage of biomedical data in two main paths. Using ‘information bandwidth’ compression in the construction of sources and detectors, some of the main components of an imaging system, the acquisition can be greatly improved. On the other hand, an adaptive decision at the time of acquiring regards for the most informative sampling based on previous data promotes a differential speed-up on current non-adaptive schemes provided the amounts of available data for data-driven assistance.

By dividing into specialised groups, the doctoral candidates can tackle specific challenges within biomedical imaging, each contributing to the broader goal of improving imaging techniques and applications. In the next page, the CONcISE specialised groups are presented.

**SMART-DOT:**

- **Objective:** Simultaneous mapping of absorption and scattering in thick biological tissues at different wavelengths.
- **Applications**: Non-invasive techniques such as optical mammography and brain functional imaging.

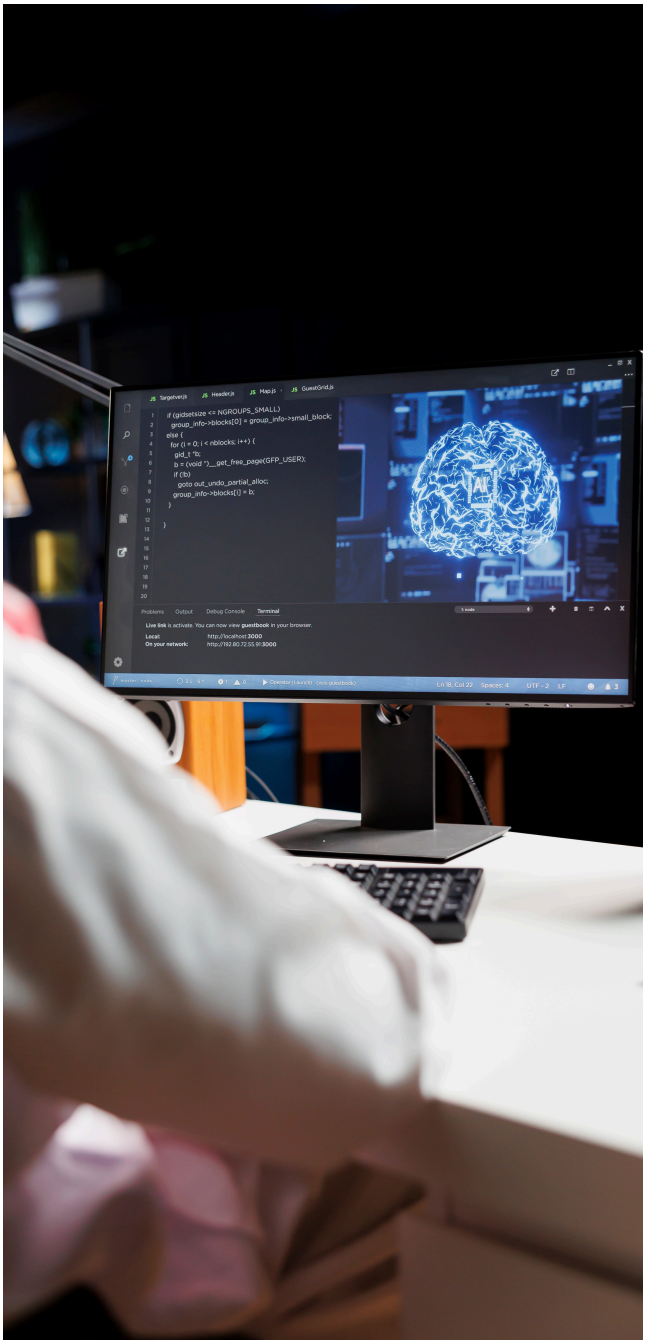
**SMART-FLUO:**

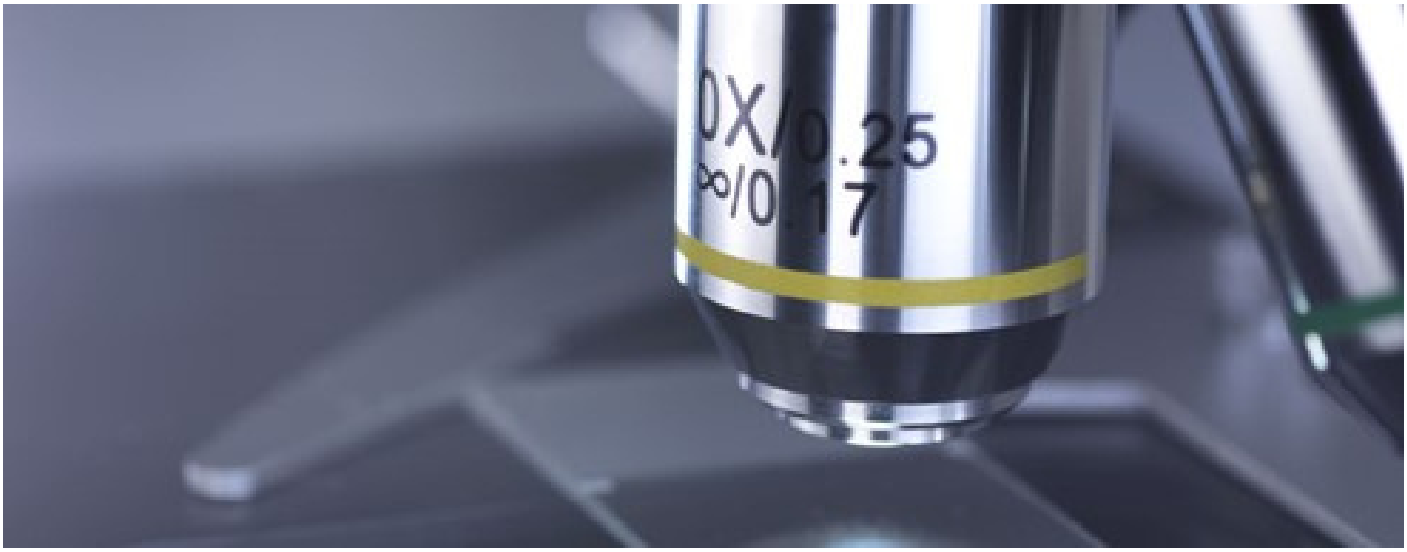
- **Objective:** Multispectral fluorescence imaging for endoscopy.
- **Technique:** Usage of structured light illumination.
- **Orientation:** More clinically oriented goal.

**SMART-2PM:**

- **Objective:** Possibility of wide-field 2-photon microscopy.
- **Techniques:** Light-structured illumination, integrated detection, and computational imaging.
- **Enhancements:** Improve penetration depth, sensitivity, and imaging speed.

Within the CONcISE network, led by the Consiglio Nazionale delle Ricerche, eight beneficiaries and four associated partners from 8 European countries participate in the development of several intersectoral programmes, providing doctoral candidates with a wide range of multidisciplinary formation in the academic and industrial sectors organised in the form of ‘topical schools’. So far these events have fostered a collaborative environment of knowledge sharing and skill development.






# SINGLE-PIXEL IMAGING MICROSCOPE

## Capturing light with patterns and a computer

We have all used a camera. In fact, with the rise of TikTok and Instagram, images are the rage of the day. Billions of photos and videos are made every day and uploaded on the internet. But have you ever wondered how your smartphone's camera works?

A digital camera is made of some lens and a sensor (and many other technical things that we do not care about) – See Figure x. The sensor is in fact a grid of light-sensitive detectors that convert light into digital image data. Each detector usually corresponds to one “pixel” of the image. To make a video, the sensor must take multiple images called “frames” (usually 24 to 60 per second), and then stitch them together into one continuous “movie”. Advancements in technology have made this complicated device cheap to make so that we have decent cameras even in affordable smartphones.

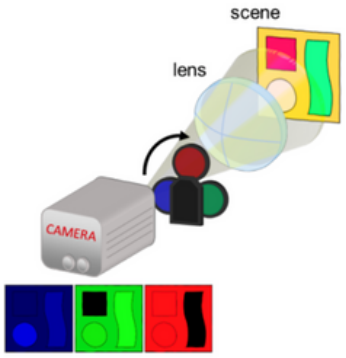



*Figure 1. Digital camera sensors and lenses*

But we cannot use such cameras to capture processes in say, living cells in a microscope, which occur in the billionth of a second! Or those that emit light over a wider spectrum than the red, green and blue (RGB) typical of a colour photo. For imaging such phenomena, we need special detectors which are fast and can even capture invisible light such as infrared. Unfortunately, they do not come cheap; making a grid of special detectors costs much more than a commercial-grade camera sensor.

> *Processes in living cells in a microscope occur in the billionth of a second!*

## Single-pixel imagining

This is where this new technique of single-pixel imaging comes in. In this method, instead of using an expensive grid of detectors, light from the entire scene is collected with a lens into a single, high-performance detector. The scene is illuminated with special, checkered patterns (See Fig. 2) instead of plain light so that details of the object are preserved. Taking multiple images with different patterns and doing a mathematical computation allows us to retrieve the original image, now enriched with the added time and spectrum data.

The simple reason this works is the principle of compression. A typical photo that we capture with our smartphone camera is stored as a JPEG, which is a highly compressed format for storing the actual digital data captured by the sensor. This is possible because the latter has a lot of redundant information.

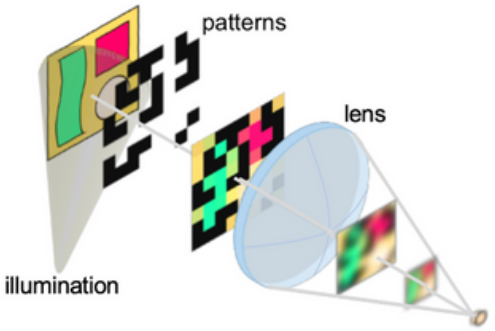



*Figure 2. Checkered patterns*

A single-pixel camera (SPC) tries to do the reverse: it directly captures the compressed information from the scene, by illuminating only parts of it at a time. This is known as *Compressed Sensing.*

> *The single-pixel camera tries to directly capture compressed information from the scene*

Thus, an advantage of this method, apart from the lower cost, is that we can decide the level of compression in advance. A smaller number of patterns means more compression and faster acquisitions; but with lower image quality. More patterns lead to better quality but takes longer to capture. One main goal of the CONcISE project is to improve the speed and reliability of this method, to make it usable for imaging live tissues during surgeries.

The main challenges are choosing the most optimal patterns for illuminating the scene and computing the real image in a reasonable time. We have recently discovered that using Machine Learning (the same technique that powers modern AI apps) can improve the performance of the SPC on both fronts. Currently, we are experimenting with integrating this new approach with the traditional single-pixel imaging microscope.

# A DAY IN LIFE AT FYLA

## John's Industrial PhD Experience

Often, students transition from university to industry after completing a degree, with a range of skills that prepare them for acquiring new specialised skills, relevant to their future workplaces. However, in academia, students are exposed to a teaching methodology within a controlled environment that does not properly represent the skills required for a real-world job. For this reason, the transition to an industrial real-world environment that requires fast, robust, inexpensive, and compact solutions can be challenging without a gradual adaptation period. In this scenario, an industrial PhD is a good alternative, allowing students to learn inside a workplace scenario and providing training that significantly increases their value to a company upon completion, compared to a traditional university-based PhD.

*Figure 3. John Rosses Monge*

My name is John (Fig. 3), and this is my case at FYLA. I am currently doing my PhD in a high-tech company specialised in the fabrication of fibre lasers. From my perspective, this experience feels different from just completing a study degree; As in a job, I have well-defined working hours, from 8 am to 5 pm, which gives me discipline in my doctoral studies. Besides, interacting with people who understand how the industry works and having a clear objective for my PhD investigation is invaluable.

The activities I undertake for this company are an important part of my studies, learning the physics behind specific products. It involves a lot of engineering, mechanics, electronics, and photonics working together. Unlike my previous experience in university labs, where I had to find solutions by myself or seek help, here I have a team ready to assist with any problem. A typical day begins with clocking in using Factorial, a software that tracks working hours and activities of the employers. After planning my day, I start with activities related to my PhD project or help my colleagues with their tasks. Although collaborating on different projects is beneficial as it provides me with a lot of knowledge, it sometimes leaves me with less time for my own research. However, this balance prepares me for my professional life, reminding me that the PhD is just another step, not the end goal. One positive aspect is that I have a particular role within the company as a student, and this is respected in terms of my responsibilities. Gradually, I am gaining more participation in other projects with my partners, and I am grateful to be here because of the supportive environment.

Team-building activities are another highlight, providing a break from daily pressures and allowing for casual interaction with colleagues, making the day more enjoyable. At the end of the day, I can leave my work for the next morning, which the discipline helps manage, recharging my energy for the next day.

Overall, my experience at FYLA is enriching, blending academic pursuits with practical industry experience, and personal and professional growth are in equilibrium.

# EVENTS ATTENDANCE

## Adaptive Optics for Industry and Medicine XIII

Our researchers, Heberley Tobon-Maya (DC6) and Samuel I. Zapata-Valencia (DC7), presented their preliminary research results on adaptive optics for non-linear microscopy of work package 3 (WP3) at the Adaptive Optics for Industry and Medicine XIII (AOIM) workshop held from March 11 -15, 2024 in Padua, Italy. The AOIM and the Industry Demo Center took place in Padua, organized by the Institute of Photonics and Nanotechnology of Padova (IFN-CNR) and Dynamic Optics. This conference was divided into two engaging parts. The first part, the Demo Center, focused on adaptive optics technologies. Heberley and Samuel received hands-on experimental training with wavefront modulators, sensors, and control systems, guided by Dr. Stefano Bonora, also a supervisor in the CONcISE project, and experts from Dynamic Optics.

In the second part of the AOIM conference, participants provided insightful sessions about their current work related to adaptive optics methods and applications. Samuel presented his preliminary research results on a method for automatic focusing of images recorded using bucket detectors in single-pixel microscopy, while Heberley presented his initial research findings on the presence of aberrations in the projected patterns used in single-pixel microscopy.

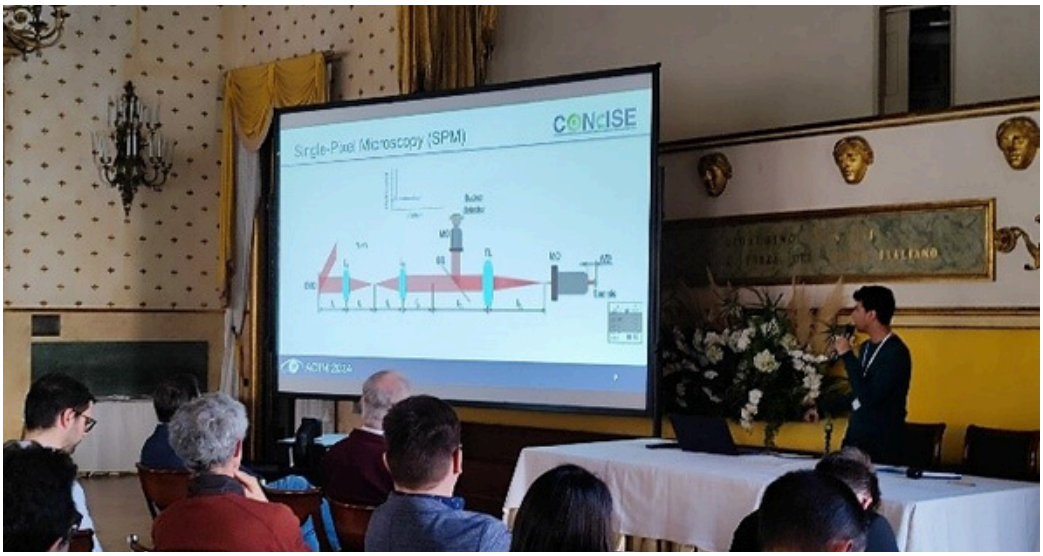



*Figure 4. Samuel presenting latest research on adaptive optics for non-linear microscopy.*

The AOIM in Padua also offered cultural experiences for attendees. The conference was hosted in the Egyptian Hall of Caffe Pedrocchi, an important historical site since the late 18th century, known for hosting numerous meetings, including scientific and secret gatherings. Participants also had a guided tour of La Specola, the astronomical observatory of Padua, where the astronomical history of the region was explained and its importance for the field was highlighted. Besides the historic places, the conference attendees had the opportunity to visit the Dynamic Optics company in northern Padua. There, they were given a tour of the company's facilities, where deformable mirrors and transmitted wavefront modulators are built.

The AOIM was an excellent opportunity for a collaborative meeting with Lyndsey Willstatter (DC8), a member of IFN-CNR and part of the AOIM organisation team (See Fig. 5). We discuss the next steps in our collaboration for Work Package 3 in the field of adaptive optics developments for non-linear microscopy and single-pixel microscopy. Additionally, we made plans for Lyndsay's upcoming secondment to Universitat Jaume I in the next few months.

*Figure 5. Samuel (left), Heberley (centre) and Lyndsey (right) in La Specola, the astronomic observatorium of Padua.*

# SINGLE-PIXEL MICROSCOPY

Expanding on the results and presentations at the AOIM conference, Heberley submitted a paper for the Optical Imaging Congress being held in July. The paper is titled “Reconstructionless autofocus method for Hadamard-based single-pixel microscopy” (See Fig. 5). The paper is co-authored by Samuel and Lindsey Willstatter along with their advisors, Enrique Tajuerce, Jesus Lancis, and Stefano Bonora.

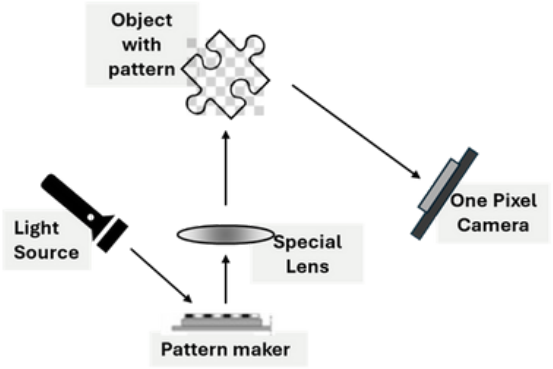



*Figure 6. Reconstructionless autofocus method for single-pixel microscopy*

Single-pixel microscopy is the idea that instead of having millions of little dots to take pictures you only have one dot to take the picture. To then make the picture again there are a few ways, one is to move the camera along and take pictures in a line and then combine them all. Or as Heberley did, was to use different special light patterns and use some special computer programming to combine the different special patterns like a puzzle and make the picture.

But if a puzzle is not cut well the pieces won’t fit together similarly it is the same for the special light patterns. If the light patterns are blurry, we won’t get a good picture. We looked at a new way to fix the blurriness without having to combine all the light patterns and make the image. We did this both using a computer to show the process and in a real experiment.

To fix the blurriness we use a special lens that can change shape. We only use a few light patterns to find the best shape of the special lens. We looked at the total brightness of the light pattern and found when it was the biggest. This meant that the blur was the smallest. We found on average it took 10 repetitions to find the best point. To show this in the laboratory we used a target that has different patterns to see how well the process works. Below shows a few repetitions of the method in action (See Fig. 7). You can see how the special lens makes the patterns the least blurry.

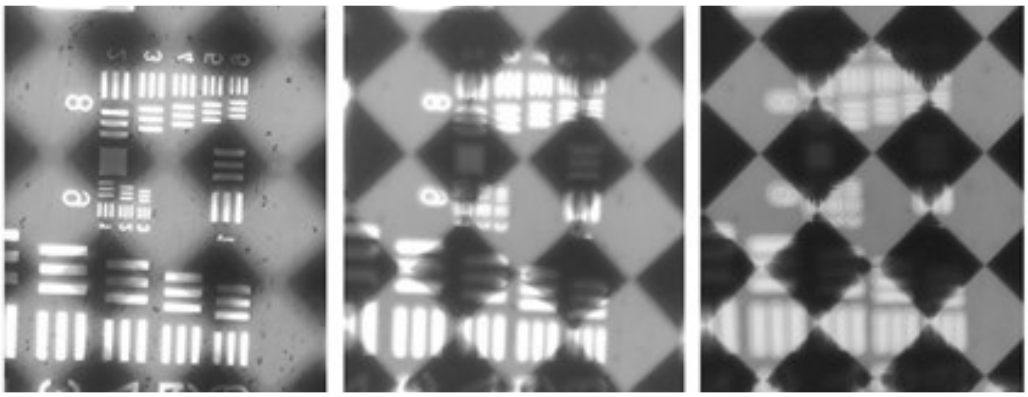
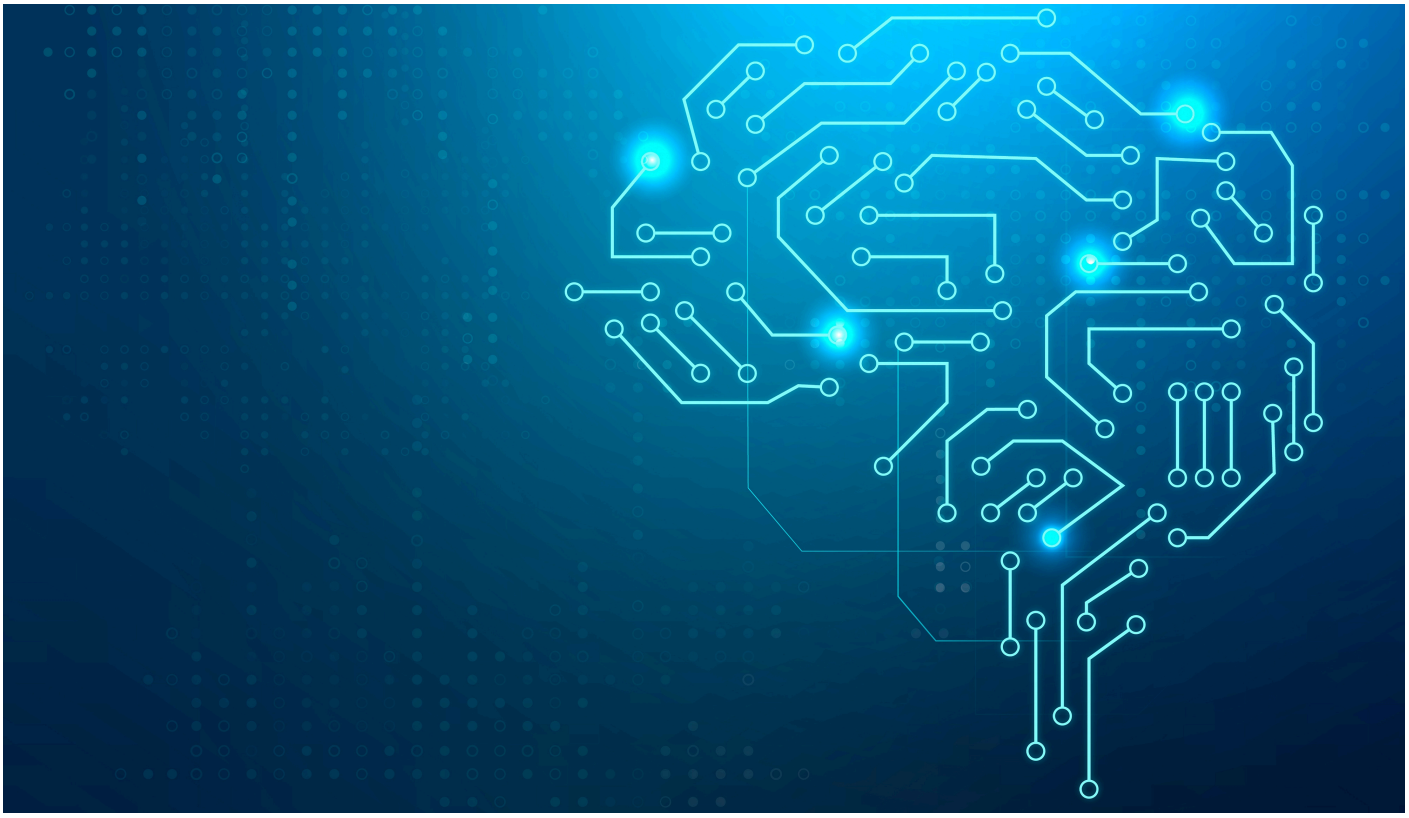


*Figure 7. Repetitions of the reconstructionless autofocus method*



# MAKING DEEP LEARNING DEMOCRATIC

Biomedical imaging, including methods such as magnetic resonance imaging (MRI), computed tomography, and ultrasound, plays a significant role in medical diagnostics and research. Semantic segmentation, an important technique within this field, involves partitioning images into meaningful segments and assigning labels to each pixel based on the object or region it represents. This segmentation provides detailed maps of various structures, such as different tissue types and anomalies like cancerous tissues.

Accurate semantic segmentation relies on understanding the contextual and spatial relations within images. When automated it often relies on convolutional neural networks (CNNs), advanced machine learning algorithms adapted to recognise patterns in images. One of the most notable CNN architectures currently used for biomedical imaging tasks is U-Net, named due to its U-shaped architecture.

CNNs are well-suited for semantic segmentation due to their ability to automatically learn hierarchical features from raw pixel data. Through the usage of multiple layers of convolution and pooling operations, CNNs extract abstract representations of images, capturing both low-level details and high-level contextual information. This enables CNNs to accurately localise objects and define their boundaries.

Leveraging CNNs for semantic segmentation however typically requires manual configuration of hyperparameters, which modify the model's architecture and learning process. This manual tuning poses a significant barrier, particularly for non-experts, limiting the technology's broader usability.

To address this challenge, researchers at Heidelberg, Germany, developed nnU-Net in 2020, an automated method for configuring U-Net for image segmentation tasks. nnU-Net streamlines the segmentation process by automatically adjusting parameters, and settings based on the provided dataset, eliminating the need for


manual tuning. It also modifies the dataset itself to extract all the informational value from it by normalising, reshaping and if needed upsizing it. This self-configuring approach enhances adaptability to diverse datasets and imaging modalities, making segmentation more accessible. Demonstrating its efficacy across various biomedical imaging tasks, including MRI analysis and cell microscopy, nnU-Net has surpassed many existing approaches, highlighting its potential to enhance image analysis in healthcare and research. Its success, underscored by the widespread adoption and subsequent citations, reflects a broader trend in the field towards democratising image analysis and making advanced techniques accessible to all.

Since U-Net's inception in 2015, there have been over 18000 citations to that first paper. Based on U-Net most researchers have opted to design their own architecture specific to their needs. The proliferation of research and technologies like nnU-Net however suggests a growing audience of more casual people interested in the field, a clear milestone in this maturing field.

At CONcISE, our research tackles increasingly complex imaging problems, and while its results will not be as easily applicable to a wider audience, there is a hope it will inspire further developments in creating user-friendly solutions for increasingly intricate challenges. As these technologies evolve, they hold the promise of unlocking new insights and discoveries in biomedical imaging, thus benefiting society.

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