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# 10,000 times faster than traditional methods: new computational framework automatically discovers experimental designs in microscopy

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**For human researchers, it takes many years of work to discover new super-resolution microscopy techniques. The number of possible optical configurations of a microscope — for example, where to place mirrors or lenses — is enormous. Researchers at the Max Planck Institute for the Science of Light (MPL) have developed an artificial intelligence (AI) framework which autonomously discovers new experimental designs in microscopy. The framework, called XLuminA, performs optimizations 10,000 times faster than well-established methods. The researchers' work was recently published in "Nature Communications".**

Currently, optical microscopy is most widely used in the biological sciences. The ingenuity and creativity of human researchers have led to the discovery of super-resolution (SR) methods, which overcome the classical diffraction limit of light at about 250 nm and enable one to resolve the organization of the smallest functional units of cellular life. Finding new microscopy techniques has traditionally relied on human experience, intuition and creativity — a challenging approach given the vast number of possible experimental optical configurations. For example, if an optical setup consists of just 10 elements, chosen from 5 different components such as mirrors, lenses, or beam splitters, there are already more than 100 million unique configurations. The complexity of this space suggests that many powerful techniques may remain undiscovered, and human intuition alone might not be enough to find them. This is where AI-based exploration techniques could be of enormous benefit, exploring this space in a fast and unbiased way. "Experiments are our windows to the Universe, into the large and small scales. Given the sheer enormously large number of possible experimental configurations, its questionable whether human researchers have already discovered all exceptional setups. This is precisely where artificial intelligence can help", explains Mario Krenn, head of the "Artificial Scientist Lab" at MPL.

To address this challenge, scientists from the "Artificial Scientist Lab" joined forces with Leonhard Möckl, a domain expert in super-resolution microscopy and head of the "Physical Glycoscience" research group at MPL. Together, they developed XLuminA, an efficient open-source framework designed with the ultimate goal of discovering new optical design

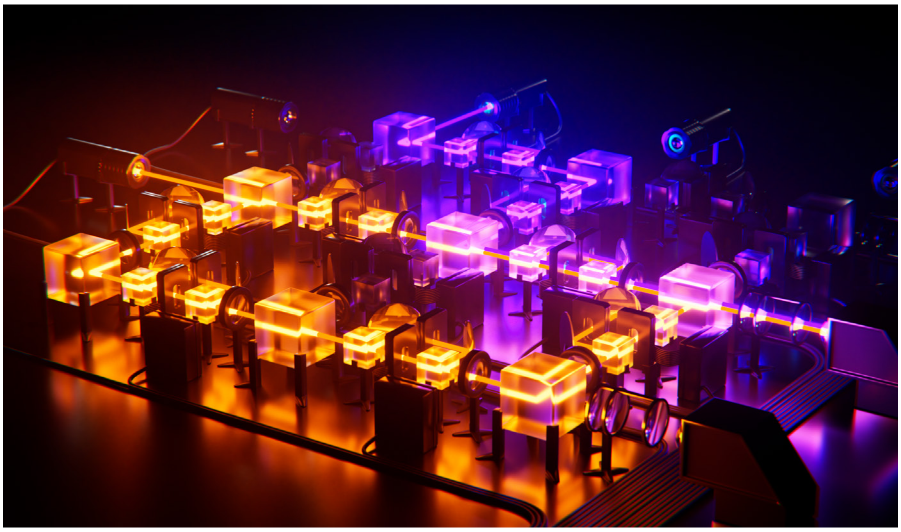

Illustration made by Long Huy Dao and Philipp Denghel

Artistic visualization of XLuminA's automated optical discovery process. The setup shows laser beams being guided through a network of optical elements including beam splitters, spatial light modulators and mirrors. This represents how XLuminA explores vast experimental configurations to discover novel super-resolution microscopy techniques. The glowing paths highlight the system's ability to find optimal routes for light manipulation automatically, enabling breakthrough optical designs previously unexplored by human researchers.



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principles. The researchers leverage its capabilities with a particular focus on SR microscopy. XLuminA operates as an AI-driven optics simulator which can explore the entire space of possible optical configurations automatically. What sets XLuminA apart is its efficiency: it leverages advanced computational techniques to evaluate potential designs 10,000 times faster than traditional computational methods. "XLuminA is the first step towards bringing AI-assisted discovery and super-resolution microscopy together. Super-resolution microscopy has enabled revolutionary insights into fundamental processes in cell biology over the past decades – and with XLuminA, I'm convinced that this story of success will be accelerated, bringing us new designs with unprecedented capabilities", adds Leonhard Möckl, head of the "Physical Glycoscience" group at MPL.

The first author of the work, Carla Rodríguez, together with the other members of the team, validate their approach by demonstrating that XLuminA could independently rediscover three foundational microscopy techniques. Starting with simple optical configurations, the framework successfully rediscovered a system used for image magnification. The researchers then tackled more complex challenges, successfully rediscovering the Nobel Prize-winning STED (stimulated emission depletion) microscopy and a method for achieving SR using optical vortices. Finally, the researchers demonstrated XLuminA's capability for genuine discovery. The researchers asked the framework to find the best possible SR design given the available optical elements. The framework independently discovered a way to integrate the underlying physical principles from the aforementioned SR techniques (STED microscopy and the optical vortex method) into a single, previously unreported experimental blueprint. The performance of this design exceeds the capabilities of each individual SR technique. "When I saw the first optical designs that XLuminA had discovered, I knew we had successfully turned an exciting idea into a reality. XLuminA opens the path for exploring completely new territories in microscopy, achieving unprecedented speed in automated optical design. I am incredibly proud of our work, especially when thinking about how XLuminA could help in advancing our understanding of the world. The future of automated scientific discovery in optics is truly exciting!", says Carla Rodríguez, the study's lead author and main developer of XLuminA.

Picture taken by Jan Olle

Dr. Carla Rodríguez, scientist in the research group of Dr. Mario Krenn at MPL.

The modular nature of the framework allows it to be easily adapted for different types of microscopy and imaging techniques. Looking forward, the team aims to include nonlinear interactions, light scattering and time information which would enable the simulation of systems such as iSCAT (interferometric scattering microscopy), structured illumination and localization microscopy, among many others. The framework can be used by other research groups and customized to their needs, which would be of great advantage for interdisciplinary research collaborations.



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*Research at the Max Planck Institute for the Science of Light (MPL) covers a wide range of topics, including nonlinear optics, quantum optics, nanophotonics, photonic crystal fibres, optomechanics, quantum technologies, biophysics, and – in collaboration with the Max-Planck-Zentrum für Physik und Medizin – links between physics and medicine. MPL was founded in 2009 and is one of the over 80 institutes that make up the Max Planck Society, whose mission is to conduct basic research in the service of the general public in the natural sciences, life sciences, social sciences and the humanities.*



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