

21st century revolution: Smart Robotic AI aided Microscopy (SRAIM)

Imaging

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Objective: Optical microscopy is one of the leading biotechnologies because it allows the study of live organisms. Its future in 21st century will be determined by the innovative technology solutions enabling researchers new applications. New hardware innovations including IOT, AI, and lab robotics technologies may turn microscopes into devices similarly autonomous as self-driving cars. In this work, we critically review the different strategies by which new optical hardware, lab robotics, and AI may produce faster, more reliable, and reproducible results, as well as the limitations of these strategies. Methods: We analyzed hundreds of publications from the past 5 years on new microscopy trends and participated in live and remote demos of multiple microscopy systems by leading manufacturers. Additionally, we performed an in-depth analysis of the innovations in fluorescent probes/labels and spectral imaging-based super-multiplexing. Results: Lab robotics is very important, because manual sample prep and handling typically takes the largest fraction of total experiment and researcher time. Optical hardware innovations most directly enable new applications and allow obtaining better results faster. Image analysis and AI-based technologies may allow a broad spectrum of new applications, but they typically require extensive setup. The abundance of available fluorescent probes (cell viability, membrane potential, $[Ca^{2+}]_i$, pH, DNA, optical mapping, protein interaction by FRET and optical tweezers, NIR/IR dyes, etc.) potentially allows simultaneous imaging/measurement of multiple cell and environment parameters; however, spectral overlap limits the number of reliably detected colors to 4-8. Further discrimination between spectrally overlapping dyes may be done by FLIM techniques but it requires special add-on hardware and software. Additional information may be collected in "label-free" mode (brightfield, phase, DIC).

Conclusions: High-level automation of robotics and AI-based analysis may dramatically speed up experiments, facilitate high-throughput applications, and allow researchers to focus on creative tasks like formulating and testing hypotheses and building theories.