Methods and areas worth watching

Deep learning in imaging

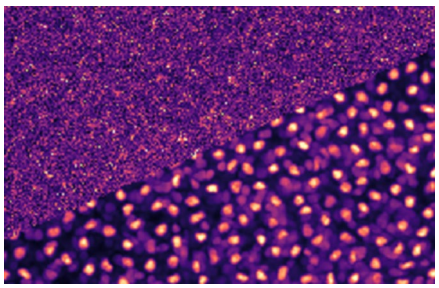
Machine learning approaches that include deep learning are moving beyond image classification to change the way images are made.

Computers are powerful tools for carrying out tasks such as image classification or identification as well as or better than human experts. Conventional machine learning approaches are widely used for segmentation and phenotyping in fluorescence microscopy. These tools are now being largely outperformed by their deep-learning-based counterparts, some of which are available as user-friendly tools (*PLoS Biol.* **16**, e2005970, 2018; *Nat. Methods* **15**, 677–680, 2018; *Nat. Methods* https://doi.org/10.1038/s41592-018-0261-2, 2018).

But a perhaps more astonishing wave of developments has recently come about through the use of deep learning not for image analysis but for image transformation. In these cases, deep convolutional networks are trained to transform one type of image into another. For example, two studies have shown the power of deep learning for the creation of fluorescence micrographs of cells directly from bright-field or phase images, to facilitate multiplexed and longitudinal imaging (*Cell* **173**, 792–803, 2018; *Nat. Methods* **15**, 917–920, 2018). Researchers have also used deep learning to go from low signal-to-noise images to high-quality images, which opens the door to extended imaging of even very light-sensitive living organisms (*Nat. Methods* **15**, 1090–1097; 2018).

Deep learning can similarly overcome obstacles associated with super-resolution microscopy. Two approaches, ANNA-PALM and DeepSTORM, were developed to improve the speed of localization microscopy, which is one of the major hurdles of the technique (*Nat. Biotechnol.* **36**, 460–468, 2018; *Optica* **5**, 458–464, 2018). Deep learning can also enable cross-modality imaging, where applications such as a shift from confocal images to stimulated-emission-depletion-microscopy-resolution images could democratize super-resolution imaging.

As with any method, the caveats associated with deep learning in such applications, such as the potential for artifacts, must be carefully considered and analyzed. Nevertheless, we think we have seen only the tip of the iceberg, and that deep learning stands to improve all aspects of imaging, from acquisition to analysis. ❐



Images of a planarian before (top) and after (bottom) content-aware image restoration. Credit: M. Weigert, T. Boothe, and F. Jug

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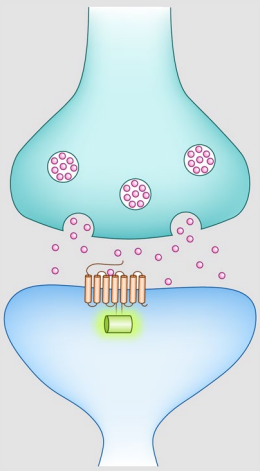
Sensing neurotransmitters

Genetically encoded neurotransmitter sensors will shed light on neuronal communication.

Neurotransmitters can be considered the vocabulary of the neuronal language. Neurons release neurotransmitters at the synapse to communicate with their receiving partners. The effects on the postsynaptic partner can be either excitatory or inhibitory. In addition, neurons can release neurotransmitters that diffuse and modulate populations of neurons. The neurotransmitter vocabulary is diverse and includes molecules such as amino acids (e.g., glutamate), monoamines (e.g., dopamine), peptides and others. Genetically encoded sensors help to decipher the communications between neurons, both at the circuit level and at a more detailed mechanistic level.

Several neurotransmitter sensors have been developed. The glutamate sensor iGluSnFR has been popular for studies of the predominant neurotransmitter in the vertebrate brain (*Nat. Methods* **10**, 162–170; 2013), and improved versions have recently been reported (*Nat. Methods* **15**, 936–939; 2018). Genetically encoded sensors for dopamine ($GRAB_{DA}$, dLight1) and acetylcholine (GACh) are now available as well (*Cell* **174**, 481–496, 2018; *Science* **360**, 1420, 2018; *Nat. Biotechnol.* **36**, 726–737, 2018).

The glutamate sensors are based on a bacterial protein, and the engineering strategy is not easily generalizable. In contrast, the dopamine and acetylcholine sensors are based on their cognate endogenous receptors—G-protein-coupled receptors—fused to a fluorescent protein. As many neurotransmitters signal through G-protein-coupled receptors, a similar design principle can potentially be used to generate sensors for other neurotransmitters, such as the monoamines norepinephrine and serotonin and the endorphin peptide family.



Visualizing neurotransmission at the synapse. Credit: Marina Corral Spence/Springer Nature

Expanding the palette of neurotransmitter sensors should help scientists better understand the intricate interplay among excitatory, inhibitory and modulatory neurotransmission. These sensors will provide a glimpse at the spatial and temporal relationships of such signaling events in neuronal circuits.

We look forward to the development of additional neurotransmitter sensors and their application in deciphering the language of the brain. ❐

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