Focus on Mapping the Brain

Recent technological advances in neuroscience are enabling researchers to study brain anatomy and function at a larger scale. Whereas scientists were previously limited to analyzing individual neurons, the field is now poised to undertake large initiatives that seek to generate large maps of brain activity and structure. Mapping large circuits and whole small brains at nanometer resolution is now feasible and methods that monitor the activity of larger groups of neurons in animals as they perform behaviors are rapidly improving. In our special Focus, we highlight this emerging field with contributions by several experts. A series of Reviews, Perspectives and a Resource present techniques that enable brain structure mapping in different organisms and at different scales and that correlate anatomy with function. A Historical Perspective and several Commentaries discuss the value of these types of maps and what will be needed beyond them to understand our minds.

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Accurate long reads for genome assembly

Short sequence read lengths have limited many applications that rely on next-generation sequencing. Piecing together a bacterial genome from scratch with short reads leaves gaps, for example—a problem that has prompted the development of hybrid approaches that require long-range information from additional sequencing libraries and technologies. Single Molecule, Real-Time (SMRT) sequencing generates reads on the order of many kilobases, but the very long reads have relatively high error rates. Korlach and colleagues now introduce the hierarchical genome assembly process (HGAP), which uses data from just one long-read SMRT sequencing library to produce high-quality finished microbial genome or bacterial artificial chromosome assemblies in an automated workflow. It includes a preassembly step that corrects errors in long reads using shorter reads from the same library. HGAP performs well on challenging repeat sequences.

Article p563

What is your resolution?

Super-resolution microscopy and nanoscopy techniques are experiencing progressively wider use and continual improvement. But with molecule localization-based nanoscopy techniques, issues such as probe density and localization uncertainty make resolution measurement far more complicated than it is with conventional light microscopy, for which the resolution can be easily determined. Rieger, Stallinga and colleagues show, through extensive simulation and testing, that Fourier ring correlation, a method developed to measure resolution in cryo-electron microscopy (cryo-EM), can be adapted to provide an accurate measure of image resolution in localization-based nanoscopy. If the method is adopted by the community as a standard way of calculating resolution, it should greatly improve the quality of reported results and help in comparing performance across nanoscopy methods.

Article p557

DMSO for stem cell differentiation

A defining feature of pluripotent stem cells is their ability to differentiate into all other somatic cell types. In practice, however, things are not always so simple. Many human pluripotent stem cell (hPSC) lines, whether of the embryonic or induced pluripotent variety, show resistance to differentiation along some lineages, at least with current methods. In the particular case of induced pluripotent stem cells, which are sometimes derived from individuals with a specific disease and genotype, this can pose a real practical problem. Melton and colleagues now revive an old approach to improve pluripotent stem cell differentiation. The simple addition of dimethylsulfoxide, they systematically demonstrate, improves the differentiation of multiple hPSC lines along all lineages.

Brief Communication p553

Cryo-EM at near-atomic resolution

In most single-particle cryo-EM studies of protein assemblies, resolution has been limited to 5–10 Å, which is much coarser than is typically obtainable by X-ray crystallography. However, cryo-EM has the advantage that crystallization is not required, so protein assemblies can be observed in their functional states up to the instant of vitrification. Cheng, Agard and colleagues now report an approach to determine near-atomic-resolution macromolecular structures using cryo-EM. Key to the method are an electron-counting camera with the ability to record a stack of successive frames and an algorithm to correct for electron beam–induced sample movement. Applying the method to the relatively small (700-kDa) Thermoplasma acidophilum 20S proteasome, an assembly with D7 symmetry, they obtained a 3.3-Å structure. The method should be applicable to a broad range of protein assemblies.

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