The power of a crowd

For some applications, a crowd of people is superior to the best computational tools available.

Crowds of people are still superior to computers for many visually based data-analysis tasks.

Given the amazing advances in software and computational infrastructure in the past decades, one would be tempted to conclude that this is a one-way path, with researchers attempting to offload as much as possible of the complex data analysis and prediction to computers. But instead, researchers are finding that for tasks that have a strong visual element to them, humans are still supreme. Harnessing the visual acuity, smarts and even intuition of many people, a crowd can outperform even the most sophisticated algorithms.

Crowdsourcing of scientific data analysis partly grew out of distributed computing efforts that harnessed personal computers to create networks whose power rivaled or exceeded that of the most powerful supercomputers. Creation of the Foldit crowdsourcing project, for example, was spurred by users of the distributed computing program Rosetta@home, who wanted to show the software how to solve protein structure problems that appeared easy to a user looking at the structure. The power of crowdsourcing protein structure analysis with Foldit was demonstrated with the solution of the crystal structure of a retroviral protease in 10 days (*Nat. Struct. Mol. Biol.* **18**, 1175–1177, 2011) and the redesign of an enzyme to increase its activity >18-fold (*Nat. Biotechnol.* **30**, 190–192, 2012).

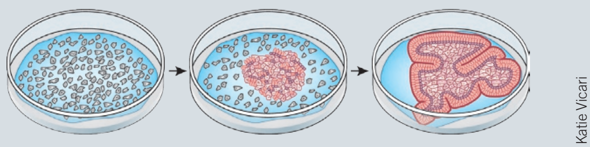
Although there is a strong desire among the public to participate in the analysis of scientific data, it can be challenging to make the tasks stimulating enough. Tracing neurites through neuronal tissue is a challenge for computers. Humans are more reliable, but neurite tracing is both tedious and exacting. When someone's attention wanes, mistakes are made. A potential solution to this quandary is to incorporate the task into a game. A company called scalable minds is working with the Max Planck Institute of Neurobiology on a crowd-sourcing effort called Brainflight to create games to help map the wiring of the brain.

It is also possible for researchers who lack the ability to distribute crowdsourcing software tools to get into the act. The Amazon Mechanical Turk allows 'requesters' to post tasks to be completed by 'workers' for a nominal fee. The structure of the service limits the types of analyses that can be performed, but the ability to restrict workers to those who have passed specified qualification requirements can be valuable.

There is no doubt that computational analysis will continue to expand and dominate most areas of biological research. For some tasks, however, a crowd of people and the right tool to connect them to the data could be superior for years to come. **Daniel Evanko**

Self-organizing stem cells

Tissue-like organoids with surprisingly complex structures can be formed by stem cells *in vitro*.



Stem cells can organize into tissue-like structures *in vitro*.

Pluripotent stem cells in culture will spontaneously differentiate into many cell types if conditions that promote pluripotency are not maintained. But in recent years, researchers have found that under the right conditions, stem cells in culture can also form structures of striking, tissue-like complexity—even reminiscent of what is seen *in vivo*, at least to a first approximation. Perhaps most surprisingly, once key enabling conditions have been identified, it seems that one need not do very much to the cells to achieve these effects.

For instance, when allowed to form three-dimensional aggregates in Matrigel, mouse and human embryonic stem cell–derived retinal pigment epithelial cells can organize into optic cups and, upon more prolonged suspension culture, into stratified neural retina (*Nature* **472**, 51–56, 2011; *Cell Stem Cell* **10**, 771–785, 2012). More recently, human pluripotent cell–derived neuroectodermal cells embedded in Matrigel and cultured in spinning bioreactors were shown to organize into millimeter-scale organoids containing structures that resemble the immature cerebral cortex, arguably one of the most complex tissues in the human body (*Nature* **501**, 373–379, 2013).

Preceding some of this work on pluripotent stem cells was the demonstration that intestinal stem cells, again under specific culture conditions and embedded in Matrigel, can organize into gut-like organoids that contain all the differentiated cell types present in the *in vivo* tissue (*Nature* **459**, 262–265, 2009; *Nat. Med.* **15**, 701–706, 2009). Similar observations have been made for both embryonic stem cells differentiating along other lineages and for adult stem cells of other tissues.

We are far from being able to generate organs *in vitro* at the wave of a wand; the culture well or bioreactor will never fully recapitulate what is going on in the body. Indeed, it is often proposed (and has in some cases been demonstrated) that implant into the *in vivo* milieu will be required for the final maturation of some cell types derived *in vitro*.

Nevertheless, as a tractable, accessible system to study normal development and tissue maintenance as well as the diseases that arise when these processes go wrong, stem cell–derived *in vitro* organoids have tremendous potential. **Natalie de Souza**