Organoids of intelligence

No man-made device of any kind, computer or otherwise, has yet come close to displaying anything like artificial intelligence on the human level. Nor has any device developed conscious awareness, and they may not for a long time. One current problem, experts suggest, is a fashion in AI research for exploring how computers can tackle the relatively easy challenge of making probabilistic associations on the basis of massive datasets — something that amounts, more or less, to high-level curve fitting. To approach real thinking, machines have to face the more profound challenge of learning to actually reason and work with the concept of causation.

But computing of the digital variety isn't the only kind possible. Indeed, biologists have been rapidly developing a technology to grow functioning and living tissues from real human cells, and have already realized complex geometrical constructs resembling real human brain tissue both in structure and function. Some show aspects of realistic neural activity, even responding to external stimuli in a coherent way. Such progress now has researchers openly concerned (see Nita Farahany et al., *Nature* **556**, 429–432; 2018) about the ethical challenges that will arise if a piece of tissue in a lab dish suddenly shows signs of having conscious states or reasoning abilities. That's still probably years away, but it may arrive well before computer-based AI, and could happen much sooner than most people think.

In the 1930s, the British mathematician Alan Turing famously set out the mathematical foundations for digital computing, inventing his concept of the Turing machine. He also speculated that such computers might one day be made to think. It's less well known that Turing later pioneered the mathematical theory of morphogenesis, using simple one-dimensional models to explore how organisms might develop from single cells into complex multicellular beings. Key to Turing's vision were concepts that went on to dominate later twentieth century physics, including an understanding of how instabilities can lead to pattern formation, breaking symmetry in the process. His early work aimed to explain phenomena such as the geometry of tentacles in *Hydra*, or phyllotaxis, the geometric patterning of leaves on a stem. Morphogenesis is also a kind of computation, one encoded not digitally, but in chemical and physical interactions, and strongly shaped also by geometry.

Many people today expect that Turing's more famous work on digital computing will lead to his vision of thinking machines. But research inspired by his 'other' vision might get there first, as biologists and neuroscientists make extremely rapid progress in gaining an ability to influence and control development, not only in living organisms, but also in artificial chemical environments. One outcome is the ability to grow artificial organoids — small but structurally and biochemically accurate versions of organs such as eyes, lungs, even brains.

Biologists have been developing technology to grow tissues from human cells, and have already made constructs resembling real human brain.

Consider the work of Stanford University biologist Sergiu Pasca and colleagues. Human stem cells can be harvested from human embryos or derived by partially reversing the earlier development of other human cells. In either case, these 'pluripotent' stem cells have the remarkable ability to develop into any cell type in the human body, including brain cells. Under the right conditions, a collection of cells in a dish of nutrients treated with appropriate molecular signalling factors will initiate development, and cells within will then grow, divide and differentiate into an array of cells with distinct functions. Following this approach, Pasca and colleagues have grown startlingly realistic brain organoids a few millimetres in dimension and containing several million differentiated cells. With the addition of a physical scaffold to encourage growth into brain-like geometry, the developing mass of cells over about ten weeks turns into a structure much like the cerebral cortex of a mostly developed human foetus, including neurons with spontaneous electrical activity and working synapses. Of course these aren't real brains, still some 10,000 times smaller and lacking other kinds of specialized cells found in real brains, including blood cells and cells able to sense the external world. But the research has come a long way.

Of course, the purpose of this research isn't to play at recreating life or intelligence, but to better understand a range of human neurological and psychiatric disorders, which are hard or impossible to study in any non-invasive way in real patients. Research on treatments becomes much easier using model brains grown so their structure and cellular make-up closely resembles that of the brains of people with specific brain disorders. In another avenue of study, researchers have already improved some cognitive abilities of mice by putting human brain cells among their own, and grown chimaera embryos of pig and human in which 1 in 10,000 cells in the developing hearts and livers were human. These chimaeras will also help better understand human illnesses, but take research into an ethical zone that will only get more bizarre with time.

The closer these organoids come to being just like real brains, the closer science, technology and medicine will come to facing some decidely uncomfortable ethical quandaries, as researchers are well aware. Today's organoids are neither intelligent nor conscious, or even close to being either, but their descendents in coming decades very possibly will be. What happens when, in the course of routine research, a lump of neural cells a few inches in size suddenly shows unmistakeable signs of conscious awareness? Or of having the capacity to feel pain or pleasure? At some point, these organoids may cross over from being complex but inanimate systems to deserving rights of their own, and perhaps requiring the protection of a legal guardian.

It's no wonder that biologists, neuroscientists and others involved in such research have held several recent meetings to discuss the ethical challenges they will almost certainly soon face. Artificial minds may be with us much sooner than we expect. ❐

Mark Buchanan

Published online: 4 July 2018
https://doi.org/10.1038/s41567-018-0200-2