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## Tissueclearing of whole organs: A challenge for chemistry

### ABSTRACT

Since the first chemical clearing of a mouse brain (Dodt et al., Nature Methods, 2007), tissue clearing has grown exponentially as a method for investigating the three-dimensional anatomy of organs in small animals such as mice and zebrafish. The technique enables the imaging of intact organs in their entirety using light-sheet microscopy combined with fluorescence labelling of structures of interest. However, attempts to render brains of larger animals fully transparent have so far been reported only sporadically, and primarily for rat brains. Extending these investigations to larger species — with the ultimate goal of clearing and imaging human brains (Oakes-Klein et al., Communications Biology, 2026) in three dimensions — would therefore represent a significant advance.

To this end, we have substantially improved our clearing technology and can now routinely produce optically transparent whole pig brains. Our approach relies predominantly on chemical methods; yet neither our group nor the vast majority of researchers active in the clearing field have a formal background in chemistry. Engaging chemists in this area would therefore be highly beneficial. A precise, chemically informed elucidation of human organs in 3D at cellular resolution holds the potential for breakthroughs in both fundamental research and clinical applications.

Dodt, H.-U., et al. (2007). Ultramicroscopy: three-dimensional visualization of neuronal networks in the whole mouse brain. Nature Methods, 4, 331–336.

Oakes-Klein, et al. (2026). activeDISCO enables large-scale exploration of human brain anatomy by light sheet microscopy. Communications Biology, doi: 10.1038/s42003-026-09935