

*A functional cellular framework for sex and estrous cycle-dependent gene expression and behavior*

<https://www.sciencedirect.com/science/article/pii/S009286742101494X>

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Knoedler et al chain together a series of cutting-edge methods for single cell transcriptomics, chemogenetics and projection mapping to show how sex and estrous cycle modify the organization and function of several subcortical nuclei to underpin sex-typical behaviors in mice. The authors begin by identifying genes which are differentially expressed as a function of sex and estrous state in several classical regions of sex-biased anatomy in the murine brain, and they then link these genes to specific sub-populations of ESR1+ neurons distributed across the examined brain regions. Next, using this information, the authors implement a chemogenetic approach to discover single cell-types that are required for sex-typical reproductive and social behaviors in each sex - which partly involve dynamic inter-regional projections. This work is not only fascinating with respect to the specific system studied, but as a worked example that illustrates the exquisite detail with which sex-biased biological factors can sculpt mammalian brain structure and function.