# Specialization of brain cell types is encoded by specific 3D genome structures

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## Abstract

During lineage commitment, cells sustain cascades of gene activation and repression to generate specific cell types that execute specialized functions. To investigate the variability of the 3D conformation of the genome in different cell types and their relation with cell-type specific patterns of gene expression, we applied Genome Architecture Mapping is specific brain cell types from the adult murine brain. We discover extensive reorganization of 3D genome topology, including the melting of long neuronal genes when highly transcribed, many of which are associated with neurodevelopmental disorders or neurodegeneration. By integrating 3D genome maps with open chromatin state and known transcription factor binding sites, we identify hubs of synaptic or addiction pathway genes in specific neurons. Our work shows that the 3D organization of the genome is highly specific of cell type and strongly related with gene expression programs.