Single-cell RNA-sequencing (scRNA-seq) has quickly become one of the most widespread methods for describing the functional identities of individual cells across a tissue or organism. Since the momentary identity of a cell is reflected in its aggregate expressed proteins, sampling the protein-encoding messenger RNA (mRNA) transcripts present in the cell by scRNA-seq provides a means of surveying cell state with high sensitivity. Moreover, current adaptations of this approach work by separately indexing transcripts across millions of cells in parallel, allowing for downstream interpretation of transcript abundance by cell origin. This is made possible by isolating each single cell and labeling its transcripts with a unique, cell-specific molecular barcode that can be read by sequencing later. Transcripts from all cells are then pooled together, sequenced, and annotated with their cell of origin based on their paired barcode.

Despite having drastically improved upon the sensitivity achievable in pooled, population-wide sequencing strategies, the implementation of scRNA-seq across diverse cell types has presented a number of challenges. Cells contain between $10^5$ and $10^6$ molecules of messenger RNA (mRNA). Because a single barcoding reaction is restricted to a comparatively low number of transcripts, a mere 5-15\% of a cell’s transcriptome is typically captured and indexed with a barcode. Many pairwise genetic relationships, particularly among lowly-expressed genes, are lost in the nearly 90\% of transcripts that are under-sampled at this step. It is then difficult to detect the transcriptional patterns underlying continuous state changes within a population of cells with high certainty, since lowly-abundant transcripts are overlooked.

To address these problems, the authors of the above paper present Markov affinity-based graph imputation of cells (MAGIC), a method that aims to denoise transcript counts by diffusing transcriptional patterns between similar cells. By imputing values of transcript abundance for cells suspected of having high transcript dropout, the authors demonstrate an improved signal to noise ratio in transcript abundance and general signal smoothing that improves cell analysis outcomes.