Measuring Cell State

MATH 612 Lecture 3

12/09/19

Elements of Cell State

1. DNA
    - The DNA sequence itself is an element of the cell state.
    - The 3D structure of this DNA is also a factor of cell state.
    - The "openness" or accessibility (geometric properties) of DNA indicates cell state; whether it is tightly compact and packaged or loose and free.
    - Methylation of the DNA sequence and of histones (chemical properties) is a factor of cell state as it can also influence accessibility of the DNA.
2. RNA
    - The expression levels of genes (number of copies) within a cell.
3. Protein
    - The amount of different proteins and of each protein present.
    - The state of the protein (ex. phosphorylated, folded, etc)
4. Phase of the cell cycle
5. Cell signalling

Cell Signalling

- Cell membranes are made up by a *phospholipid bilayer*.
- Proteins exist in the membrane and can be found as *channels* or *receptors*.
- Receptors can alter other proteins within the cell via *phosphorylation* and these targets can further downstream alteration of other proteins and/or gene expression.

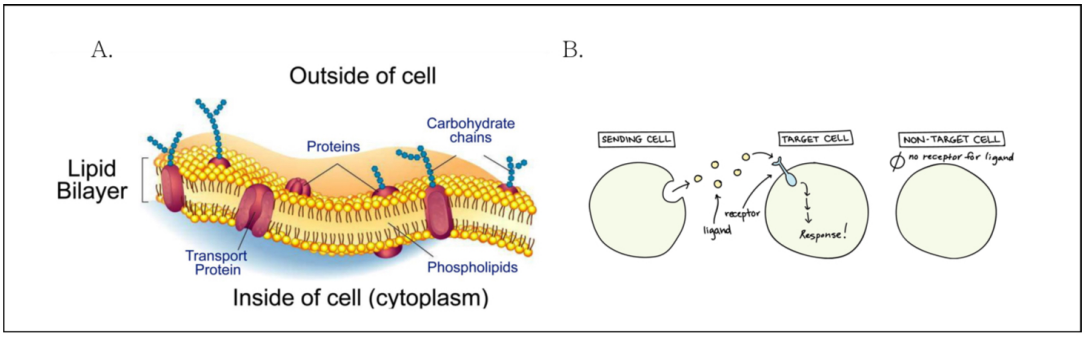

Figure 1: A. Structure of the cell membrane made up by a phospholipid bilayer that contains integral membrane proteins. B. Cell signalling through the production of a ligand from the "sending" cell, which is recognized and induces a response in the "target cell."

Measuring Cell State

1. Microscopes
    - Fluorescent tags can be used to visualize different proteins using antibodies.
2. DNA Sequencing
    - Sequencing by synthesis
        - Input: library (collection) of DNA
        - Output: collection of reads
        - Add library to a manufactured chip which contains fragments of DNA. Complementary sequences from the added library will bind and get elongated. Each different base that gets added to the growing sequence induces a flash of a different coloured light. One can read the sequence of the growing strand of DNA from the sequential flashes of light as different bases are added.
    - RNA Sequencing
        - Extract RNA from a cell
        - Make *cDNA* via *reverse transcriptase* from the RNA
        - Amplify the cDNA via a technique called *polymerase chain reaction* (PCR)
        - Sequence and obtain reads
        - Align to genome transcriptome

– Estimate number of RNA molecules for each gene

$$Output = \begin{bmatrix} gene_1 \\ gene_2 \\ \vdots \\ gene_m \end{bmatrix} \tag{1}$$

- Single Cell RNA Sequencing
  - Prepare a population of cells from an organism or tissues (used as input)
  - Isolate single cells

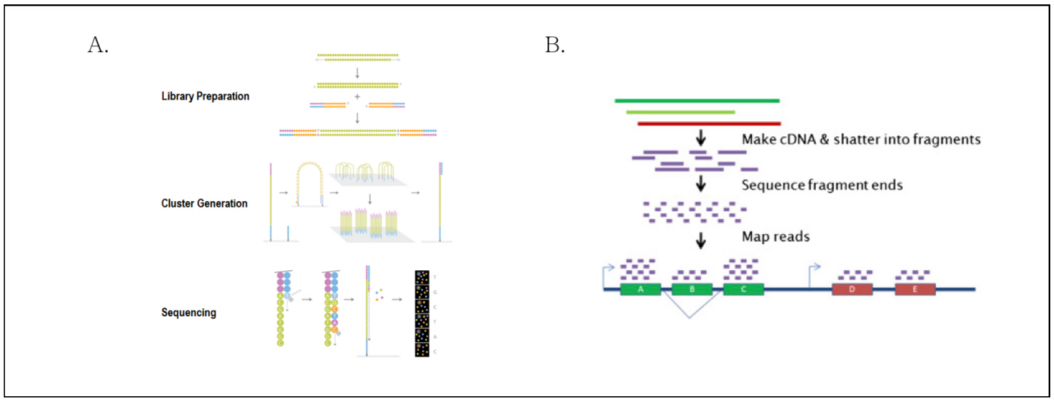

Figure 2: A. DNA sequencing by synthesis steps. B. RNA sequencing steps.