New Data Science in Nucleic Acids Chemistry (16): Cellular Compartment Size as a Critical Factor in the Stability and Function of Nucleic Acids

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In living cells, organelles create compartments of varying sizes, effectively isolating specific biomolecules from the rest of the cell.[1] This physical separation provides a controlled microenvironment, enabling more efficient regulation of biological processes. For these processes, G-quadruplex (G4) structures play a crucial role, with their stability being highly influenced by the surrounding environment.[2] Given that organelles range in size from 30 nm to 7.0 μm, we explored whether compartment size affects directly the stability of G4s in these distinct microenvironments.

To explore the impact of compartmentalization, we mimicked organelle sizes using large unilamellar vesicles (LUVs) and giant unilamellar vesicles (GUVs) to generate compartments ranging from 0.1 μm to 10 μm in diameter (Figure 1), which are widely used for creating artificial cells and mimicking viral membranes.[3] The vesicles contained an aqueous layer enriched with K^+ ions to replicate physiological conditions (Figure 1). Thermal melting studies revealed that the melting temperature (T_m) of G4 inside vesicles with a diameter of 0.1 μm (LUV) was decreased compared to dilute conditions. The decrement became more pronounced in GUV-sized vesicles. These findings demonstrated that compartment size affects strongly G4 DNA stability, highlighting the potential role of compartmentalization in regulating the gene expression efficiency of nucleic acids.

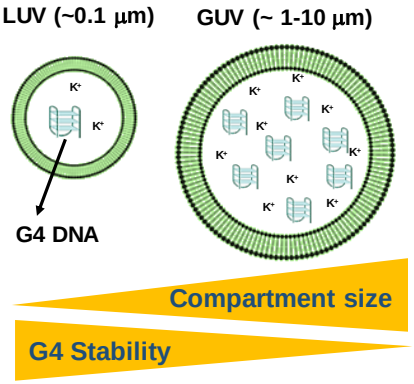

Figure 1. Schematic illustration of different sizes of vesicles ranging from 0.1 μm to 10 μm. The vesicles were formed using a 2:1 ratio of 1-palmitoyl-2-oleoyl-sn-glycero-3-phosphocholine (POPC) and cholesterol to ensure stability and effective encapsulation of G4 DNA.

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