

Novel HIV matrix shell structure and potential functions

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The structure of the HIV matrix shell has not been fully elucidated. In this article, I highlight contributions that led to a model composed of adjacent hexagons forming a sphere and mentioned studies that were subsequently impacted. A cross disciplinary group of students in my lab tested this hypothesis and conclusively demonstrated that this model was incorrect. I provide a summary of our results with emphasis placed on contributions made by students.^b

In the winter of 2015, a brilliant student from the Northern Alberta Institute of Technology (NAIT) approached me looking for opportunities to do research during the spring and summer terms. Eduardo Reyes Serratos had taken my Applied Genetics class and I knew his tremendous potential. A few weeks later, I assembled a **group of 6 students** and received a research grant to prepare a project for the iGEM 2015 competition in Boston. Three of the students, including Eduardo, were so pumped by the experience at Massachusetts Institute of Technology (MIT) that upon arriving home that November they requested to continue their research involvement in my lab. At the time, the structural biology scientific community was trying to decipher the super structure of the HIV matrix (MA) shell and I challenged my students with this unsolved computational biology problem.

duce experimentally determined results, namely the flat [2] and the cylindrical [5] configurations of the MA shell. With some basic python scripting and simple fundamental trigonometry, we finished this part of the project in a few weeks (Figure 2).

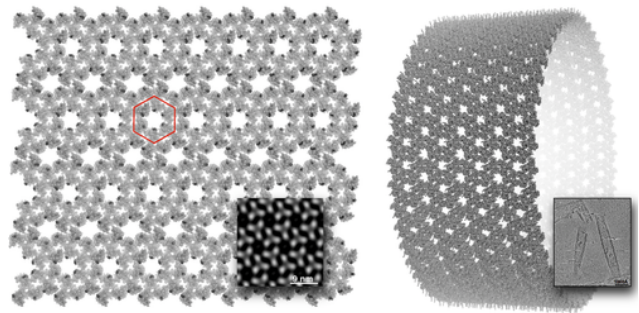


Figure 2: Flat and cylindrical hexagonal arrangements of the MA shell [2, 5] supporting these configurations. A hexagon is shown in red. Hexagons are permissive in flat (left) and cylindrical (right) arrangements of the HIV MA trimers.

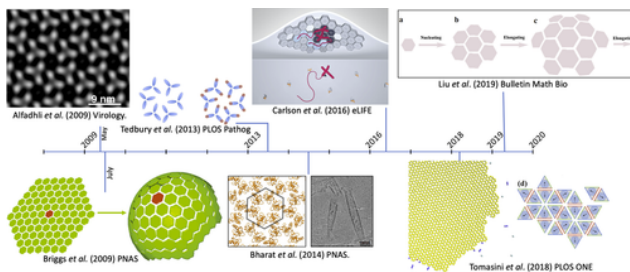


Figure 1: Key Developments in the elucidation of the HIV MA shell superstructure and its impact on the field.

An important key piece of evidence came from work performed by Alfadhli et al [2]. This study demonstrated that HIV MA trimers would arrange themselves in a hexagonal pattern if purified MA trimers were on a flat surface. Shortly thereafter, researchers around the world made the assumption that the structural configuration of the HIV spherical shell was hexagon-based, as shown in a figure published by Briggs et al [3]. A selection of studies [4–8] that were impacted by this hexagon-based model is shown in Figure 1.

My team of students attempted to reconstruct this 3-dimensional model using X-ray crystallography MA structures [9, 10]. Our first objective was to repro-

Our next objective was to assemble a sphere made from these hexagons. We learned, after many attempts, that the configuration was mathematically impossible. In fact, this geometrical fact had been discovered in 1758 by Leonhard Euler [11]. With his famous equation, $F + V - E = 2$, he demonstrated that a regular hexagon sphere is not possible (Figure 3).

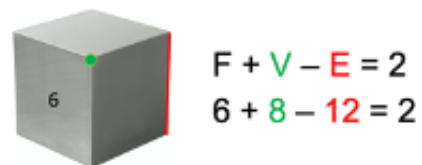


Figure 3: A cube follows Euler's equation. If we add the total number of faces (F) to the total number of vertices (V) and subtract the total number of edges (E), the answer is always 2. This is true for any convex polyhedron and is false if a hexagon is used in the formula.

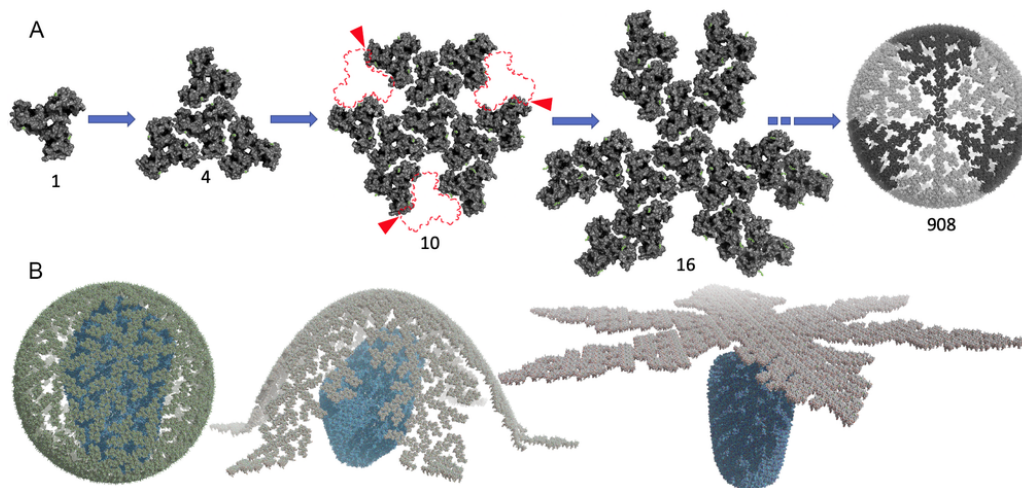


Figure 4: Construction of the HIV MA shell. (A) At 10 trimers, it is not possible to close the hexagons (red arrows and highlighted areas). Doing so results in over imposed trimers. (B) New HIV MA shell models and their putative transitions from sphere to flat. The HIV capsid is shown in blue.

My lab rediscovered this principle and applied this math to the 3-dimensional structure of the HIV MA shell to conclusively demonstrate that the established dogma for the superstructure of the HIV MA shell was incorrect [1]. We then proceeded to create a new model of the MA shell that would respect the geometrical restrictions imposed by the curve of a sphere. Using more [sophisticated math](#) applied by my student Weijie Sun, we followed a simple principle (Figure 4A). Starting from a single trimer resting inside a sphere, we added MA trimers wherever there was space. We built over 10,000 possible structures ranging in diameter from 100 to 200 nm. All structures followed the same general configuration. Adjacent branches of trimers would bend around the spherical surface but would never reconnect. This resulted in a shaped that resembled a flower with 6 petals, mathematically referred to as a 6-lune hosohedra (Figure 4B).

This novel structure led us to predict a new mechanism of viral entry and perhaps viral assembly. Our institute published a [story](#) shortly after to celebrate the achievement of these students.

Notes

- a. Email: marcelo@ualberta.ca
- b. Original version of this article is Ref. [1]

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