COVID Information Commons (CIC) Research Lightning Talk

Transcript of a Presentation by Wai-Yim Ching (University of Missouri- Kansas City), January 13, 2021

Title: *Structural Refinement and Intramolecular Binding in SARS-CoV-2 Spike Protein*

Wai-Yim Ching CIC Database Profile

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Youtube Recording with Slides

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Transcript

Wai-Yim Ching:

Slide 1

I'm Wai-Yim Ching from the University of Missouri-Kansas City, and I'm a theorist, a computational theorist, and so my result would be very condensed. I think if anybody is interested, send me an email. I will answer all their questions. We have a very small team which consists of Dr. Adhikari and two very capable graduate students— Ph.D. students, Mr. Jawad and Mr. San, and an undergraduate student, Ms. Namiq. We are supported by an NSF RAPID project which is in the Condensed Matter and Materials Theory section of NSF. Since we are computational scientists, we have to rely a huge amount on computational resources. This was provided by the Department of Energy Supercomputer Center and called the NERSC. I wanted to start the next slide.

Slide 2

I'll say something about the background and why we want to study the spike protein, because this protein bonds to the host cell receptor. Most of the people know what is going on there. It plays a critical role in the infection. The structure and the properties of this internal bonding is not fully understood. So we have to use the world-class supercomputer facilities to do an initial calculation based on density functional theory for this large molecular system. This type of calculation is very layered because it's very resource-consuming, and it's very challenging. Our goal is to have a fundamental understanding based on quantum mechanical methods and the inter-atomic and intra-atomic amino acid network, including the hydrogen bonding. Also, of course, the main focus is to train the next generation of scientists in this

very important area of material science, because I was trained as a material researcher, and I work in condensed metaphysics in chemistry and biophysics. Okay, so biomaterials are very important.

Slide 3

I want to first report some of the latest achievements. We have the structural optimization of seven basic structure domains in the spike protein, which is right here. This is the three chains. The chain A has seven different domains, and each of them consist up to several thousand atoms. We have to do the computation for all these seven domains together and investigate their covalent and hydrogen bonding and the partial charge distributions. We also developed a key parameter called amino acid bond pairs, which would allow us to do three-dimensional amino acid interactions. We, so far, have published three papers. If any of you are interested, please send me an email.

Slide 4

Currently, the ongoing project we did is interface modeling, in which we combine the molecular dynamics of DFT calculation, and this is even more challenging. We also try to calculate the rigidity of each of their spike domains. The rigidity is very important in any biological system when they are under temperature change or stress. We are also currently working on the mutation modeling, which is the D614G. If A is in the news, those are the variants of different coronavirus, and it's in the news almost every day. We also want to improve the computational methods and the codes used for large data generation. This is a figure about the mutation model with water molecules included, and this is the preliminary result on the rigidity. We have three manuscripts currently under preparation. The work takes us at least two or three months. So this comes down to the, one of the, last slides.

Slide 5

Our project will finish by May 31st, which is only a one-year project for the NSF RAPID. Before we end the project, we will extend our computational modeling to drug design of some selected models by adding very short peptides. This is an example of two models which we would, sort of, start to model. It is called LCB1 and LCB3. These are the two shorter peptides to be inserted at the interface. We also work for extensive mutation modeling and on the analysis of the following cases. In addition to the one we are currently working on, there are many new variants, according to the B.1.1.7 report from COG-UK. These are the four examples, and there are many more. The longer goal is to extend computational modeling to cover much larger biomolecular systems. Even though we are doing our initial calculation, and at this moment it is one of the largest computations that can be envisioned, we are more ambitious. We want to extend it to even larger systems. On the other hand, we are very ambitious. We want to advocate the use of large-scale computational modeling for biomolecular systems that can rival or even complement the experimental techniques in accuracy and at a much reduced cost. Thank you very much. That's the end of my talk.