Researchers take mathematical route to fighting viruses

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Mathematicians at the University of York have joined forces with experimentalists at the University of Leeds to take an important step in discovering how viruses make new copies of themselves during an infection.

The researchers have constructed a mathematical model that provides important new insights about the molecular mechanisms behind virus assembly which helps to explain the efficiency of their operation.

The discovery opens up new possibilities for the development of anti-viral therapies and could help in the treatment of a range of diseases from HIV and Hepatitis B and C to the "winter vomiting bug" Norovirus and the Common Cold. The research is published in the *Proceedings of the National Academy of Sciences* (*PNAS*).

The researchers led by Professor Reidun Twarock, of the Departments of Mathematics and Biology at York, have established a theoretical basis for the speed and efficiency with which viruses assemble protective protein containers for their genetic information – in this case an RNA molecule - during an infection.

By incorporating multiple specific contacts between the genomic RNA and the proteins in the containers, and other details of real virus infections, the research team's mathematical model demonstrates how these contacts act collectively to reduce the complexity of virus formation, thus solving a longstanding puzzle about virus assembly – a

form of Levinthal's Paradox. This also ensures efficient and selective packaging of the viral genome and has evolved because it provides significant selective advantages to viruses that operate this way.

Professor Twarock, a member of the York Centre for Complex Systems Analysis (YCCSA), said: "This truly interdisciplinary effort has provided surprising insights into a fundamental mechanism in virology. Existing experimental techniques for studying viral assembly are unable to identify the cooperative roles played by all the important components, highlighting the need and power of mathematical modelling. This model is a paradigm shift in the field of viral assembly. It sheds new light on virus assembly in a major class of viruses and their evolution, and opens up a novel strategy for antiviral therapy."

Professor Peter Stockley, of the Astbury Centre for Structural Molecular Biology at the University of Leeds, added: "These results provide a new perspective for our understanding of virus assembly, highlighting important features in the process that had previously been overlooked. We have already obtained proof of principle in a simple model virus that these functions can be targeted by drugs. The new opportunities for anti-viral intervention opened up by our paper also apply to viruses for which therapeutic options are currently limited. The new approach is enticing because it enables us to target co-operative aspects of viral assembly that are conserved across different viral strains, making it less likely that drug therapy would elicit resistance mutations. "

More information: The paper 'Solving a Levinthal's paradox for virus assembly identifies a unique antiviral strategy' is published in *Proceedings of the National Academy of Sciences*: www.pnas.org/cgi/doi/10.1073/pnas.1319479111