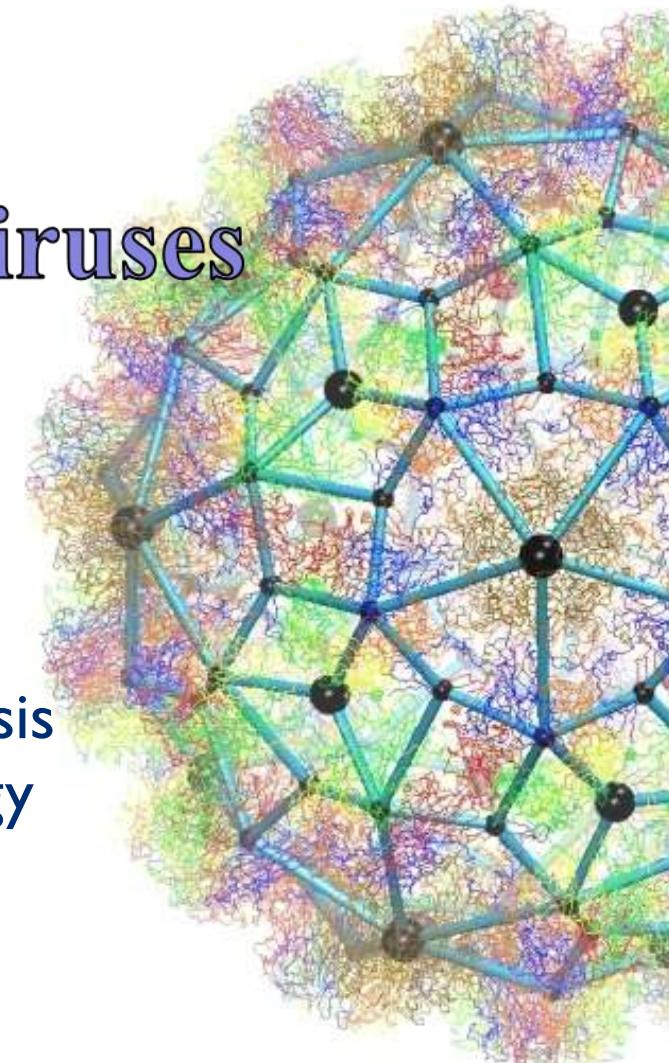


Using Maths to Attack Viruses

Prof Reidun Twarock

York Centre for Complex Systems Analysis
Departments of Mathematics and Biology

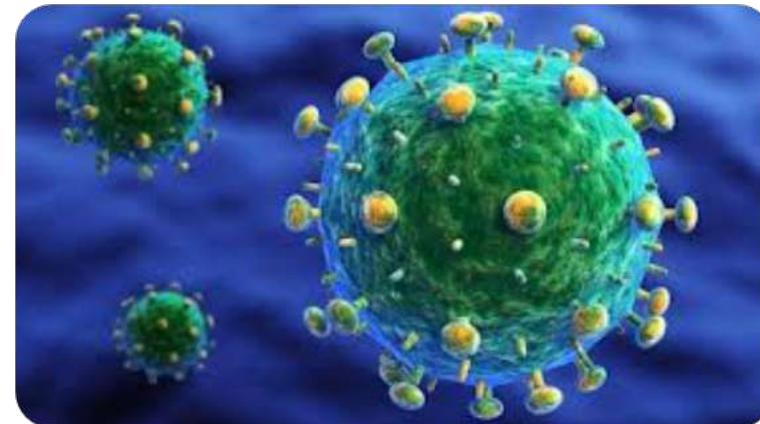


The challenge

Viruses are responsible for a wide spectrum of devastating diseases in humans animals and plants, yet options for anti-viral intervention and vaccination are still limited.

Examples:

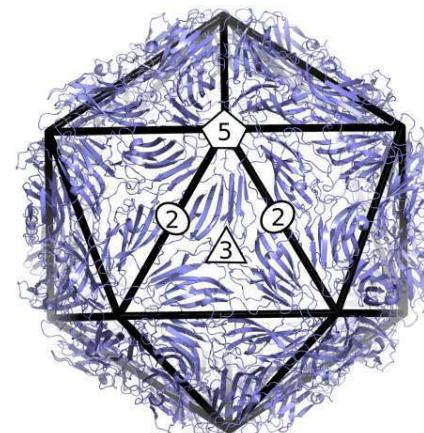
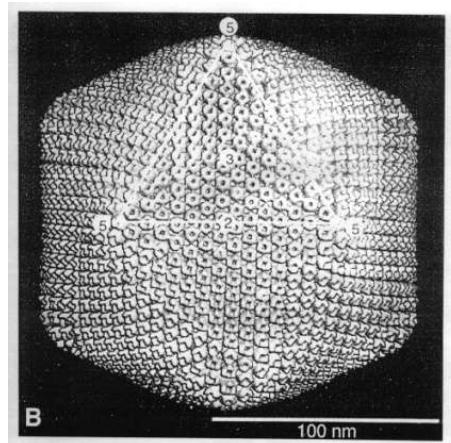
- HIV
- Hepatitis C
- Cancer-causing viruses
- Picornaviruses linked with type I diabetes
- Common cold



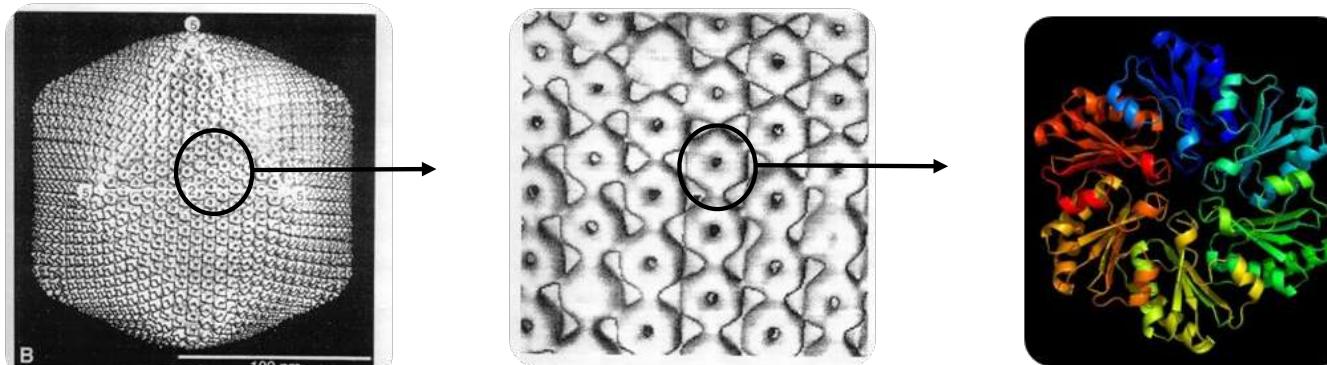
New solutions

New mechanistic insights in how viruses form provide new opportunities for anti-viral strategies.

Mathematics can help!

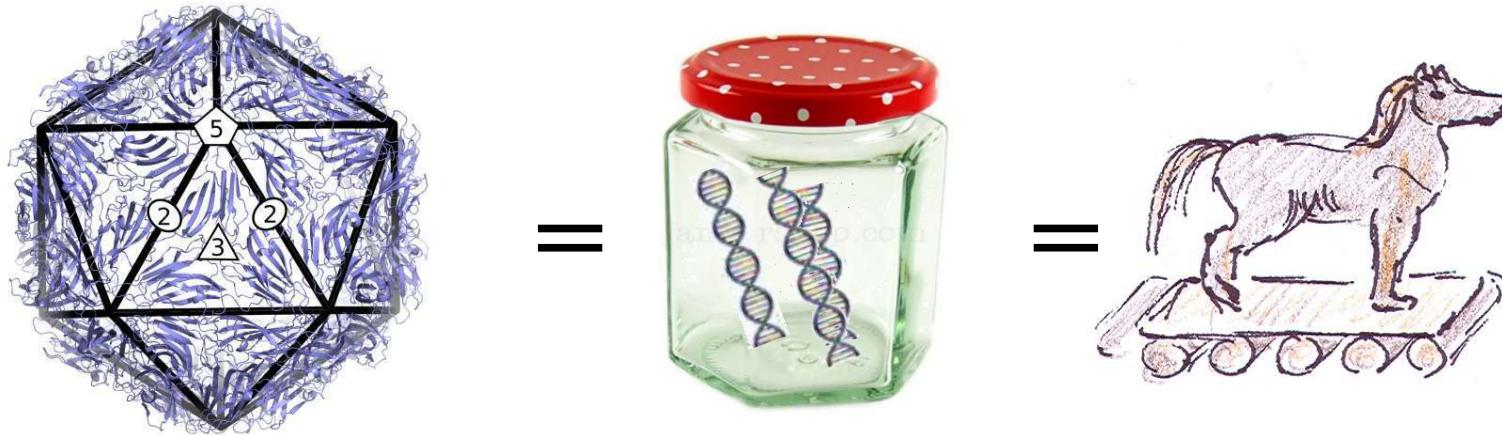


Viruses and mathematics



Viruses are fascinating examples of order and symmetry in Biology.

Viral Capsids act like Trojan Horses



Vital roles of the genomes in container formation have previously been overlooked

An interdisciplinary research programme

A **Leverhulme Trust Research Leadership Award** enabled a highly interdisciplinary research programme

Highlights:

- Novel mathematical tools provide new insights into the geometric principles underlying virus structure
- Mathematical models provide a new understanding of the functional roles of viral genomes in virus formation and evolution

New mechanistic insights

Our work on virus formation has initiated a paradigm shift in our understanding of virus assembly:

Viral genomes play vital cooperative roles in the formation of viral capsids



In collaboration with experimental groups at:

- the Astbury Centre for Structural Molecular Biology in Leeds
- the University of Helsinki

Self-packing suitcases

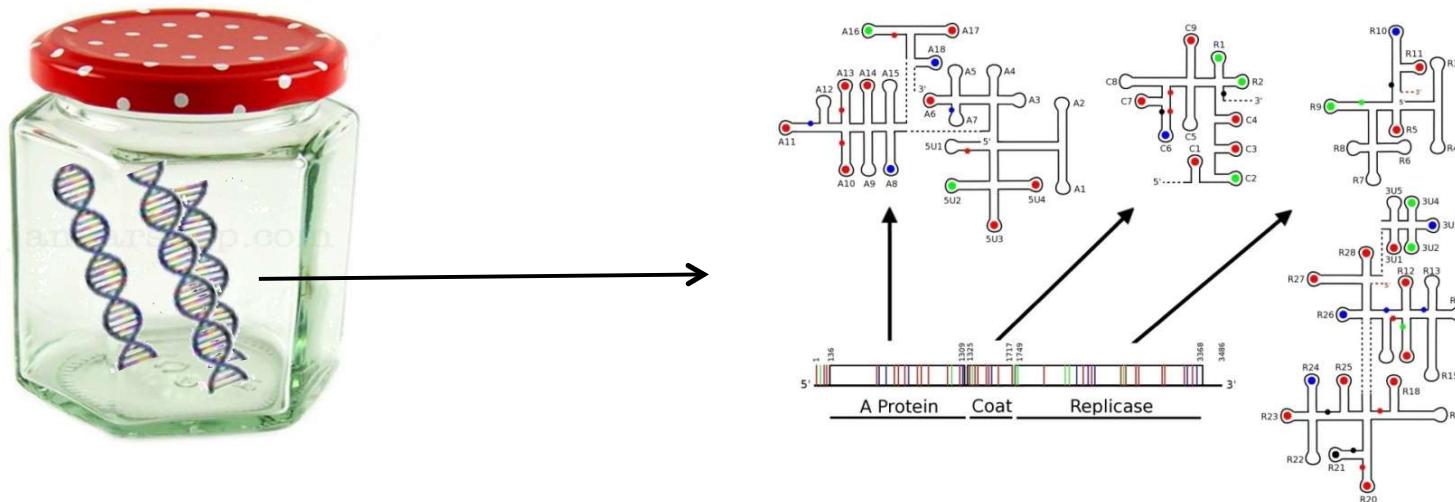


Prof Peter Stockley (Leeds) – Huffington Post –
Nature's Nanoscale Suitcases

The packaging signal paradigm

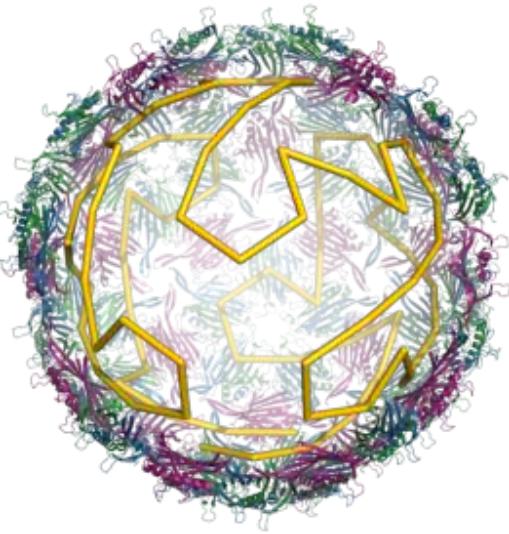
In ssRNA viruses, viral genomes are more than passive passengers:

Multiple dispersed interactions with capsid protein are essential for efficient capsid formation



Work in collaboration with experimental
groups at the Astbury Centre for Structural
Molecular Biology in Leeds

The role of mathematics

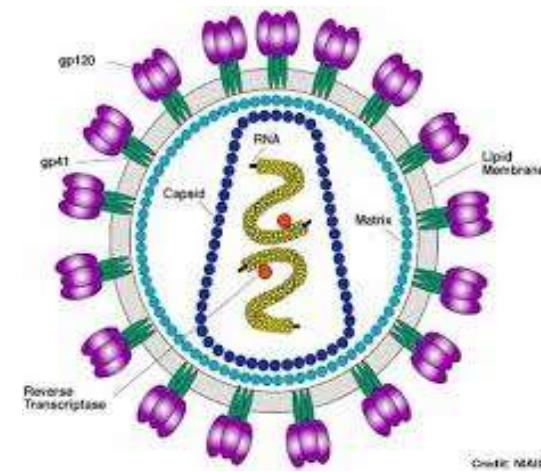


- Identify the motifs of the packaging signals;
- Identify the positions of the packaging signals;
- Demonstrate their cooperative roles in capsid formation;
- Identify suitable drug targets.

A highly interdisciplinary approach, carried out in close collaboration with experimentalist.

Solution to a fundamental problem

- Escape mutants can occur when viruses are challenged by a drug;
- Small changes in capsid structure make drugs less likely to bind (problems with the “key-lock” principle).



The solution:

Our mechanistic insights provide a new solution, because they allow us to target evolutionarily stable features.

A new anti-viral strategy

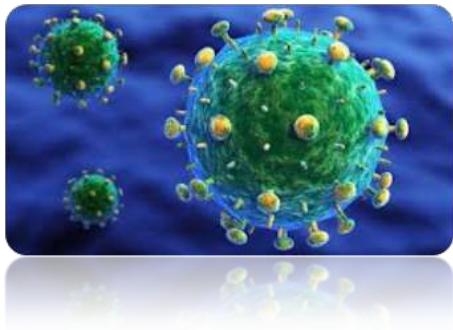
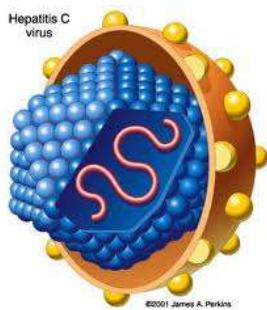
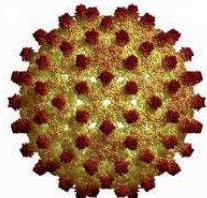
Our highly interdisciplinary approach has resulted in a new anti-viral strategy that avoids the problem of escape mutants.

Mathematics has played a key role in this discovery

A patent:

University of York, in collaboration with the Universities of Leeds and Helsinki, has **filed a patent in September 2013, proposing a novel anti-viral strategy in RNA viruses** based on these discoveries.

The next steps



- We are currently in the process of exemplifying this strategy in a wide range of viral systems, including:
 - Hepatitis B and C
 - HIV
 - SARS
 - Norovirus
 - Foot-and-Mouth disease virus
- **We expect to be ready to approach industrial partners from Spring 2014.**

Mathematical Virology in YCCSA

This project is only one in our portfolio of research activities, which span:

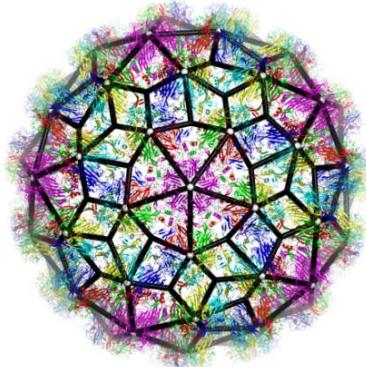
- Development of new mathematical tools for applications in bio-nanotechnology
- Development of new analysis tools for data analysis
- Blue sky research into evolution based on viral systems
- Modelling of other aspects of viral life-cycles
- More mathematical strands also have applications also in chemistry (carbon cage structures) and physics (quasicrystals).

Funding: EPSRC, Leverhulme Trust, Wellcome Trust, EU

The conference Mathematical Virology 2014
will be held in YCCSA in August 2014.

Explore further...

Viral geometry and design:
Visit Briony Thomas' exhibit in the atrium



Watch our **3Sixty presentations**, including videos on our virus research by Alex Polack, a YCCSA summer research student, and Matt Bedder, Yoggya De Silva Kande, Ashley Meredith & Holly Tobin.