

Virus Presentation Notes and Exercise Solutions

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Presentation Notes:

SLIDE 2:

Viruses give many opportunities to emphasize important concepts in contemporary cell and molecular biology:

Structure-Dynamics-Function: The relationship between structure and function drove the development of structural biology. However, recently there has been emphasis on dynamics as a missing link between these two important concepts. An essential aspect of biological macromolecules is that they are highly dynamic (they are constantly squirming and wiggling around, and these motions are what allows a protein to perform its function). Virus capsid proteins do a great job of showing that these protein motions are often functionally significant. An example of functional dynamics in virology is the transition of tomato bushy stunt virus between the low-pH and high-pH states (as shown in movie 2; this motion opens the capsid, releasing the genetic material).

Systems Biology: Viruses are large, complex assemblies of many different proteins in which the individual pieces work together to accomplish a common goal: find and enter a host cell. By studying the individual parts and how they interact with each other, scientists are able to get a handle on how an entire virus functions.

Self-Assembly: Students must often wonder how the large, complex biomolecular structures, such as viruses, that they see in their text books are made inside the cell. Amazingly, the answer is often very simple: they make themselves. Viruses, because of their simple geometry, make it easier to see that the components of a virus are structured such that when thrown together, they spontaneously assemble themselves into a complete virus.

Model Systems: The history of virology has clearly illustrated that knowledge about a complex system is often obtained by studying a related phenomenon in a simplified

model system.

Physics and Chemistry: Physical principles often impose constraints on the structure and function of biological systems. This is particularly apparent with viruses since the structure of viral capsids is governed by something even more fundamental: simple geometry.

Engineering Concepts: Viruses have many practical applications in the laboratory. For example, viral vectors are used to transfer genes into cells and viral promoters are used to ensure that a cell expresses a gene of interest. Since viruses are so closely linked with basic methods of molecular biology, they present an opportunity to discuss bioengineering concepts.

SLIDE 3:

Understanding the size scale of the viral world is important. Viruses are sub-cellular; the poliovirus, for example, is approximately the size of a ribosome.

SLIDE 4:

It's important to appreciate that the molecular diversity of the viral world is tremendous. Viruses infect every type of living cell, including being specialized to cells of particular tissues in multicellular organisms (tissue tropism).

SLIDE 5:

One of the great things about studying viruses is that it's never dull. These are two really cool things I've come across in the field. First, viruses are not always bad. One example of this that students sometimes hear of is that infection by a virus often provides protection against infection by a more dangerous virus (which is the basis the smallpox vaccine). Another even more interesting example is that some species, such as certain species of parasitic wasps live in a state of mutual symbiosis with species of viruses. These wasps lay their eggs inside of a caterpillar; the hatching wasps then devour the caterpillar from the inside. However, the immune system of the caterpillar is able to destroy the wasp eggs before they hatch. To overcome this, the wasps have come up with a clever form of bioterrorism: along with their eggs, they inject the caterpillar with a virus that destroys the caterpillar's immune system. So in this case, the wasp eggs are not destroyed and the mama wasp helps the virus find new hosts. The second example is of

Seneca Valley Virus 1, a recently discovered virus that very selectively infects certain types of lung cancers. This has given rise to the field of oncolytic virotherapy, which uses viruses to treat cancer.

SLIDE 9:

The movie shows a detailed, cryo-electron microscopy (cryo-EM) image of a human papilloma virus.

These several slides are intended to show how far the field of structural virology has come in the past few decades.

SLIDE 10:

It's important to consider some of the design constraints of viral capsids to fully appreciate their structure. The need to be a dynamic structure is particularly important, which allows the virus to “come alive” when it interacts with its host cell. The types of motions that the virus capsid undergoes while entering the host cell and releasing its genome occur in a “programmed” series of steps. Today, some scientists believe that the functional dynamics of a viral capsid is encoded by the amino acid sequence of the capsid proteins, much like the instructions for a computer program are encoded by the source code. This kind of thinking is related to the view that viruses are “nano-machines.”

SLIDE 15:

That viral capsids are composed of a repeating asymmetric subunit is the first principle of viral capsid architecture. If we consider the constraint that a virus must be able to contain all of the genetic material needed to encode all of its proteins, the requirement of a repeating asymmetric subunit becomes apparent.

SLIDE 16:

The jellyroll fold is a fold that is unique to viral capsid proteins. As far as researchers can tell, there are no cellular proteins that have this fold, which presents scientists who study the evolution of viruses with an interesting puzzle: how did viral capsid proteins evolve if they are structurally unique from all other cellular proteins?

SLIDE 18:

The quasi-equivalence of viral capsid proteins is due to the fact that the structure of capsid proteins is slightly distorted when they are packed together into an icosahedral shell. The structural distortion results in an isolated capsid protein being “quasi-equivalent” to a capsid protein that's part of an icosahedral shell.

SLIDE 22:

It's important to understand that if one shakes this physical model long and hard enough, the pieces will always self-assemble into a complete virus.

SLIDE 23:

It's important to consider how the structure and dynamics of a virus influences the various stages of its lifecycle. The role of the hemagglutinin membrane protein in host cell entry of the influenza virus by membrane fusion is a good example of the structure-dynamics-function relationship.

Exercise Solutions:

As was explained in the presentation, larger virus capsids tend to have higher T-numbers. This is because the T-number of a capsid indicates how many capsid proteins are needed to tile one equilateral face of the icosahedron (of which there are twenty) and the fact that most viral capsid proteins are approximately the same size.

Most viral capsid proteins tend to be positively charged. The positive charge allows the capsid proteins to bind to the strongly negatively charged nucleic acid that the virus contains. These favorable electrostatic interactions help the virus to assemble by bringing together the capsid proteins and viral genome and neutralizing the high negative charge of the genetic material.

Highly conserved regions of the virus capsid proteins include: (1) binding sites for receptors, (2) important contacts at the interface between two capsid proteins, (3) the beta strands comprising the jellyroll folds, (4) other special regions that are specific to certain virus families. If a region belongs to (1), it should have high solvent accessible surface area. If a region belongs to (2), it will be listed as forming a contact to another capsid protein in the residue contact table and will be buried (have low solvent exposed surface area). Regions that correspond to (3) will have a very distinct appearance in the structure

(antiparallel beta sheets that are characteristic of the jellyroll fold).

A region that corresponds to an antigenic site of a virus can be identified by performing a multisequence alignment of several strands of the same virus. Such regions are highly variable. Hence, they will not be conserved in the alignment. These regions will also not have contacts to other capsid proteins listed in the residue contact tables and have high solvent exposed surface area.