

Bioinformatics



Viruses, etc

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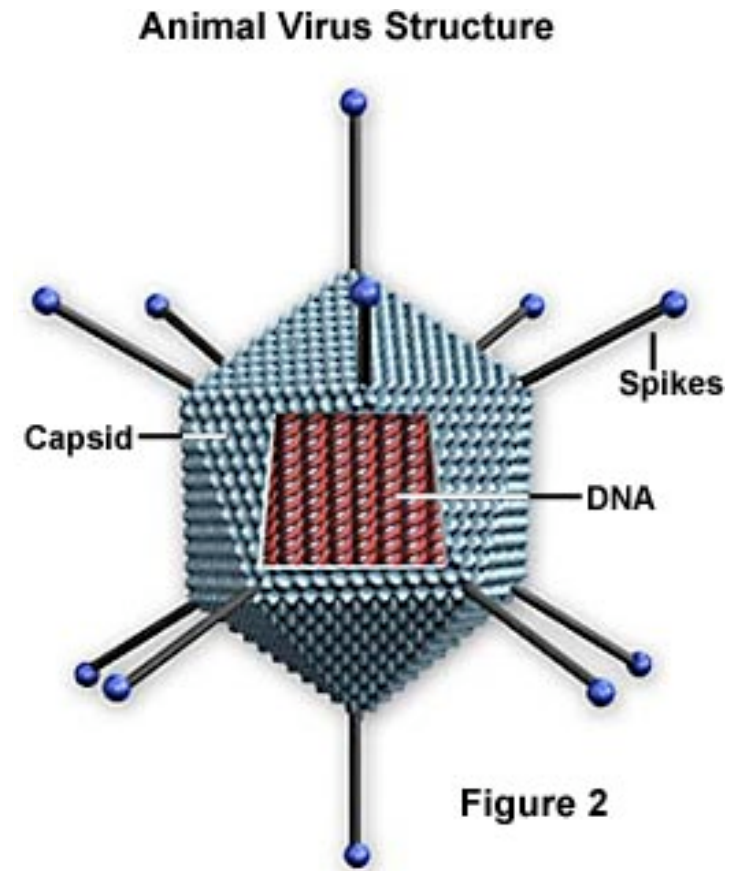
Incorporating notes by Ali Al-Shahib, David Leader, and Wikipedia

Lecture contents

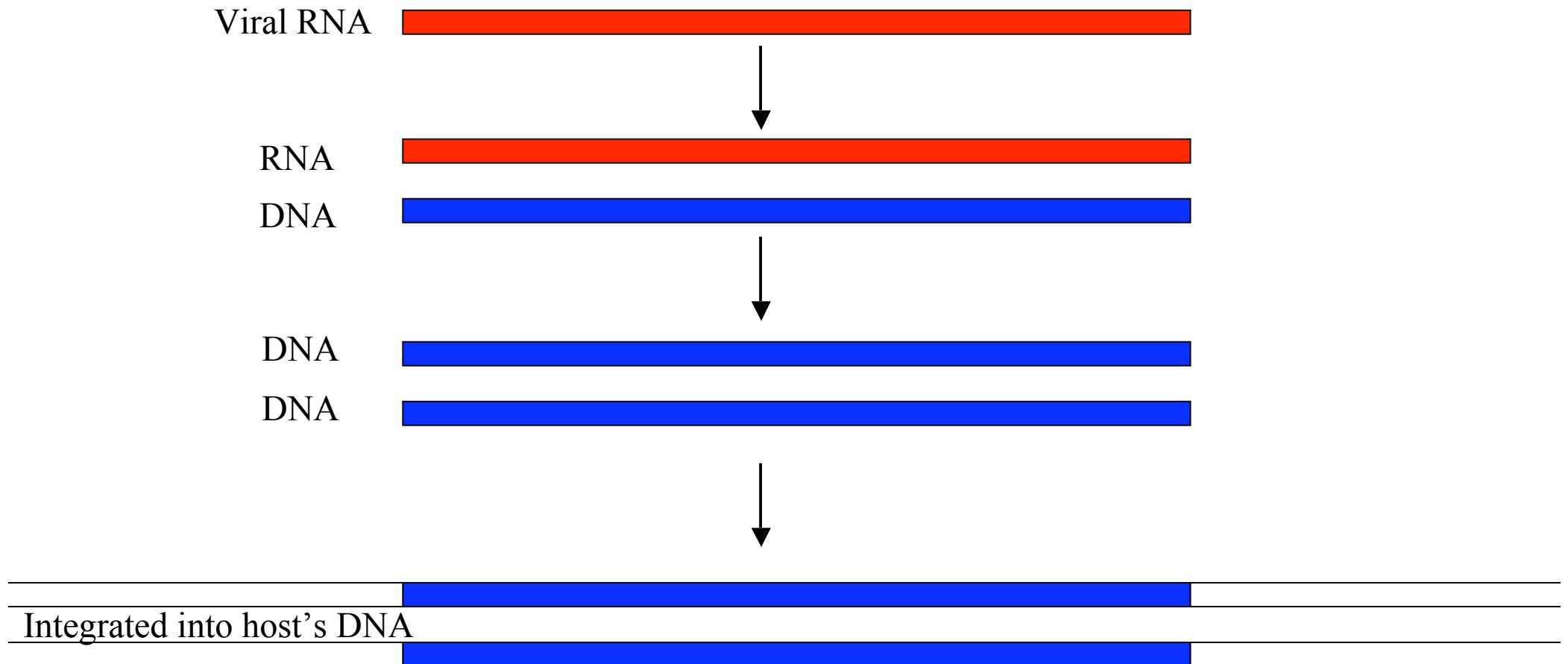
- Viruses
 - Types
 - Life cycle
 - examples
- Retroviruses
- Mobile/copying DNA:
 - Transposons, retrotransposons

VIRUSES

- Not Computer Viruses...
- Non-living agents
- Exist outside of cells as particles called **virions** (waiting!)
- Store their genetic information as either DNA or RNA (not both).
- Vary greatly in size and shape
- Reproduce by using or taking over the host cell's machinery for DNA replication and protein synthesis.

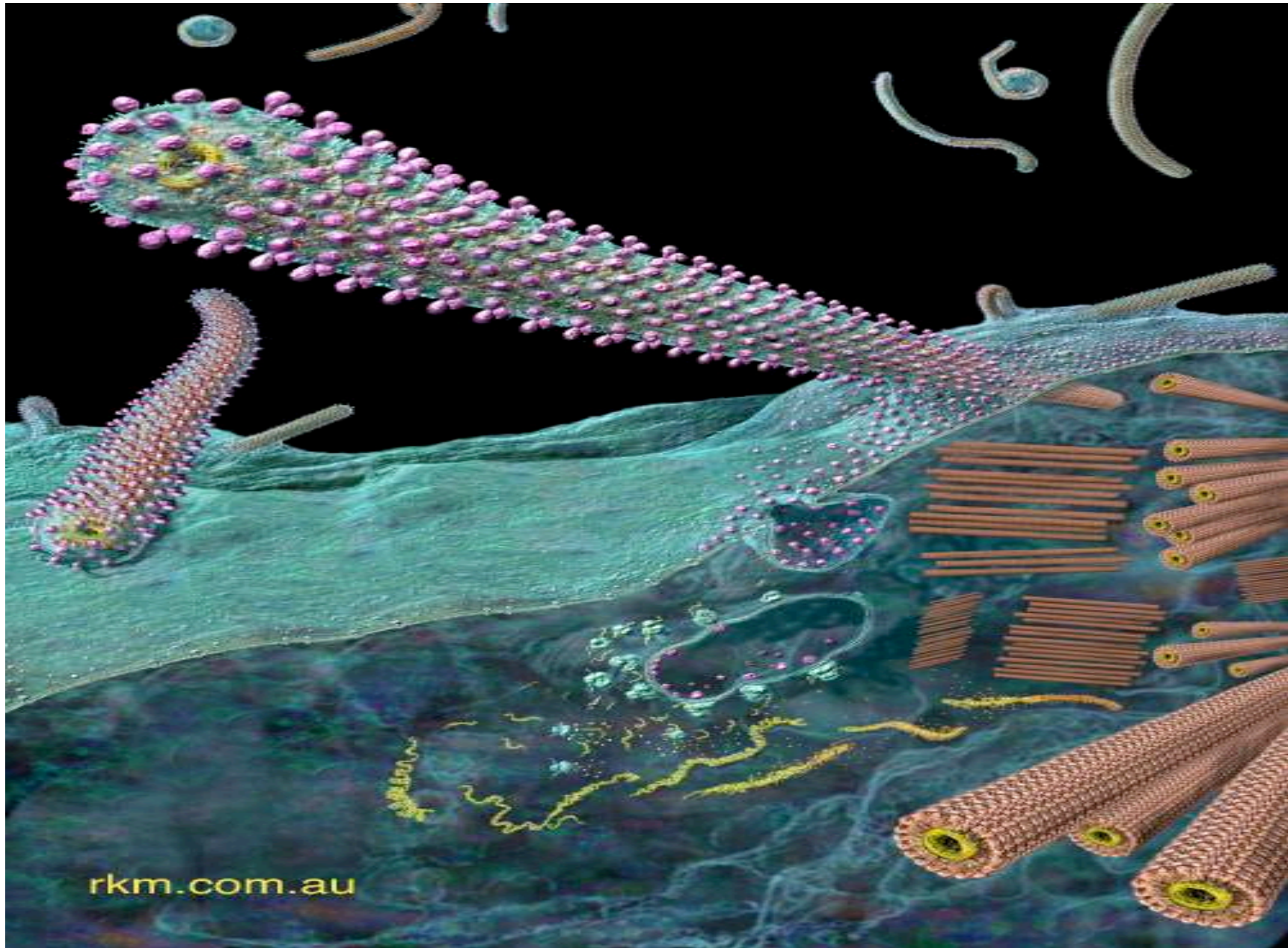


Reverse flow of Genetic Information: Retroviruses



Retrovirus

- Genome consisting of RNA molecules
- Relies on the enzyme reverse transcriptase to perform the reverse transcription of its genome from RNA into DNA, which can then be integrated into the host's genome with an integrase enzyme.
- The virus itself stores its nucleic acid genome and serves as a means of delivery of that genome into targeted cells, which constitute the infection.
- Once in the host's cell, the RNA strands undergo reverse transcription in the cytosol and are integrated into the host's genome, at which point the retroviral DNA is referred to as a provirus.
- When retroviruses have integrated their genome into the germ line, their genome is passed on to a following generation. These endogenous retroviruses (vs. exogenous) now make up 8% of the human genome.



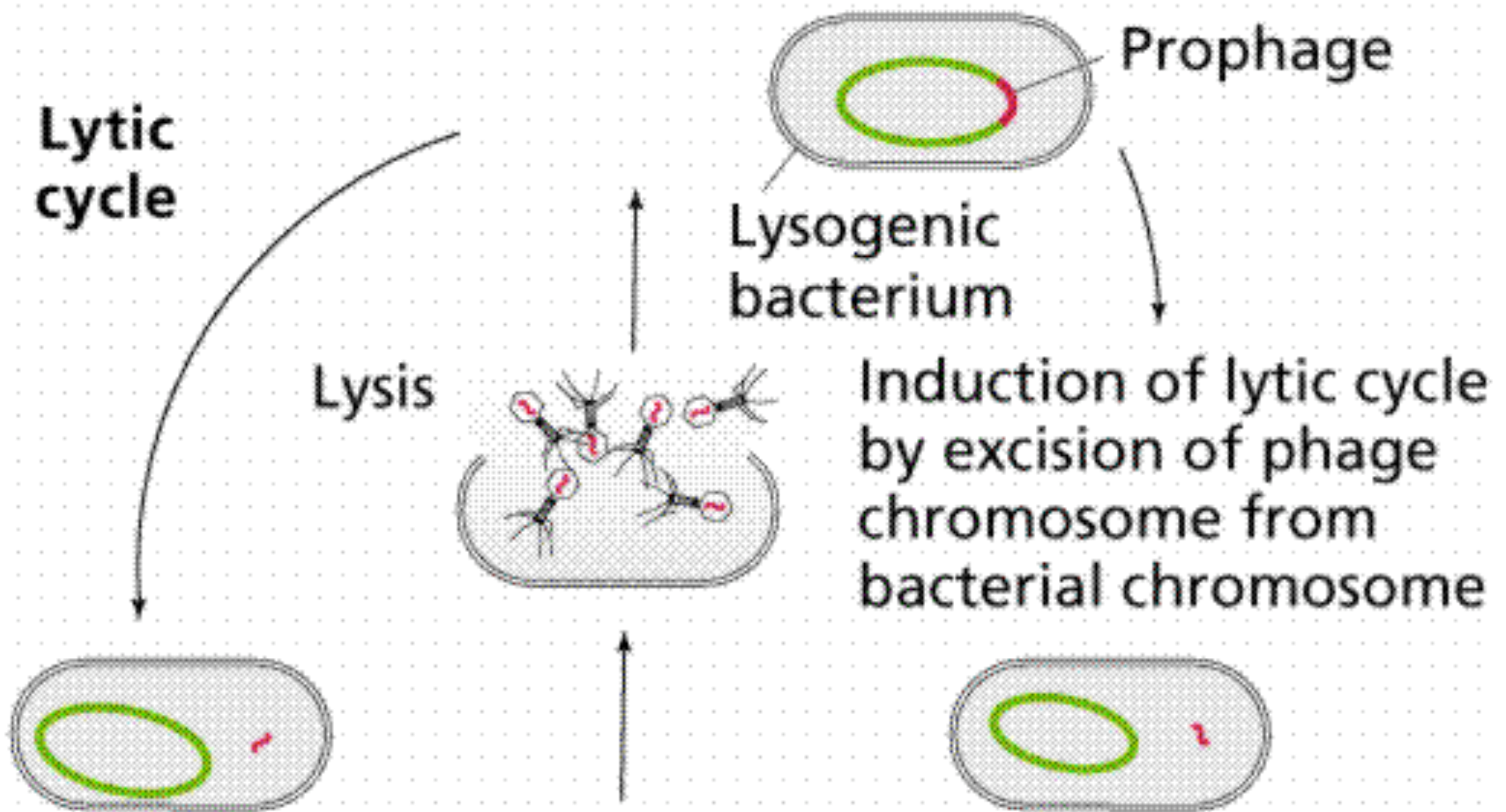
VIRUSES - life cycle

- Viruses have a variety of life cycles once they infect their hosts:
- Some viruses have **Lytic life cycle** and cause lytic infections in their hosts
 - Virulent viruses force the host cell to make thousands copies of the virion.
 - Result: Virus bursts (lysis) to release new virions \Rightarrow Death of cell.
- Others have **Lysogenic life cycle**
 - Viral genetic material inserts into the host's DNA
 \Rightarrow Provirus

Lytic life cycle

- Three-stage process.
- **Infection**
 - When a virus infects a cell, it first binds with the cell membrane using receptor molecules on the virus's surface. The virus then injects its genetic material, which can be either DNA or RNA, into the cell's nucleus.
- **Growth**
 - The viral nucleic acid takes over and uses the host cell's organelles to make many copies of the virus.
 - In the case of DNA viruses, the DNA transcribes itself into messenger RNA (mRNA) molecules that are then used to direct the ribosome.
 - In retroviruses, or RNA viruses, a unique enzyme called reverse transcriptase transcribes the viral RNA into DNA, which is then transcribed again into mRNA.
- **Replication and lysis**
 - After many virus copies are made, they are assembled into complete viruses.
 - The cell eventually becomes filled with viruses (typically 100-200) until it bursts, or lyses; this end process gives the cycle its name.
 - The new viruses are free to infect other cells.

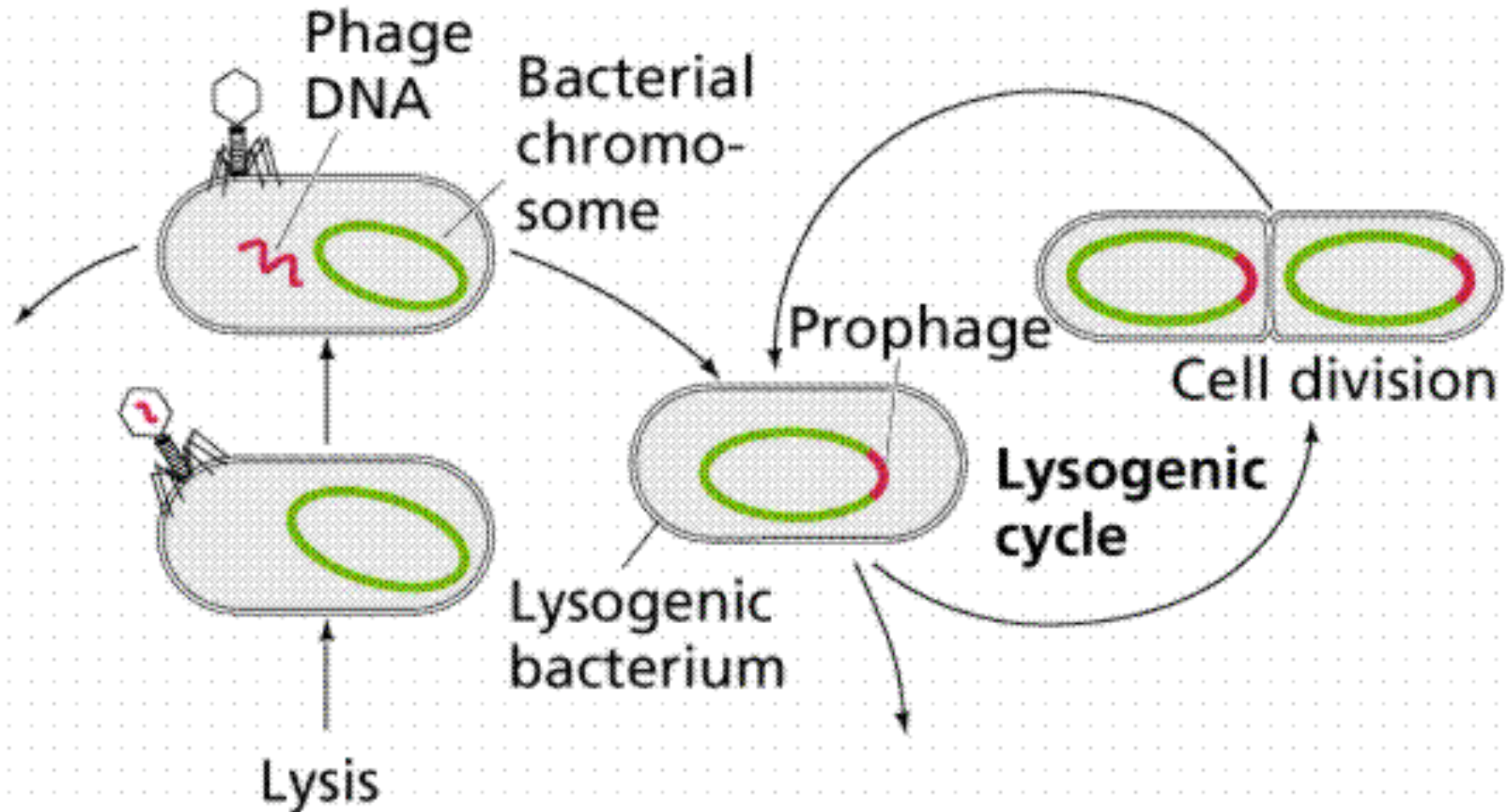
Lytic Cycle



Lysogenic life cycle

1. Viral genome enters cell
2. Viral genome integrates into host cell genome
3. Host cell DNA polymerase copies viral chromosomes
4. Cell divides and virus chromosomes are transmitted to cell's daughter cells
5. At any moment when the virus is "triggered", the viral genome detaches from the host cell's DNA and enters stage 2 of the lytic cycle.
 - While it is unclear as of yet what exactly constitutes a "trigger" that activates the viral DNA from the latent stage entered in Step 4, common symptoms that appear to "trigger" the viral DNA are hormones, high stress levels (adrenaline), and free energy within the infected cell.
- An example of a virus that enter the lysogenic cycle is **herpes**, which first enters the lytic cycle after infecting a human, then the lysogenic cycle before travelling to the nervous system where it resides in the nerve fibres as an episomal element. After a long period of time (months to years) in a latent stage, the herpes virus is often reactivated to the lytic stage during which it causes severe nervous system damage.

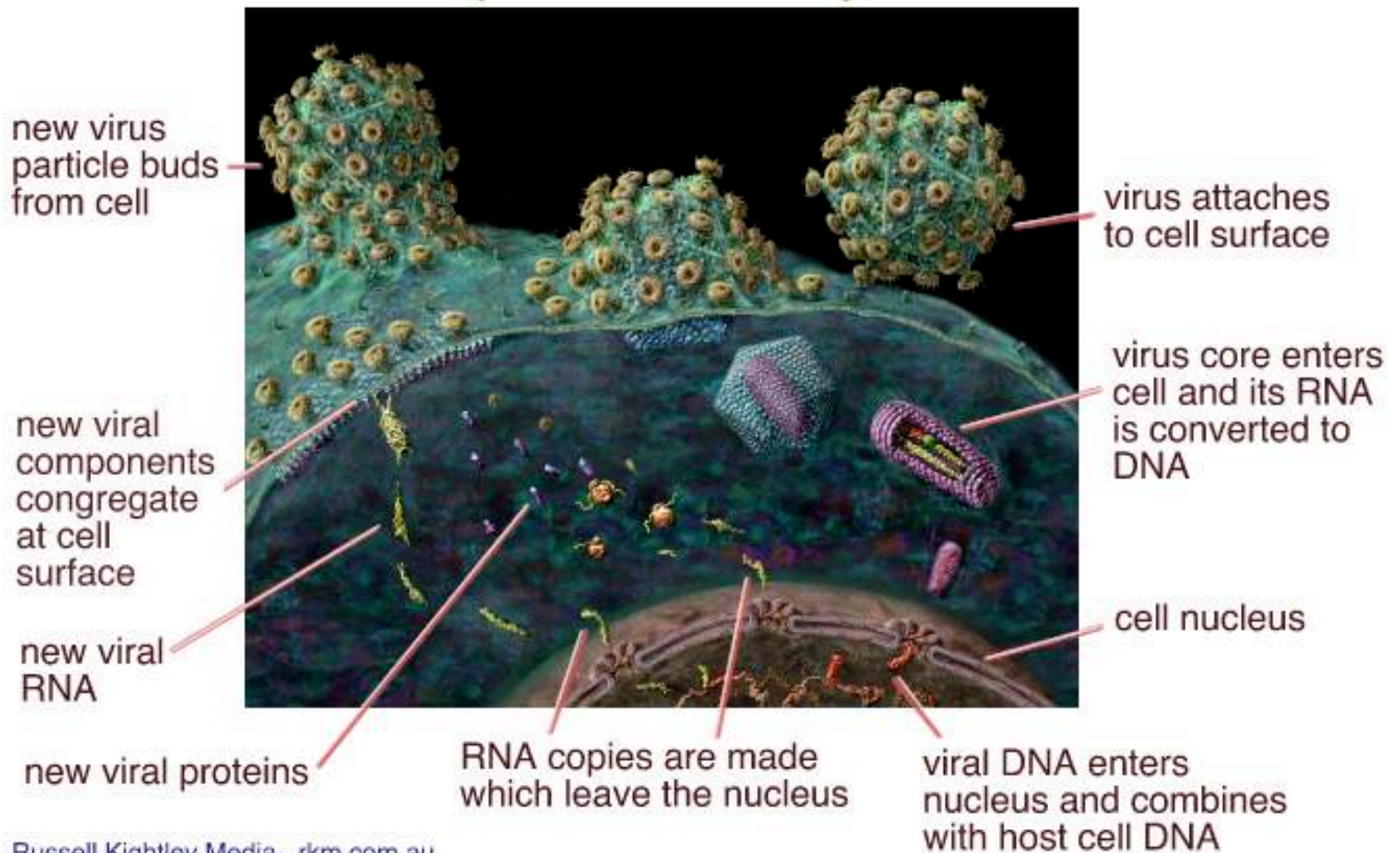
Lysogenic Cycle



VIRUSES - infections

- Proviruses are the cause of **latent infections** where the virus can exist without causing symptoms, sometimes for decades. Example Herpes virus.
- Other viruses slowly release a small number of virus particles, by a process called budding, from the host cell without killing it. This type of virus infection is called a **persistent, or chronic, infection**.
- Some viruses exhibit slow infections, in which the virus density gradually increases over long periods of time. Example HIV.

simplified HIV life-cycle



Russell Kightley Media, rkm.com.au

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Viruses

AIDS

- Retrovirus
 - First shown to cause cancer
 - Single Stranded RNA genome
 - Reverse Transcriptase
- A global pandemic, with over 50 million people estimated to have been infected. About 6 million new infections are estimated each year.
- 30 million people are estimated to be infected in Africa. Possibly from Monkeys! (as food!)
- Up to 10 year period of slow infection.
- No certain cure (few possible cures)

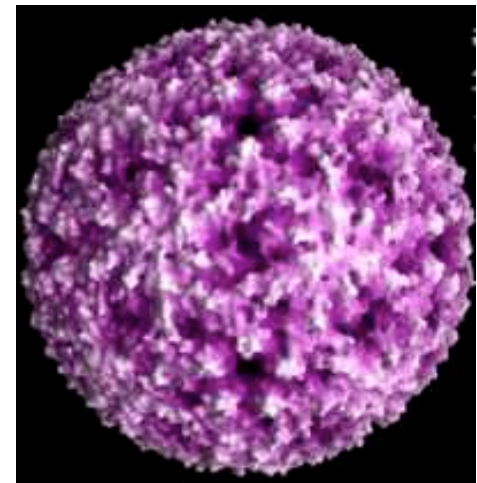
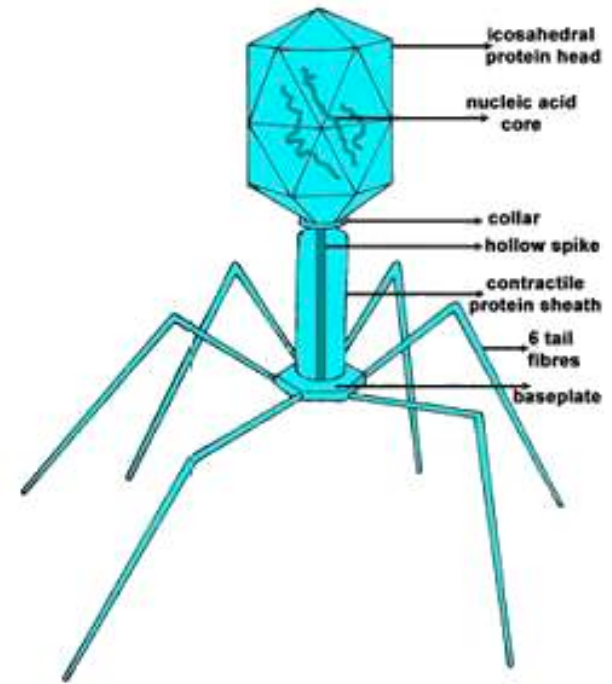
VIRUSES - examples

Bacteriophages

- Bacteria's most dreaded enemy
- Infect bacteria
- Has extended 'legs' (!)
- Double stranded DNA

Foot & Mouth

- Aphthovirus (Picornaviridae family virus)
- One of the most contagious animal diseases, with important economic losses
- Hosts are Bovidae (e.g. cattle), sheep, goats, swine, all wild ruminants and suidae (also camel)
- Transmission can be through direct or indirect contact (droplets)
- Occurs mostly in Asia, Africa, Middle East and South America
- Diagnosis: incubation period is 2-14 days
 - Variable diagnostic procedures in animals



Retrovirus, retrotransposons

- Most insertions have no known function and are often referred to as "junk DNA" (Noncoding DNA).
- However, many endogenous retroviruses play important roles in host biology, such as control of gene transcription, cell fusion during placental development, and resistance to exogenous retroviral infection.
- Reverse transcriptase transcribes RNA into DNA. "retro" in retrovirus refers to the reversal of the central dogma of molecular biology.
- Reverse transcriptase activity outside of retroviruses has been found in almost all eukaryotes, enabling the generation and insertion of new copies of *retrotransposons* into the host genome.
- Because reverse transcription lacks the usual proofreading of DNA transcription, this kind of virus *mutates* very often. This enables the virus to grow resistant to antiviral pharmaceuticals quickly, and impedes, for example, the development of an effective vaccine against HIV.

Transposons

- Sequences of DNA that can move around to different positions within the genome of a single cell, a process called transposition.
- In the process, they can cause mutations and change the amount of DNA in the genome.
- Transposons are also called "jumping genes" or "mobile genetic elements".
- Class I mobile genetic elements, or retrotransposons, move in the genome by being transcribed to RNA and then back to DNA by reverse transcriptase
- Class II mobile genetic elements move directly from one position to another within the genome using a transposase to "cut and paste" them within the genome.
- Transposons make up a large fraction of the genome sizes of eukaryotes: ~45% of the human genome is composed of transposons and their defunct remnants.

Retrotransposons: LINEs, SINEs

- Class I type of mobile elements, 2 sub-types
 - long terminal repeat (LTR) - apprx 8% of the human genome, and
 - non-LTR retrotransposons: LINEs & SINEs
- LINEs (long interspersed elements): move by copying themselves (instead of moving, like transposons do) hence *enlarge* the genome. ~500,000 copies, ~16% of human genome. Used to generate genetic fingerprints.
- SINEs (short interspersed elements): do not encode a functional reverse transcriptase protein and rely on other mobile elements for transposition. ~ 1 million copies, ~ 11% of the human genome.
- Previously believed to be "junk DNA". Recent research suggests that LINEs & SINEs have a significant role in gene evolution, structure and transcription levels. Their distribution implicated in some genetic diseases and cancers.
- Retroviruses, (e.g. HIV-1) behave like retrotransposons.