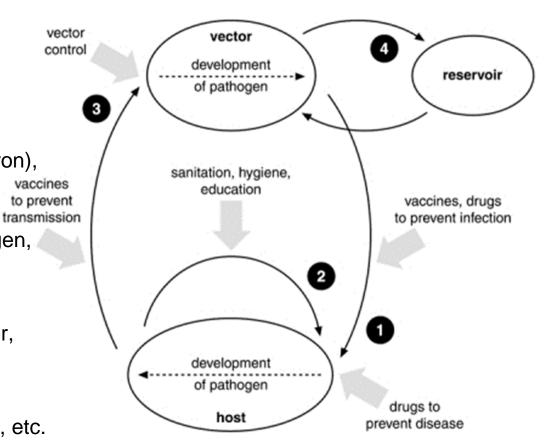
## Host-Pathogen Relationship in 3D

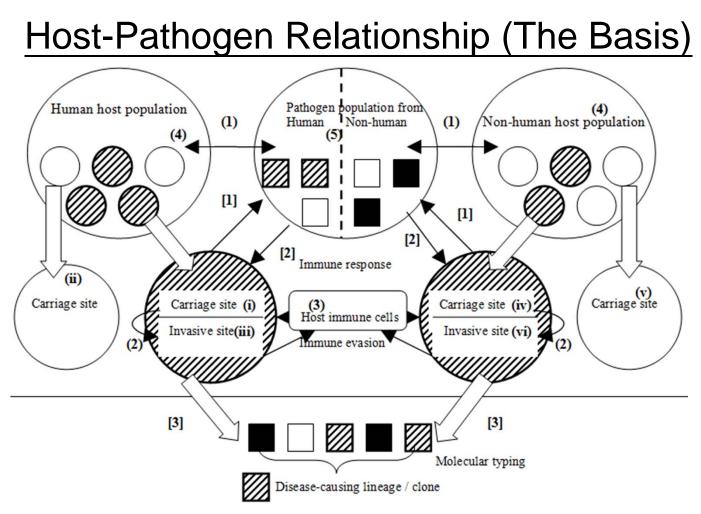
Name: Ma Hok Lun, Helen (PhD, Yr 2) Date: 2010-12-7

### Host-Pathogen Relationship (The Basis)

- Definition of pathogen:
- Microorganisms that are capable of causing disease
- <u>Types of pathogens:</u>
- By organism identity:
- Viruses, Bacteria, Fungi, Protozoa, (Piron), etc.
- By ability to cause infection:
- True pathogen vs. opportunistic pathogen, etc.
- Types of hosts:
- Definitive (Final), Intermediate, Transfer, Reservoir, etc.
- Types of Host-pathogen interaction:
- Commensalism, Mutualism, Parasitism, etc.

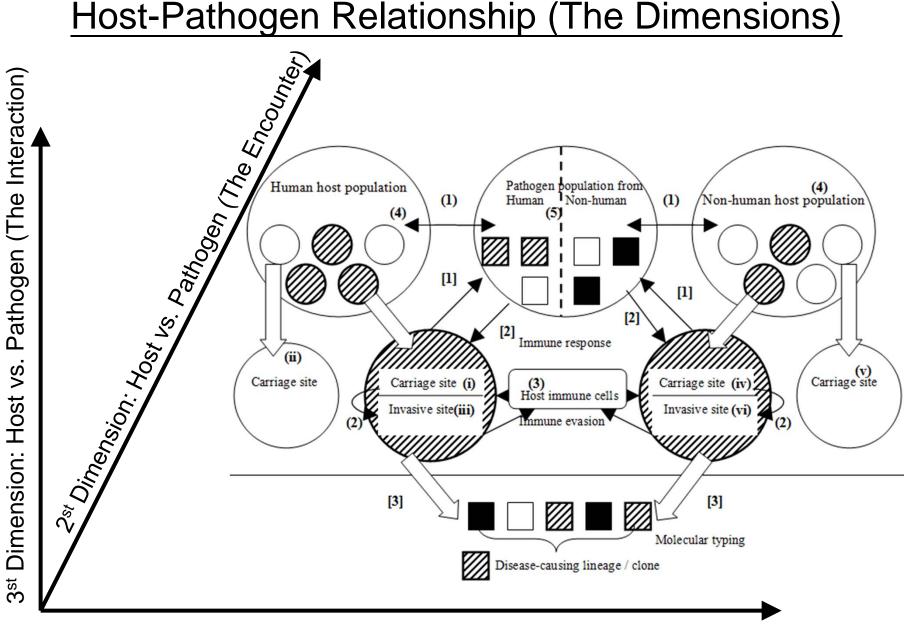


Bethesda, NIH, 2007 http://www.icp.ucl.ac.be/~opperd/parasites/types3.htm



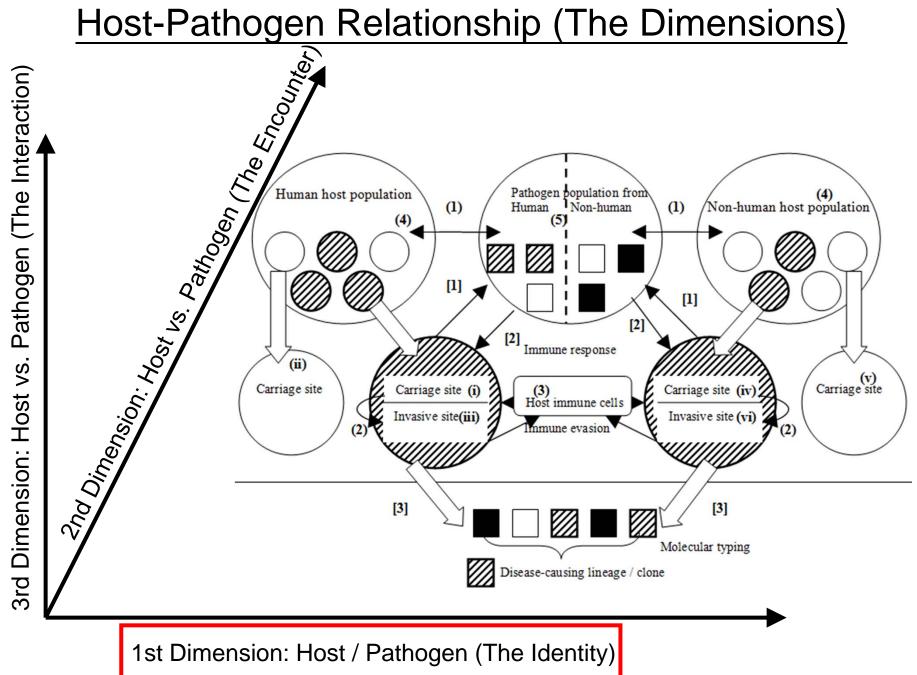
- Schematic diagram of Host-Pathogen Interaction:
- (1) Transmission between host and pathogen
- (2) Transmission within host (carriage vs. invasive sites)
- (3) Host immune response vs. Pathogen immune evasion
- (4) Individual factors of particular host that affect (1) to (3)
- (5) Strain-dependent factors among pathogens

Willey J *et. al.*, 2008 Ip M and HLH Ma, 2010



1<sup>st</sup> Dimension: Host / Pathogen (The Identity)

Ip M and HLH Ma, 2010



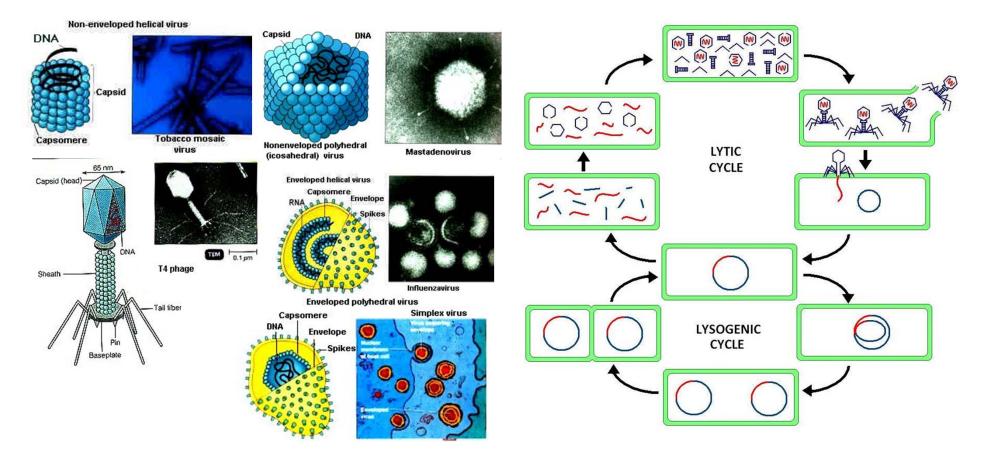
Ip M and HLH Ma, 2010

#### • Our usual understanding on viruses:

• An envelope of nucleic acid that takes over host's machinery to reproduce

#### • Our usual understanding on viral life cycle:

• Lytic vs. Lysogenic cycle



http://www.prism.gatech.edu/~gh19/b1510/virus.htm

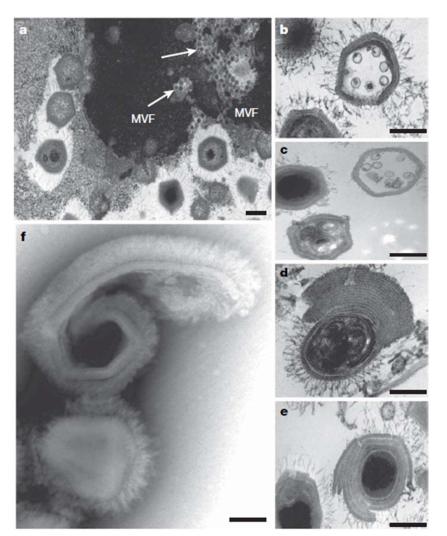
http://en.wikipedia.org/wiki/Lytic\_cycle

#### • Pathogen:

- Acanthameoba polyphaga mimivirus (mamavirus, APMV)
- The largest known virus

#### • Host:

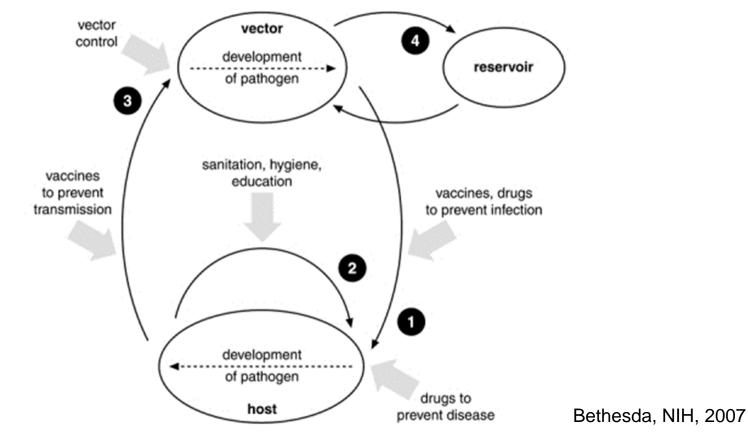
- Ameoba (Acanthameoba polyphaga, Acanthameoba castellanii, etc.)
- Pathogen's "pathogen":
- Sputnik, icosahedral viron particle
- A currently unknown family of virus
- Take over the ameoba machinery taken over by mamavirus to reproduce
- Identified as "Virophage" (compared to bacteriophage)

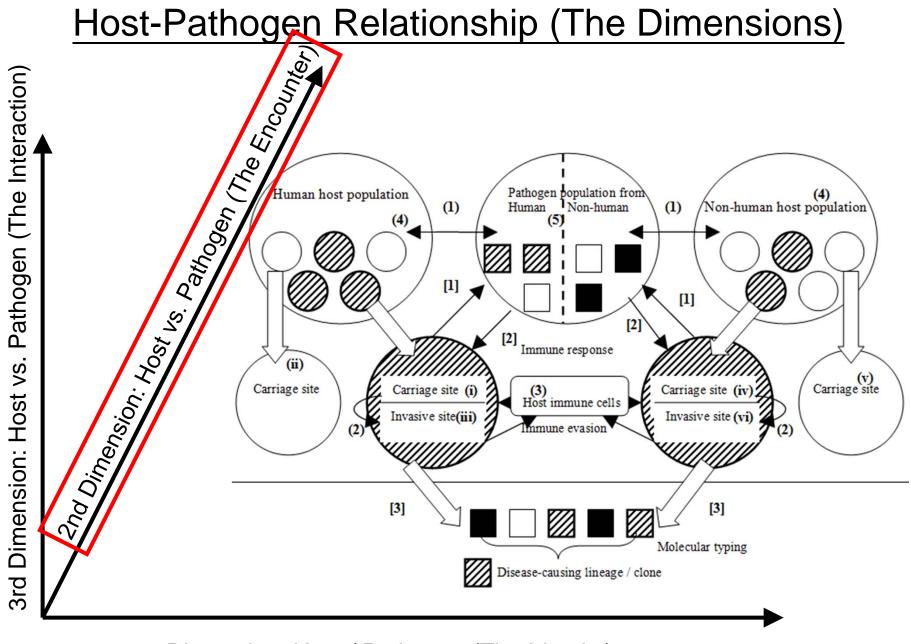


#### Pathogenicity is the ongoing evolution between a parasite and a particular host.

Faklow S, 2007 Scola BL *et. al.*, 2008

- Pathogenicity is the **ongoing evolution** between a parasite and a particular host.
- The identity of a "Host" and a "Pathogen" is not fixed.
- The rationale we use for defining "Host-Pathogen" relationship is oversimplified.



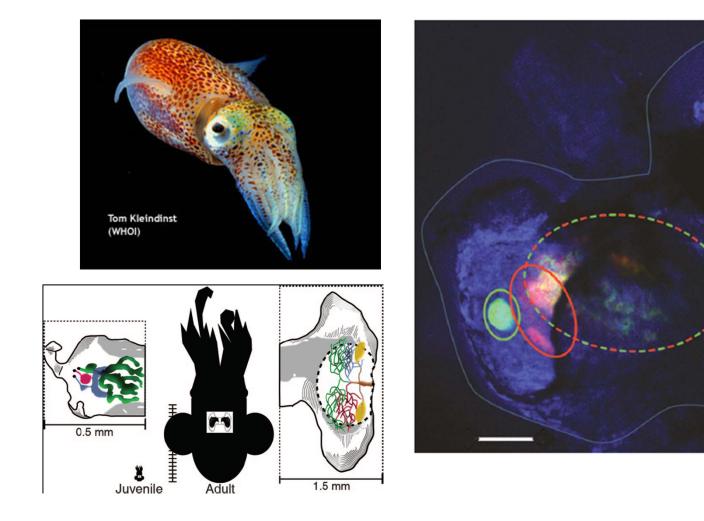


1st Dimension: Host / Pathogen (The Identity)

Ip M and HLH Ma, 2010

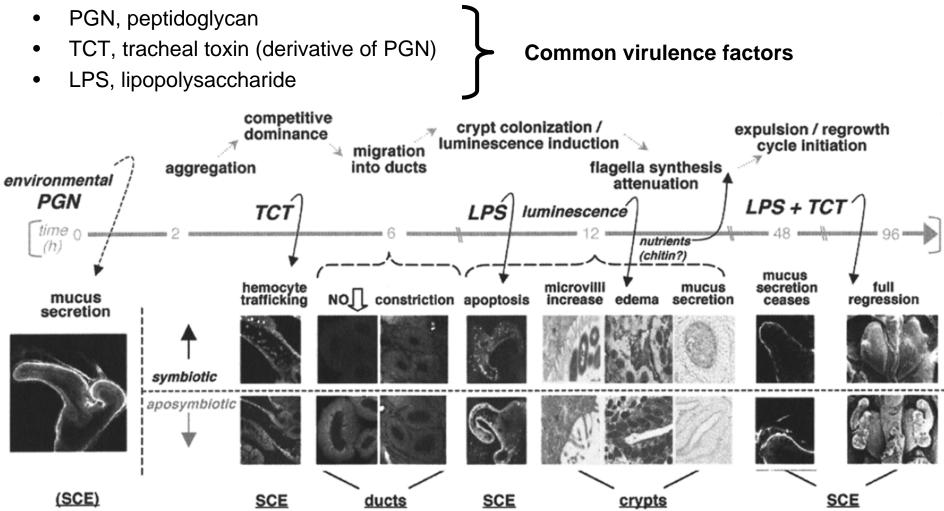
### 2nd Dimension: Host vs. Pathogen (The Encounter)

- "Pathogen": Vibrio fischeri, produce biofilm in host, responsible for Bioluminescence
- Host: Various marine animals, such as Hawaiian bobtail squid (*Euprymna scolopes*)



#### 2nd Dimension: Host vs. Pathogen (The Encounter)

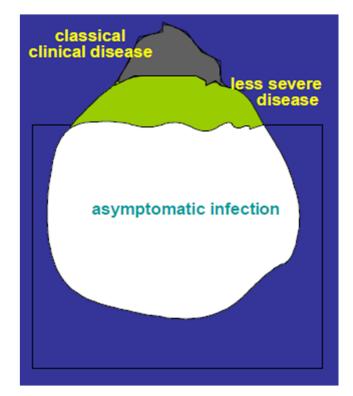




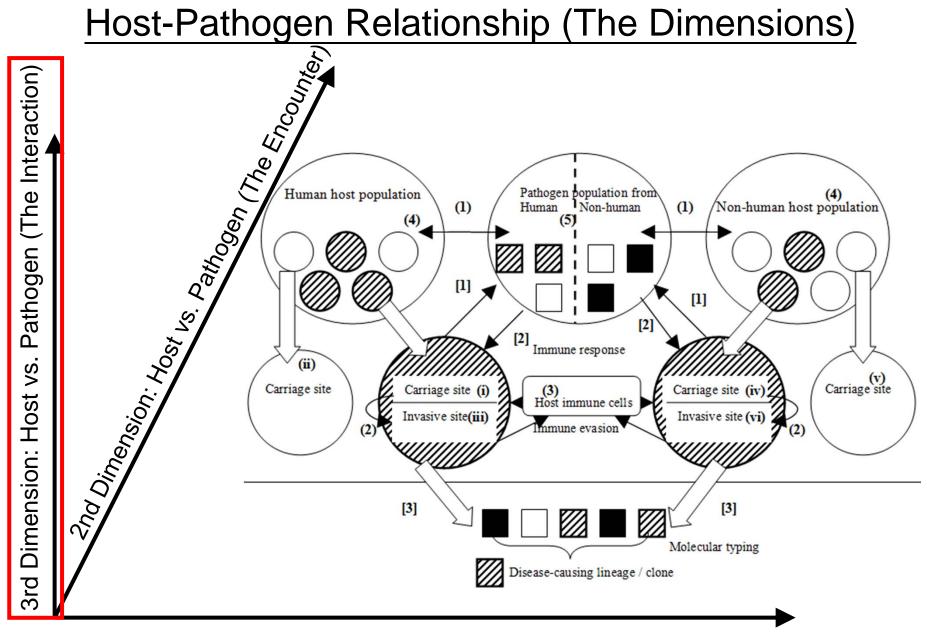
The real identity of virulence factors are signaling molecules!

#### 2nd Dimension: Host vs. Pathogen (The Encounter)

- The real identity of virulence factors are signaling molecules!
- Types of Host-pathogen interaction:
- Commensalism, Mutualism, Parasitism, etc.
- Definition of Infection:
- When a pathogen invades and begins growing within a host.
- Definition of Disease:
- Consequence of the invasion and growth of a pathogen, tissue function is impaired.
- The Iceberg Concept of Infection:
- <u>"Disease is the more the exception than the rule."</u>



Bethesda, NIH, 2007 Faklow S, 2007



Willey J *et. al.*, 2008 Ip M and HLH Ma, 2010

#### 3rd Dimension: Host vs. Pathogen (The Interaction)

- A more practical issue: How we study Host-Pathogen Interaction?
- Host: changes in gene expression, cytokine release, changes in metabolism, etc.
- **Pathogen:** changes in gene expression, life-cycle, etc.

glucose metabolism

purine biosynthesis

Fibroblast

cell cycle

PI3K signaling

amino acid catabolism

• E.g. in Trypanosoma cruzi,

cell proliferation response to wounding immune response response to stress

apoptosis

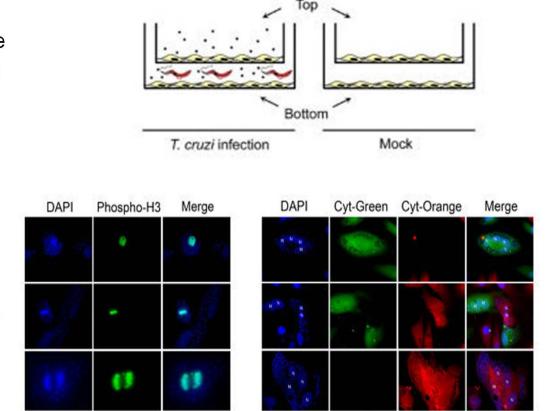
Endothelial

lipid metabolism

steroid metabolism

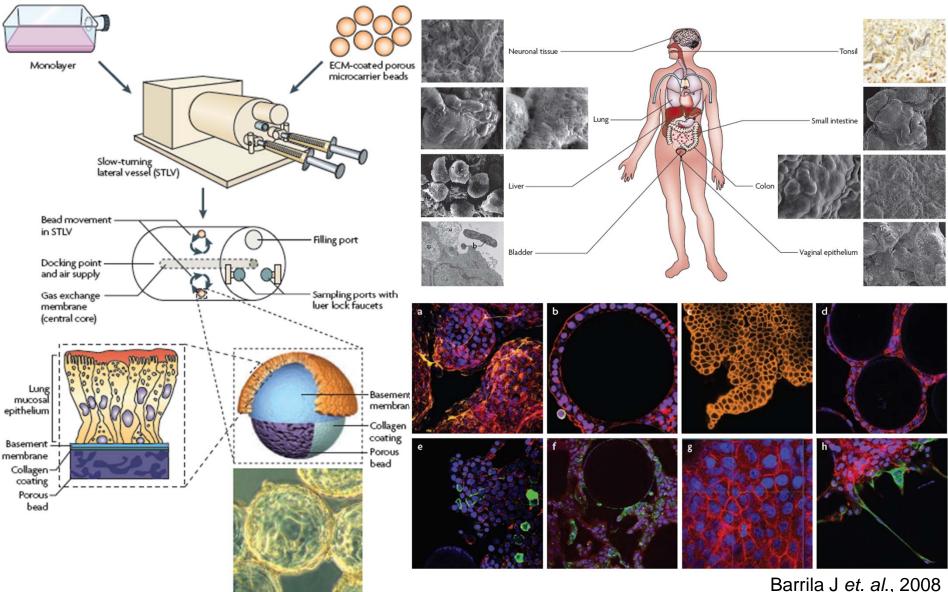
Smooth muscle

- an intracellular protozoa that cause
- South-American sleeping sickness



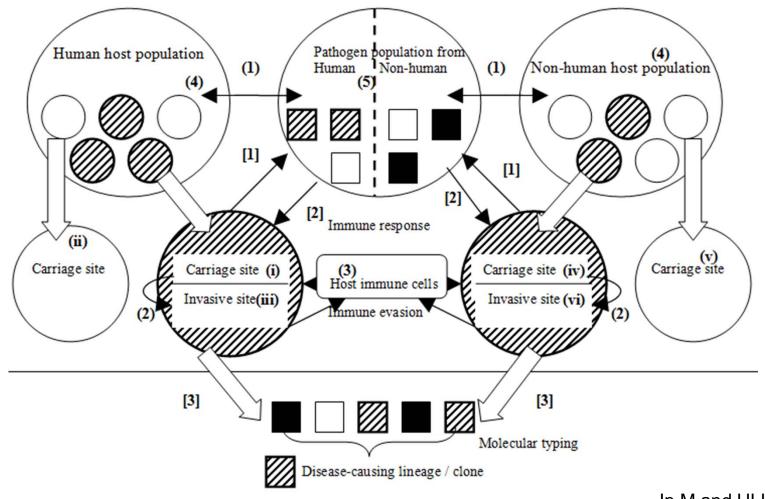
### 3rd Dimension: Host vs. Pathogen (The Interaction)

It depends on what question we ask:



#### 3rd Dimension: Host vs. Pathogen (The Interaction)

- Various choice of methods to study <u>"Host-Pathogen Relationship"</u>
- The question we ask may "simplify" or "complicate" the answer.

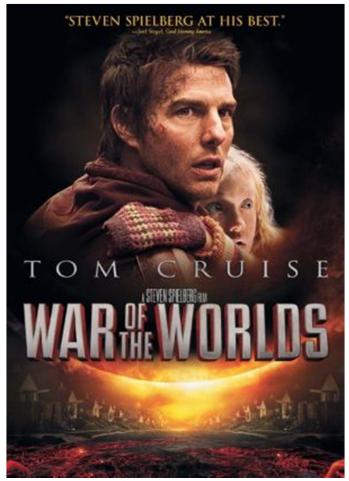


Ip M and HLH Ma, 2010

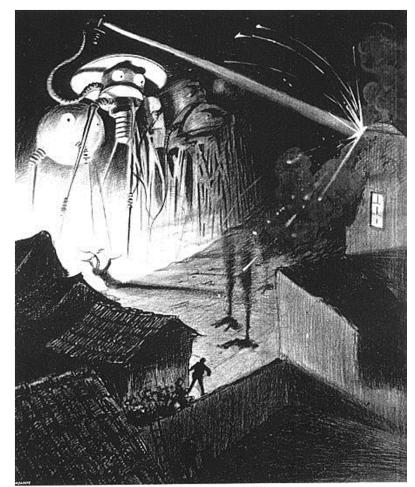
#### Host-Pathogen Relationship (Among the Dimensions)

- <u>1st Dimension: Host / Pathogen (The Identity)</u>
- Pathogenicity is the **ongoing evolution** between a parasite and a particular host.
  - The identity of a "Host" and a "Pathogen" is not fixed.
- The rationale we use for defining "Host-Pathogen" relationship is **oversimplified**.
  - <u>2nd Dimension: Host vs. Pathogen (The Encounter)</u>
    - "Disease is the more the exception than the rule."
  - The **real identity of virulence factors** are signaling molecules!
    - <u>3rd Dimension: Host vs. Pathogen (The Interaction)</u>
  - Various choice of methods to study "Host-Pathogen Relationship"
  - The question we ask may "simplify" or "complicate" the answer.

- Host-Pathogen Relationship in Science Fictions:
- In film "War of the Worlds" (H.G. Wells, adopted by Steven Spielberg),
- Alien creatures die out as they lack immunity against microbes on Earth.

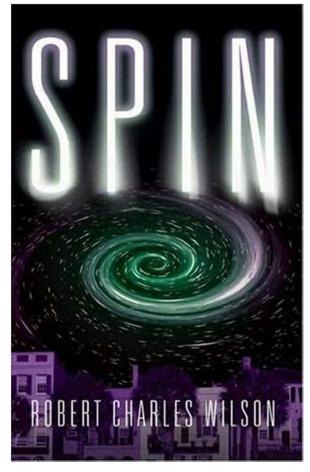


http://scifilounge.blogspot.com/2010/10/war-of-worlds.html

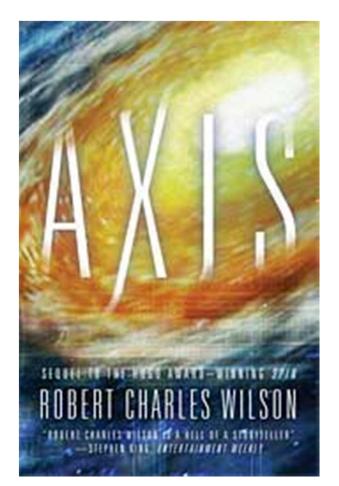


http://en.wikipedia.org/wiki/The\_War\_of\_the\_Worlds

- In "Spin" and "Axis" (R.C. Wilson, winner of Hugo Award),
- Human moves to live on a new planet, and was said to <u>immune to</u> <u>all alien pathogens as they lack appropriate receptors to interact.</u>



http://en.wikipedia.org/wiki/Spin\_(novel)

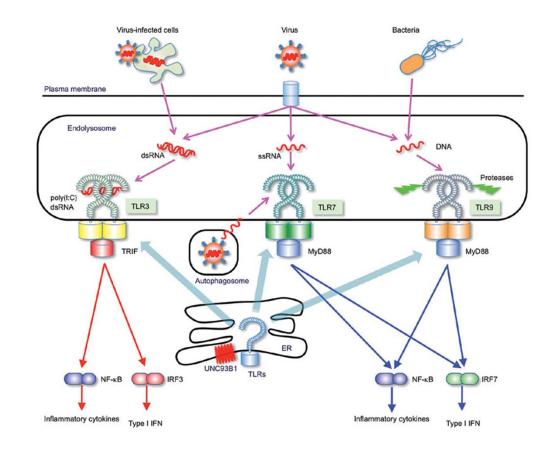


http://en.wikipedia.org/wiki/Axis\_(novel)

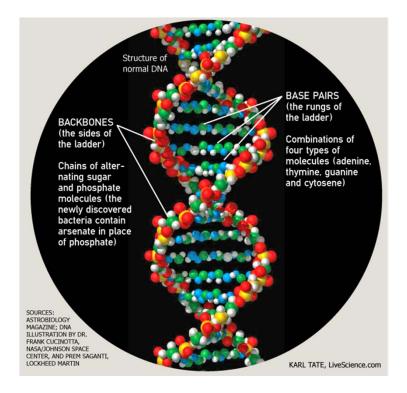
#### Infection vs. Immunity

If we encounter alien microbes, are we prone to infection or not?

- Molecular level of Host-Pathogen Interaction
- Translated as Multiple Ligand-Receptor Binding
- Resulted from ages of Host-Pathogen Co-evolution
- Virulence (Pathogen) vs. Resistance (Host)



- Infection vs. Immunity
- If we encounter alien microbes, are we prone to infection or not?
- <u>1st Dimension:</u> <u>Host / Pathogen (The Identity)</u>
- <u>2nd Dimension:</u> <u>Host vs. Pathogen (The Encounter)</u>
- <u>3rd Dimension:</u> Host vs. Pathogen (The Interaction)



# END