

Virologie vétérinaire

Chapitre 1 Les origines de la virologie, les origines des virus



Il y a 10^{31} virus sur la terre (approximativement)

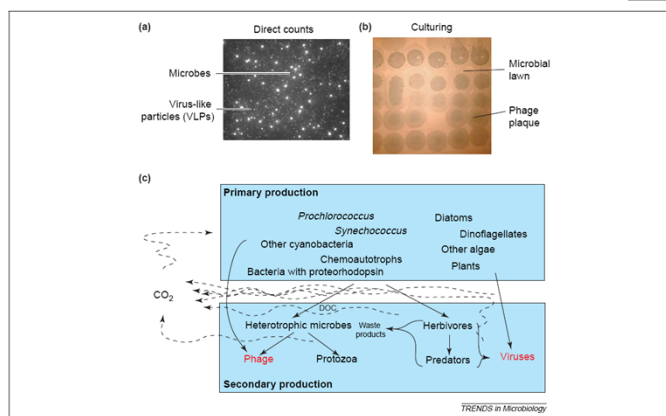


Figure 1. Methods and models used to study viral ecology (a) Epifluorescence micrograph showing microbes and virus-like particles (VLPs) from seawater stained with a nucleic acid stain. The microbes are the larger brighter spots, whereas the VLPs are small pinprick dots. (b) Phage isolation accomplished by plating on a bacterial lawn. A bacterial host is first cultured from the environment of interest and then plated as a lawn on top of an agar plate. Phage are spotted on top of this lawn and the clear areas represent regions where phage have lysed the host. (c) Ecological roles of viruses. Carbon dioxide is fixed into sugars by primary producers. The sugars and downstream metabolites are then used to make biomass (production), perform metabolism (respiration) or are released into the environment as dissolved organic carbon (DOC). Secondary producers, such as herbivores, eat the new primary producer biomass and heterotrophic microbes eat the DOC. Herbivores are then eaten by predators and the microbes are grazed by protozoa or viruses. A rough rule of thumb is that ~50% of the fixed carbon is shunted into heterotrophic microbes via DOC and approximately half of the new microbes are killed by viruses. This means that ~25% of the fixed carbon is respired as CO₂ due to viral lysis. Viruses also directly kill primary producers and other secondary producers.

Breitbart et Rohwer, Trends in Microbiology, 2005, 13, 278)



Virologie vétérinaire – BMV3 - E. Thiry

> Israël - OLP: la paix brisée (p.52)

L'EXPRESS

Les virus
attaquent

D'anciennes maladies résistent
De nouvelles apparaissent
Un défi permanent pour la médecine (p.38)



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<small>Interministeriële Influenza Commissie</small> <small>Eurostation II</small> <small>Place Victor Hortaplein 4D Bte/Bus 10</small> <small>1000 Bruxelles/Brussel</small>	<small>Interministerieel Commissariaat Influenza</small> <small>Eurostation II</small> <small>Victor Hortaplein 4D Bus 10</small> <small>1000 Brussel</small>	<small>Commissariat Interministériel Influenza</small> <small>Eurostation II</small> <small>Place Victor Horta 4D Bte 10</small> <small>1000 Bruxelles</small>
<h2>H1N1 flu, be cautious !</h2>	<h2>H1N1 griep, wees waakzaam!</h2>	<h2>Grippe H1N1, soyons vigilants !</h2>
<p>Are you coming back from a country where cases of the H1N1 flu have been reported?</p> <p>Please be cautious if you show the following flu symptoms within 7 days after your return :</p> <ul style="list-style-type: none"> - Fever - Painful muscles and/or articulations, headache - Cough - Diarrhoea, vomiting <p>Stay at home and immediately call for your GP, and tell him about your travel.</p> <p>More info on : www.influenza.be</p>	<p>Komt u terug uit een land waar gevallen gemeld werden van de H1N1 griep?</p> <p>Wees dan waakzaam indien u de volgende griepsymptomen vertoont binnen de 7 dagen na uw terugkeer :</p> <ul style="list-style-type: none"> - Koorts - Pijnlijke spieren en/of gewrichten, hoofdpijn - Hoesten - Diarree, braken <p>Blijf thuis en verwittig onmiddellijk uw huisarts en breng hem op de hoogte van uw reis.</p> <p>Meer informatie op: www.influenza.be</p>	<p>Vous revenez d'un pays où des cas de grippe H1N1 ont été mentionnés ?</p> <p>Soyez très attentifs si, dans les 7 jours qui suivent votre retour, vous ressentez des symptômes grippaux tels que :</p> <ul style="list-style-type: none"> - Fièvre - Courbatures (douleurs articulaires et/ou musculaires), maux de tête - Toux - Diarrhée, vomissements <p>Restez à la maison, appelez immédiatement votre médecin généraliste et informez-le de votre voyage !</p> <p>Pour en savoir plus : www.influenza.be</p>
0 8 0 0 / 9 9 . 7 7 7		
www.influenza.be - info@influenza.be		



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la virologie et les virus

- D'où vient la virologie ?
- D'où viennent les virus ?

Viruses are packages of genes and genetic elements with millenia of biological experience
(Walter Doerfler, 1994)

C. Chastel, La naissance de la virologie, *Virologie*, 1997, 1, 103-110.
F. A. Murphy, University of Texas Medical Branch, The Foundations of Medical and Veterinary Virology: *Discoverers and Discoveries, Inventors and Inventions, Developers and Technologies*

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Bas-relief de la 18^e dynastie égyptienne (1500 AJC)

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Homme mordu
par un chien
Freer Gallery of Art,
Smithsonian Institution,
Washington, DC.

Manuscrit irakien du 13^e siècle,
écrit par Abdallah ibn al-Fadl de l'école de Bagdad



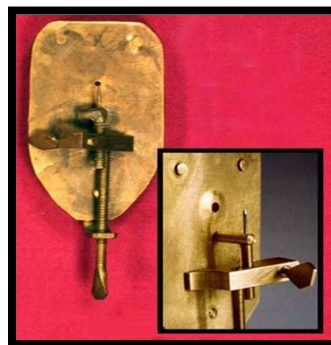
Rabies (derived from the Sanskrit, “rabhas” meaning “to do violence”) was first described in the 23rd century BC in the Eshuma Code of Babylon — it is the oldest documented disease of humans.



Virus (latin) : jus, poison, écoulement, puanteur

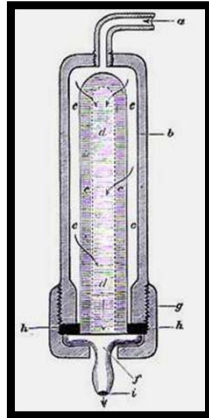
- XIX^e siècle : microscope optique et bougies filtrantes

Microscope optique



One of Leeuwenhoek's microscopes
(simple, that is with a single convex lens, yet capable
of a magnification of x200-300, whereas the compound
microscopes of the day achieved only x20-30)

Filtration: les bougies et le concept de « virus filtrant »



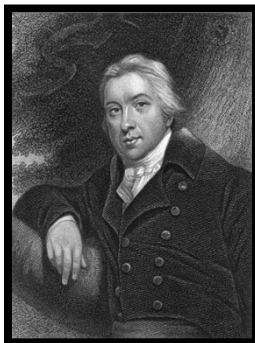
Virus filtrants ou ultravirus

- Virus filtrants :
 - Responsables de maladie
 - Ne se multiplient pas sur les milieux de culture de bactéries
 - Invisibles au microscope
 - Ne sont pas arrêtés par les filtres bactériologiques courants
- XIX^e siècle : Les virus sont des « êtres de raison »
 - Les bactéries sont visibles
 - Les virus sont du domaine de l'inconnu

Les précurseurs

- Edward Jenner
 - (vaccination contre la variole, 1796)
- et Louis Pasteur
 - (vaccination contre la rage, 1885)
- ont tenu en main des virus, sans le savoir

Vaccination par Jenner, 1796



Edward Jenner
(1749-1823)



Pasteur, le « père » de la microbiologie



À Arbois, lieu de villégiature



À Dole, lieu de naissance

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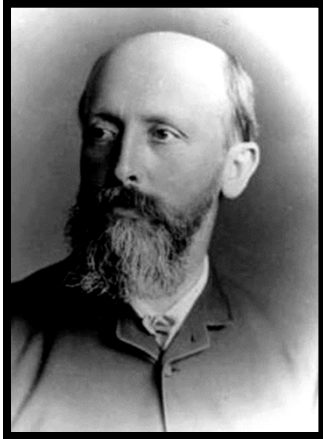
Joseph Meister, age 9 the first person treated with Pasteur's vaccine 6 July 1885



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La mosaïque du tabac : première description de la maladie en 1886



Adolf Mayer (1843-1942)

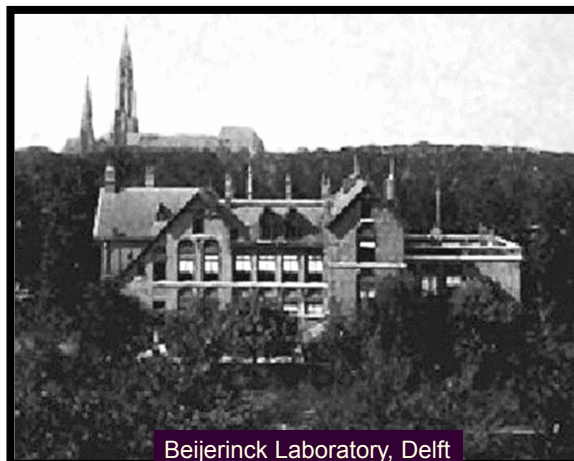
Tobacco mosaic disease
from Mayer's work, 1866Université
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Dmitri Ivanovski (1864-1920)

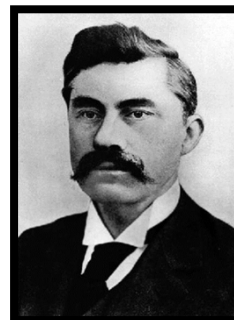
- Transmission expérimentale de la mosaïque du tabac, de plant malade à plant sain, avec du filtrat de de feuilles broyées (premier virus filtrant) (1882)

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Beijerinck : principe filtrant qui transmet la mosaïque du tabac: *contagium vivum fluidum*



Beijerinck Laboratory, Delft

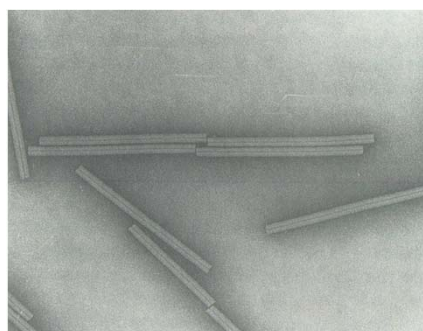


Martinus Willem
Beijerinck
(1851-1931)

Mosaïque du tabac

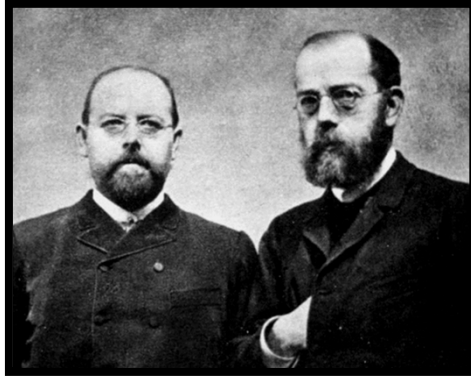


Virus de la
mosaïque du tabac
(*Tobamoviridae*)



Le triomphe de la virologie vétérinaire

- Friedrich Loeffler (ici avec Robert Koch) et Paul Frosch (Greifswald, île de Riems)



Friedrich Loeffler (1852–1915) , Robert Koch (1843-1910)



Paul Frosch (1860-1928)

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Découverte du virus filtrant de la fièvre aphteuse (1898) par Loeffler et Frosch

Friedrich Loeffler and the Isle of Riems

"The history of Riems is part of the history of research into foot-and-mouth disease and of veterinary viral research" (Otto Waldmann, 1936).

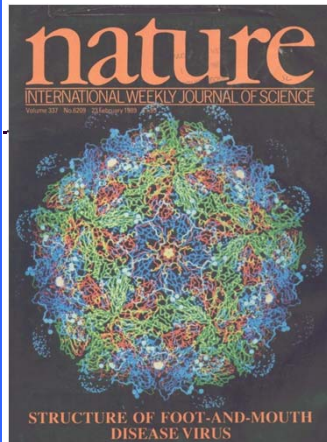
It may be an oddity that one of the roots of the first virological institutes in the world can be traced back to the offer of a reward by the Prussian Ministry of Agriculture. In 1893, 3,000 Reichsmarks were offered for the person who "identifies and, if possible, isolates" the contagious matter causing FMD "and demonstrates its effectiveness by means of decisive experiments on animals". Ten applicants tried to achieve this without success until 1895.



The Isle of Riems in 1910

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Virus de la fièvre aphteuse (Picornaviridae)



Fièvre aphteuse (bovin)

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Loeffler and Frosch gave an account of their investigations which had led to three fundamental observations: the filterability, the *in vivo* replication and the corpuscular nature of the agent of foot-and-mouth disease. These observations laid the basis for a new line of research: virology. After his return to Greifswald in 1898, Loeffler continued his investigations together with Uhlenhuth, accompanied by increasing criticism and complaints from the surrounding farmers about FMD outbreaks in the closer or more distant neighbourhood as a result of the experiments; finally, on February 26, 1907 this led to the prohibition of his work by the Minister of Culture. The fact that Friedrich Loeffler was well aware of the dangers and tried to prevent them wherever possible is evident from his words of 1906 when, for the first time, the idea of an island as a suitable research site was mentioned.

"... that the location of a future institute should really be such that by itself it could completely exclude any spread of the infective matter. Undoubtedly, an island would be suited best for this purpose".



Institut d'Hygiène,
université de Greifswald

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L'île de Riems : premier laboratoire de haute biosécurité (10 octobre 1910)



Construction of the first cable car to the island, 1926



Control before leaving the island



The isle of Riems in 1927

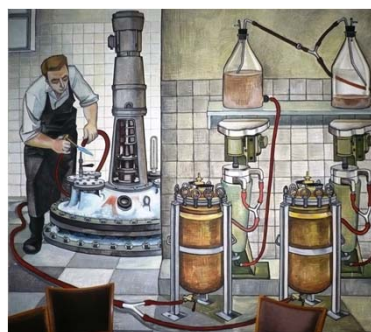


Laboratoire de F. Loeffler, île de Riems, ouvert en 1910, état actuel

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L'île de Riems : site actuel du FLI, le Friedrich Loeffler Institut



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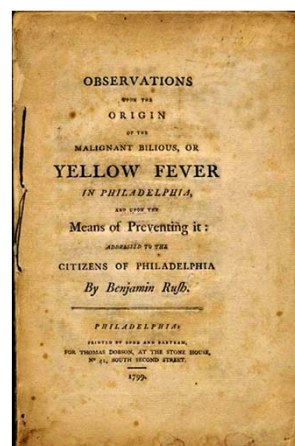
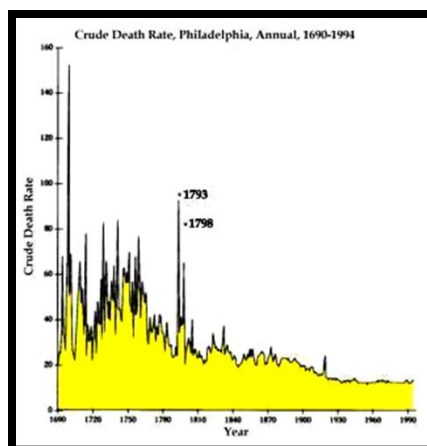


Who discovered the first virus?

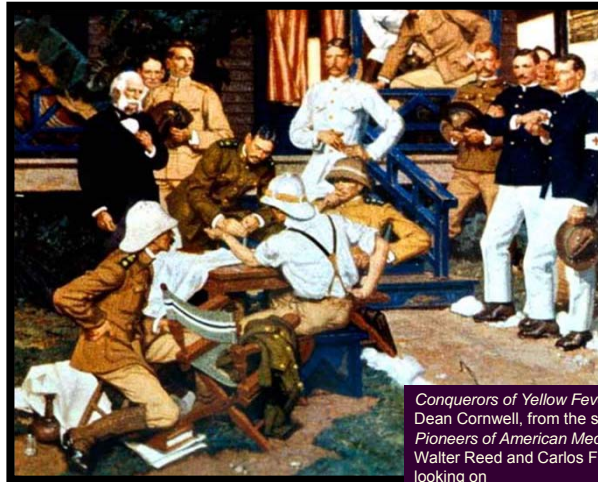
(an opinion on the priority of the work of Ivanovsky, Beijerinck and Loeffler and Frosch by Marc van Regenmortel, 2006)

- Although all historical accounts of the beginnings of virology refer to the work of Ivanovsky, Beijerinck, and Loeffler and Frosch (working with Koch), there is disagreement among authors about who should be credited with the discovery that viruses were a new type of infectious agent. This debate concerns the question of what is a scientific discovery.
- Although Ivanovsky was clearly the first one to show that the agent causing tobacco mosaic disease passed through a bacteria-retaining filter, all his publications show that he did not grasp the significance of his observation. He believed that the filter he used might have had fine cracks and that small spores of a microbe might have passed through the filter.
- Beijerinck on the other hand, realized he was dealing with something different from a microbe but he thought that the virus was an infectious liquid and not a particle.
- Only Loeffler and Frosch correctly concluded that the virus causing foot-and-mouth disease was a small particle that passed through a Chamberland filter, but was stopped by a fine-grain Kitasato filter.
- The debate about who should be considered the founder of virology may be settled only if it is accepted that, in order to make a discovery, it is not sufficient to make a novel observation (i.e. the filterability of an infectious agent) but that it is also necessary to interpret the observation correctly. Good science does not consist only in making new observations but it requires also unbiased, imaginative thinking which enables the scientist to arrive at the correct interpretation of his experimental findings.
- *Loeffler and Frosch's interpretation of their filtration experiments came the closest to the modern concept of a virus and so they should be acknowledged as the founders of virology.*

Epidémie de fièvre jaune à Philadelphie, 1793

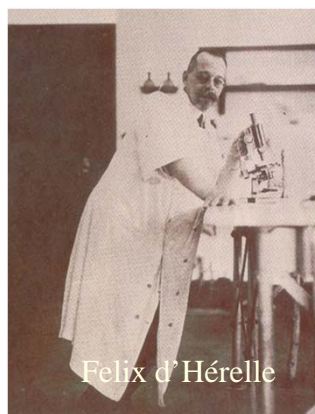


Walter Reed : découverte du premier virus humain (1902) : le virus de la fièvre jaune



Conquerors of Yellow Fever by Dean Cornwell, from the series *Pioneers of American Medicine*. Walter Reed and Carlos Finlay looking on as Jesse Lazear exposes James Carroll to an infected mosquito

1917 : découverte des bactériophages par F. Twort et F. d'Hérelle



Felix d'Hérelle



Frederick W. Twort

60 ans après Beijerinck : la définition moderne du virus

« Les virus sont les virus »

(Lwoff, 1957)

Ce ne sont ni des organismes, ni des
microorganismes; c'est l'originalité des virus

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La définition du virus (A. Lwoff, 1957)

- « *Les virus sont infectieux et potentiellement pathogènes ;*
- *ce sont des entités nucléo-protéiques possédant un seul type d'acide nucléique (ARN ou ADN) ;*
- *ils sont reproduits (par la cellule) à partir de leur matériel génétique ;*
- *ils sont incapables de croître et de se diviser ; ils sont dépourvus de système de Lipmann »*

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Prix Nobel de physiologie ou médecine, 1953



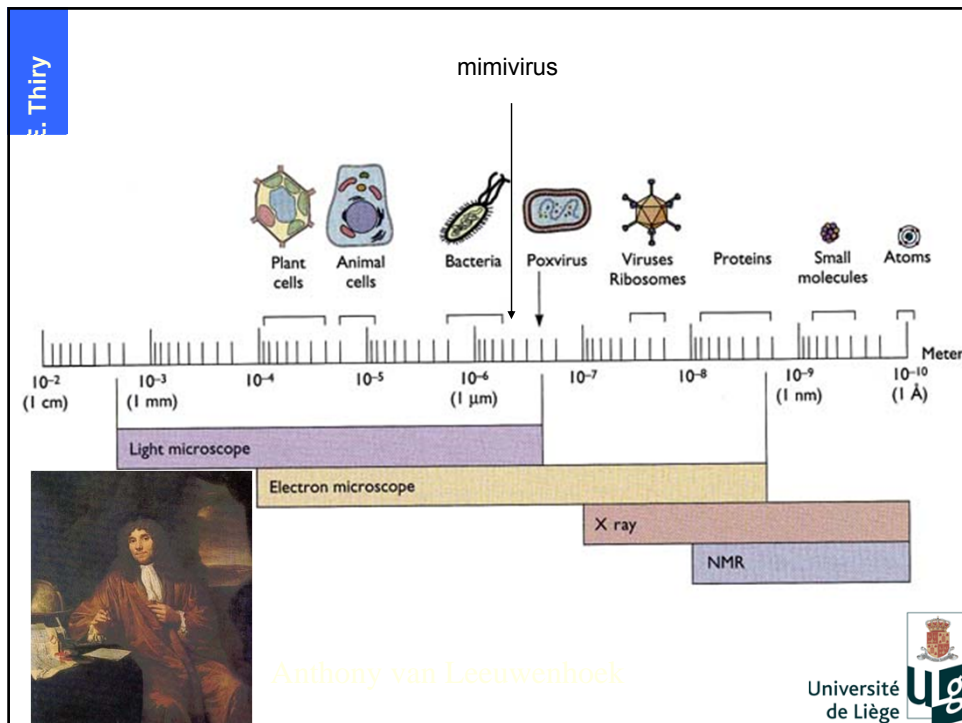
Hans Adolf Krebs (UK)
découverte du cycle
de l'acide citrique



Fritz Albert Lipmann (USA)
découverte de la coenzyme A

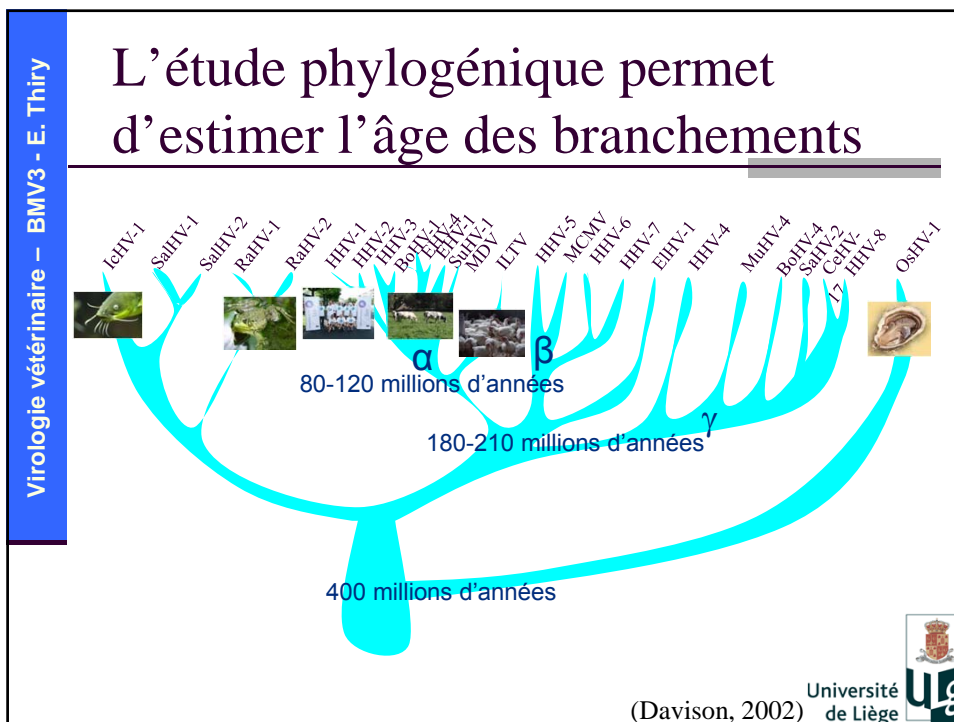
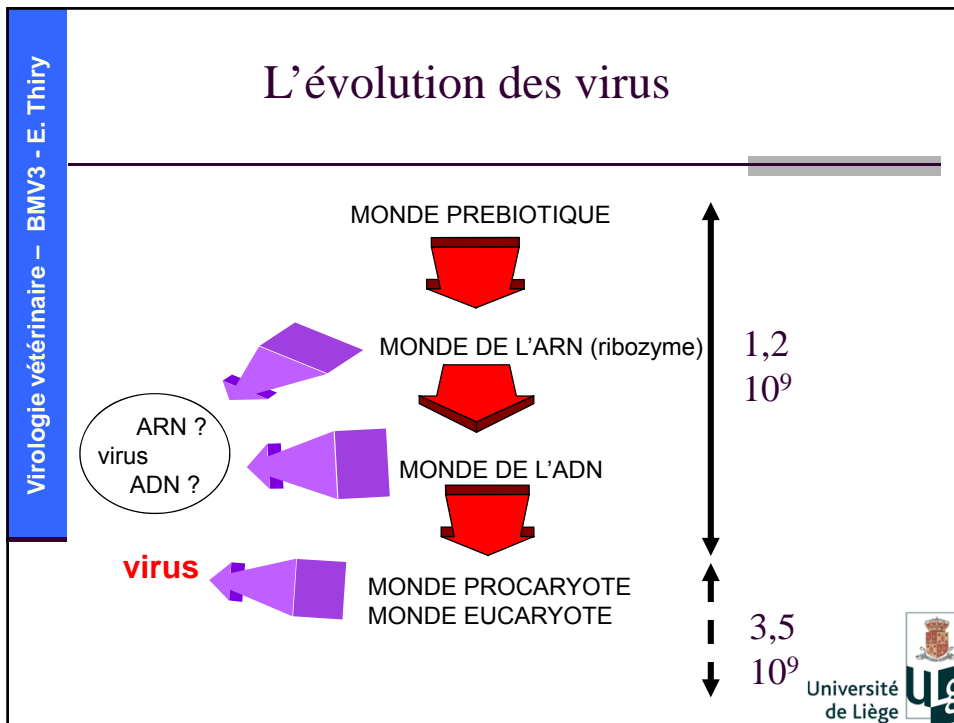
La définition du virus

- Unité infectieuse
- requiert l'environnement intracellulaire
- un seul type d'acide nucléique
- deux phases
 - phase extracellulaire : virus inerte
 - phase intracellulaire : multiplication virale
- acide nucléique (souvent) infectieux
- virion et virus
 - le virion est la particule virale complète



Les origines des virus

- Hypothèse de Green-Laidlaw
 - virus = représentants dégénérés de microorganismes de plus grande taille
- hypothèse de l'origine prébiotique
 - vestiges de l'ancien monde prébiotique ou précellulaire
 - virus à RNA
- hypothèse de l'origine endogène
 - éléments génétiques échappés de la cellule
 - virus à DNA et à transcriptase inverse



Évolution des herpèsvirus: herpèsvirus humain 1 et les migrations



Taux de mutation estimé chez l'HHV-1 :
 $3,5 \times 10^{-8}$ substitutions synonymes/site/an

Contacts

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 - secrétariat : 04/366.42.63
 - <http://www.dmipfmv.ulg.ac.be/virovet/>
- Axel Mauroy, assistant
 - mail : amauroy@ulg.ac.be
 - Tél. : 04/366.42.51

Virologie vétérinaire et
maladies virales animales,
Département des maladies infectieuses
et parasitaires

Organisation du cours

- Virologie :
 - 13 heures de cours
 - 8 heures de TP par groupe
- Notes de cours
 - Cours régulièrement mis à jour
 - e-campus

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Organisation du cours (2)

- Évaluation :
 - Examen écrit : 16 points
 - interrogation de TP de virologie : 4 points
- Examen en janvier

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En résumé

- Le concept du virus est récent
- L'association entre maladie et virus « filtrant » date de la fin du 19^e siècle
- Exemple de F. Loeffler et de l'île de Riems
 - La fièvre aphteuse
 - La biosécurité
- Le virus occupe une niche particulière dans la biosphère et la classification des « êtres vivants » : *le virus est un virus*
- Le virus est un parasite intracellulaire obligé