Making Microbes Complex: Parasites, Epidemics and the Intellectual Origins of Disease Ecology

Two-day summer workshop and conference, 7-8 July 2016
Lecture Room 126, Geography Building, Mile End Road campus, QMUL

Thursday, 7 July

9:00–10.00: Registration with tea/coffee bar

10.00–10:15: Welcoming remarks

10.15–12.30 The Development Of Medical Ecology In France

Frédéric Vagneron (University of Zurich), *'La Grippe Existe-t-elle?' Research on Influenza in France Before 1918 and the Predominance of Ecological Conceptions of Disease.*

Pierre-Olivier Méthot (Université Laval, Québec), *Charles Nicolle: Inventing Medical Ecology.*

Jon Arrizabalaga (Institución Milà i Fontanals, Spanish National Research Council) , *Between Medical Geography and Disease Ecology: Mirko D. Grmek's historical epidemiology views.*

12:30–13:30 Lunch

13:30–15:00: Revisiting Key Figures In Disease Ecology

Warwick Anderson (University of Sydney), *The Calculus of Disease Ecology Emerging from Cold-War Canberra.*

Mark Honigsbaum (QMUL), *Accidental Ecologist: René Dubos, the Rockefeller and the 'road less travelled by.'*

15:00–15:30 Tea/coffee break

15:30–16:30: Microbes and Globalisation

Andrew Mendelsohn (QMUL), *Modelling Epidemics and Policies in the Age of Extremes, 1915-1946.*

Anne-Marie Moulin (University of Paris), *Governance of Complexity or the Political Ecology of the Microbial Diseases in a Global World.*

Friday, 8 July

8:30–9:15 Coffee bar

9:15–11:30 Soviet Approaches To Plague Ecology

Susan D. Jones and **Anna A. Amramina** (University of Minnesota), *Entangled Histories of Plague Ecology in Russia and the USSR.*

Christos Lynteris (CRASSH) and **Michael Y. Kosoy** (CDC), *Natural Focality of Disease: Origins, Development and Legacy of a Soviet Disease Ecology Paradigm*.

Nils Chr. Stenseth (University of Oslo) – *A Unified Biology: Six Blind Scientists and the Elephant in the Room, a Parable for Environmentally Mediated Diseases (With a Focus on Plague).*

11:30–12:00: Tea break

12:00–13:00: Keynote Address

David Morens (National Institutes of Health), *Miasmatism, Contagionism, and Infection: The Evolution of Ideas to Explain Diseases.*

13:00–14:00 Lunch

14:00–15:30: Ecologies of Prevention and Control

Christoph Gradmann (University of Oslo), *Natural History by the Bedside: Hospital Hygiene, Antibiotics and Infectious Disease 1950-1990.*

David Heymann (LSHTM), *Emerging Infections: Shifting the Paradigm from Rapid Detection and Response to Prevention at Source.*

15:30–16:00: Tea break

16:00–17:00: General discussion

Chair: **Andrew Mendelsohn** (QMUL)

19:00 Conference dinner at Coburn Arms, 8 Coborn Road, E3 2DA.

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ABSTRACTS

Warwick Anderson (University of Sydney).
The Calculus of Disease Ecology Emerging from Cold-War Canberra.

During the Cold War, Frank Fenner (protégé of Macfarlane Burnet and René Dubos) and Francis Ratcliffe (associate of A.J. Nicholson and student of Charles Elton) studied mathematically the coevolution of host resistance and parasite virulence when myxomatosis was unleashed on Australia's rabbit population. Later, Robert May called Fenner the "real hero" of disease ecology for his mathematical modelling of the epidemic. While Ratcliffe came from a tradition of animal ecology, Fenner developed an ecological orientation in World War II through his work on malaria control (with Ratcliffe and Ian Mackerras, among others)--that is, through studies of tropical medicine. This makes Fenner at least a partial exception to other senior disease ecologists in the region, most of whom learned their ecology from examining responses to agricultural and animal husbandry problems in settler colonial society. But in the 1960s, Fenner also came under the influence of Adelaide animal ecologists Charles Birch and Herbert Andrewartha, who led him along a different ecological path from Burnet's prewar speculations. In this paper, I will consider again the local ecologies of knowledge in Southeastern Australia during this period, and describe the particular intellectual niche in which Fenner and Ratcliffe found themselves.

Jon Arrizabalaga (Institución Milà i Fontanals, Spanish National Research Council). *Between Medical Geography and Disease Ecology: Mirko D. Grmek's historical epidemiology views.*

During the 1960s Mirko D. Grmek (1924-2000) was highly concerned about providing history of collective diseases with a theoretical framework (1963, 1969), the coined concept of pathocenosis (*pathocénose*) having been his most relevant theoretical contribution. Later, in the 1980s, he applied it to diseases in Western Antiquity (1983), and to the new pandemic nowadays known as HIV-AIDS (1989). The trace of evolutionism in pathocenosis has been recently analysed with particular attention to the influences exerted by Theobald Smith and Charles Nicolle (Méthot, 2016). In addition to examining another relevant inspiration source in Grmekian historical epidemiology views, namely Jacques M. May (1896-1975), this paper is aimed to analyse how Grmek reshaped his concept in the course of the time in order to adapt it to different agendas –from the earliest one in relation to a *longue durée* history of "dominant diseases" (*maladies dominantes*) to the latest one focused on the new epidemiological threat of emerging infections– as well as to assess the fortune of pathocenosis in current disease ecology.

Christoph Gradmann (University of Oslo).
Natural History by the Bedside: Hospital Hygiene, Antibiotics and Infectious Disease 1950-1990.

Antibiotic therapy, upon entering clinical medicine in the 1940s, seemed to complete a transformation of hospitals that had originated with late nineteenth century's laboratory revolution. To promote former death sinks into harbingers of therapeutic progress. Yet, the story took a different turn quickly. The arrival of pathologies caused by resistant bacteria and of nosocomial infections whose spreading was helped by antibiotic therapies seemed to be intimately related to modern anti-infective therapy. Worse, it soon became clear that the place where such problems culminated were hospitals! From institutions that symbolized the conquest of infectious disease they now came to be viewed as dangerous environments were attempts to combat infectious diseases in hospitals had instead created hothouses of disease evolution. Among the many dimensions of this crisis the paper shall focus on one. It brought clinical medicine to pay attention to a dimension in the biology of infectious disease it had mostly ignored so far: With swiftly evolving pathologies, evolutionary biology – previously a matter of mostly theoretical interest - came to be useful in explaining phenomena such as the transfer of resistance factors between different bacterial species or widespread nosocomial infections of patients with compromised immunities. The paper will follow discussion on these issues from the 1950s to the 1990s.

Mark Honigsbaum (QMUL)
Accidental Ecologist: René Dubos, the Rockefeller and the 'road less travelled by.'

Reflecting on his scientific career in 1982, the French-educated Rockefeller microbiologist René Dubos asserted that though he had never taken a course in ecology and had rarely used ecological terminology before the 1960s, he had always "looked at problems from an ecological point of view." Dubos traced the genesis of his ecological perspective to the early 1920s when as a 23-year-old editor working in Rome he had chanced on an article by the Russian soil scientist Sergei Winogradsky and had become "entranced" by the idea that even the smallest living organisms were influenced by environmental conditions. It was this insight, Dubos later claimed, that had led to his discovery in 1932 of a soil enzyme that decomposed the polysaccharide capsule of pneumococcus, the major cause of lobar pneumonia, and his isolation in 1939 of the first antibiotics, tyrothricin and gramicidin. And it was this that in turn had led him to emphasize the relationship between health, disease and the environment in his popular writings and to decry short-term technological fixes, including efforts to eradicate specific diseases, that he feared might upset the delicate ecological balance between people and microbes. In so doing, Dubos presented his flowering as an ecological thinker as a story of linear progression – the inevitable product of the intellectual seeds planted in his youth. But to what extent can we trust Dubos's account of "the road taken," to paraphrase the title of his 1974 essay on Louis Pasteur? Rather than accepting Dubos' retrospective biographical readings, this paper aims to ground a study of his intellectual development in his scientific practices and experimental choices. In particular, I focus on Dubos' studies of the biochemical and morphological properties of bacteria and the resistance to infection in animal models.

These studies, which began in the 1930s, initially focused on pneumonia and tuberculosis but by the 1960s had expanded to encompass the role of diet and the microbiota of the digestive tract in regulating immunity to disease. I argue that these studies coincided with an important shift in Dubos's thinking about role of physiochemical processes and environmental stressors in shaping bacterial variation and the adaptations of microbes, as well as his conceptualization of virulence generally. The result is that whereas other ecologically-minded medical researchers in the period, such as Frank Macfarlane Burnet, looked to animal ecology for a theoretical framework with which to make sense of their epidemiological and immunological observations, Dubos never engaged with the work of Charles Elton or the Chicago School. Instead, his ecological viewpoint was idiosyncratically his own.

Susan D. Jones and **Anna A. Amramina** (University of Minnesota)
Entangled Histories of Plague Ecology in Russia and the USSR.

A vibrant framework of disease ecology coalesced during the late Tsarist and early Soviet periods in Russia around the problem of recurrent outbreaks of plague. This framework linked climate, soil and other environmental factors with a complex assemblage of microorganisms, insects, and mammals; humans became infected when they ventured into these plague ochags, or "hearths" of the disease. Russian and Ukrainian scientists who created the theories, methods and practices of this framework included D.K. Zabolotny (1905), Lev Zil'ber (1937), E.N. Pavlovsky (1938-39) and others who quickly expanded the framework to other diseases. As Lynteris and Kosoy will discuss in another paper, this Russian/Soviet disease ecology program was developed by Pavlovsky and his followers into a very influential school of "natural focality of disease" during the middle decades of the 20th century. The development of this school of thought brings up several important questions. How was this school, and the broader framework out of which it grew, affected by the political environments of the revolution, the Stalinist purges, and the Cold War? How did this framework of disease ecology develop with the particular resources, constraints and goals of the Russian and Soviet periods? What happened to outliers—the ideas, people, and methods that were not placed centrally in the school of natural focality as time went on? To what extent did other scholarly ideas at home and abroad, and the exchange of scientific knowledge between Soviet Russia and the West influence the emergence of this theory? This paper argues that the Russian/Soviet framework of disease ecology grew in particular ways out of entanglements with the scientific, political, and economic goals of its proponents. It emerged not only from late 19th-century excitement over bacteriology, but also out of the field sciences and the colonial ambitions of the late Tsarist regime. As the USSR sought to incorporate territories in the 1920s and 30s, this framework of disease ecology was a crucial tool for assessing the fitness of landscapes for settlement and resource extraction. During and after World War II, it provided the basis for plague eradication regimes that one Western observer called "unprecedented control" over particular plague landscapes. Although plague and other disease outbreaks were generally held as state secrets, this Russian/Soviet disease ecology framework did not develop in isolation but was entangled in global cross-currents of scientific and political allegiances and competitions. Using non-published archival and oral history sources as well as published scientific books and articles,

this paper situates the intellectual development of this Russian/Soviet disease ecology framework within dynamic political as well as scientific contexts.

Christos Lynteris (CRASSH) and **Michael Y. Kosoy** (CDC), *Natural Focality of Disease: Origins, Development and Legacy of a Soviet Disease Ecology Paradigm*.

The theory of "natural focality" (or nidality) was pioneered by the Soviet academician Evgeny Nikanorovich Pavlovsky and is often referred to in contemporary literature as the precursor or origin of landscape epidemiology. This theory or so-called "doctrine" revolved around the idea that the natural focus (aka nidus) of a disease contains a particular pathogen, which can be maintained in specific ecosystem that includes reservoirs and vectors as necessary components for a long-term circulation of the infection. Central to this was the premise that pathogens originate and persist as components of ecosystems independently from humans. Rather than being simply the idea of one man, following its original exposition in 1939, this soon became a dominant school of thought in the USSR. Applied to the study of a wide range of zoonotic diseases and involving zoologists, bacteriologists and parasitologists, natural focality hence became the epistemic basis of a long-term research in disease ecology funded and deployed to a scale unparalleled in the West. In spite of growing interest in the particular theory, and recent developments in disease ecology arriving closely to ideas discussed by Soviet scientists (e.g. zoonotic 'spatial refugia'), access to this body of work to non-Russian speakers has been largely limited to Pavlovsky's landmark "Natural Nidality of Transmissible Diseases". With the exception of conference proceeding translated in English, the main corpus of work produced by this school of disease ecology remains unexamined by historians. This paper aims to approach the concept of natural focality of zoonotic diseases through a systematic examination of the rich corpus of work produced in the USSR between 1939 and 1991. Rather than seeking to "translate" it into contemporary landscape epidemiology, our aim is to examine the extent to which this formed an autonomous theory of disease ecology. Specifically, the paper will examine the development and employment of the concept of 'natural focus' in the study of plague, generally considered as its most prolific and influential area of application. On the one hand, we will explore the intellectual origins and development of the 'natural focus' in Soviet and pre-Revolutionary Russian plague research and its reception in the West. At the same time, the paper will discuss the extent to which the theory of natural focality may serve today as a complimentary opposition to the concept of emerging zoonoses, currently dominating the study of disease ecology.

Pierre-Olivier Méthot (Université Laval, Québec)
Charles Nicolle: Inventing Medical Ecology.

According to current historiography, ecological perspectives of disease developed against the backdrop of reductionist germ theories during the first three decades of the twentieth century in postcolonial settler societies. Local case-studies are accumulating but it remains to be explained in more general and particular terms how scientists came to postulate an "evolutionary time scale" and "integrative models" instead of a more static relation between

environment and disease, as found in former medical geography approaches. Adding to the confusion, terms such as "virulence," "pathogen," and "infection" have been defined in different ways across (and within) the fields of biology and medicine. And although local scientific traditions and research styles often profoundly differ from one historical context to another, scholarship has so far mostly concentrated on "dominion" sciences, and especially on German, American, and British sciences. Last but not least, prominent scientists have themselves contributed to shape the historiography of disease ecology, notably in identifying their prestigious forerunners. As an attempt to untangle some of these historiographical issues, this paper proposes to examine the work of Charles Nicolle (1866-1936), a leading scientific figure and once head of the Pasteur Institute in Tunis, who contributed to infuse a dynamic view of diseases within the French colonial context. Trained in bacteriology, Nicolle drew upon history and biology to study the "fate of diseases" at individual, collective, and historical levels. Widening the notion of "specificity" beyond the one-germ, one-disease paradigm, he described the plasticity of microbial virulence in terms of a "mosaic of powers." Typhus and other "inapparent infections" he studied in Tunisia revealed the importance of "reservoirs" of potentially pathogenic germs that could remain hidden in between epidemics. Through the lens of Nicolle's theories of disease change based on his work in North Africa, this paper explores the "invention" of medical ecology in the periphery of France and looks at Nicolle's legacy in the second half of the twentieth century. Rather than treating him as "precursor" of emerging infections, I seek to place his contributions within the broader microbiological and medical context.

Anne-Marie Moulin (University of Paris)
Governance of Complexity or the Political Ecology of the Microbial Diseases in a Global World.

In 2016, in France, as one noted the (universal?) decline of confidence in vaccines, the French ministry of Health, after ordering a report from the Senate. announced a popular consultation, prior to a discussion of a revised Public Health Law, bearing, between other items, on recommended versus mandatory vaccines. This evolution is related to changes having occurred altogether in popular mentalities and microbiological and immunological knowledge. Vaccinology addresses this complexity from the viewpoints of both biomedical and social sciences. Smallpox inoculation was viewed for Michel Foucault (Conférences au Collège de France, 1975) as the model of emerging biopower in Europe, based on what he called the "governementality of the body." Vaccination has become an issue of a growing complexity. The vaccinal agenda, once restricted to infants and children, spans over all ages of life. Microbes are no longer viewed as the enemy to be eradicated, and the management of microbial diseases refers to a profoundly revised version of the immune system. The multiplication of company-produced vaccines (including some whose efficacy and efficiency turn to be inferior to the vaccines of the past) leads some authors to question the historical choice of vaccinal strategy. My presentation will present the political dimension of microbial disease ecology, which will bring together the unrest in some countries of the South and the public debates in Europe.

Andrew Mendelsohn (QMUL).
Modelling Epidemics and Policies in the Age of Extremes, 1915-1946.

Where did the modern, ecological understanding of infectious disease come from? I address the conference question by exploring ways in which it is only half the story. In a paper first given 20 years ago, I described an international conceptual shift in the early 20th century from epidemics as invasions to epidemics as disturbances of equilibrium between microbes and their host populations. Eradication and laboratory-administrative disease control were thrown into doubt. Here, I revisit this change and some of the same research and intervention programs and institutions in Britain, Germany, and the United States, but with different questions and goals. These are prompted by a fuller picture of the period. It witnessed rejection of laboratory-administrative disease control, but also its intensification. Thus what had seemed to me a shift was equally a process of fission and polarization of science, policy, and expertise. Two features stand out in this dichotomous landscape. The first is the confluence, on either side, of type of research pursued, policy advocated, and valuation of expertise and its limits; of perception of the nature of spatial and biological relations in populations; assessment of how complex or simple the natural and human world is and therefore how difficult or easy it is to know and control; of extreme versus subtle modes of intervention, along with correspondingly aggressive or moderate professional persona; and, finally, of stance in national politics and with respect to ideologies and movements of welfare and socialism, technocracy and criticism of the "machine age," nationalism and internationalism, fascism and Nazism. The consistency of this topography across widely variant national contexts is its second striking feature. So I aim not to explain historical change, but to identify and understand a pattern. Why is the pattern so? What holds the rival camps and their heterogeneous elements together? Are these elements adequately described using standard ways of talking about science, politics, ideology, policy, intervention, or is another vocabulary needed?

Nils Chr. Stenseth *(University of Oslo)*
A Unified Biology: Six Blind Scientists and the Elephant in the Room, a Parable for Environmentally Mediated Diseases (With a Focus on Plague).

This is the century of biology – a statement I will start out defending (as well as spelling out the condition for this being so). A key condition for this century being the century of biology is that we bring together the various fields of biology (as well as other fields). This is not the least important if we are to deal with many of the disease-linked issues facing the world today – and if we, in that effort of ours, are to take a One Health perspective – often being an Elephant in the room. After these introductory remarks, I will review recent work on plague and how its ecological dynamics are linked to climate variation – all being framed within a unified biology perspective. Here are a few points to be highlighted:

1. Plague is a wildlife disease which needs to be understood as such: humans are a dead end for the bacterium.
2. Plague is affected by climate variation – but differently so in different part of the world.

3. Local/regional plague dynamics might have global consequences.

The presentation will end with some reflecting comments going back to the start of the talk.

Frédéric Vagneron (University of Zurich)

'La Grippe Existe-t-elle?' Research on Influenza in France Before 1918 and the Predominance of Ecological Conceptions of Disease.

The return of an ecological approach of disease is partly due to the narratives of bacteriologists in the Interwar period, and later historians of the "bacteriological revolution"; they framed the Golden Age of this discipline between the 1880s and the early 20th century (Mendelsohn, 2002). But the unified bacteriological paradigm associated with the "one germ - one disease" postulate was also supposed to have reduced the complexity of the genesis of diseases and epidemics, which was then "rediscovered" after World War I. Yet, despite the emergence of new vocabulary and laboratory practices, the dynamics of certain epidemics such as typhoid or influenza was not explained in terms of presence or absence of specific bacteria in the Pasteurian bacteriological culture of the 1890s. Rather, it demonstrates the variability attributed to both bacterial virulence, the environment or the "terrain" and the interaction between these factors. Our paper tackles these conflicting interpretations of disease through the lens of influenza research in France between 1890 and 1914. The argument is the following: while historiography has largely described the "Spanish" flu as the key moment in the controversy over the role of Pfeiffer's bacillus (accepted as the influenza microbe since its "discovery" in 1892), scientific controversies in France on the etiology of pandemic flu show that this consensus had been crumbling as soon as the late 1890s. In fact, the identity of this disease was openly discussed at the turn of the century, in debates confronting bacteriologists, epidemiologists and clinicians, and their methods of observation, conceptions of disease origins and processes, and more broadly the relationship between specialties in medical sciences. A vivid scientific controversy, which occurs in 1905 during a more severe seasonal flu epidemic and rapidly spread in the general press, provides my case study to inquire about the conflicting medical conceptions of this disease. In the bacteriological discussion on the role of Pfeiffer's bacillus, which launched the controversy, the specificity of the microbe but also the disease it-self became questioned. "Does the flu exist?", brazenly questioned some bacteriologists, yet did not come to a definite answer. Nevertheless, we can observe the emergence of a consensus among French scholars on the complementary role of the environment, the individual « terrain » and interactions between microbes in the genesis of pandemic influenza. Consequently, when the 1918-1919 pandemic occurred in France, the epidemic was interpreted in line with these on-going discussions: the new laboratory arguments against the Pfeiffer bacillus fit in continuity with earlier expressed positions. The specific issue of the specific influenza microbe was only one etiological factor among others, in an ecological conception of the disease that lasted until the end of the Interwar period in France. This conception was robust enough to resist the first research on influenza virus in England and the US at the beginning of the 1930s.

Keynote

David Morens (National Institutes of Health)

Miasmatism, Contagionism, and Infection: The Evolution of Ideas to Explain Diseases.

Since ancient times, epidemic disease occurrence has powerfully provoked explanatory theories, not only from scientists and healers but also from theologians, intellectuals, and ordinary citizens. In pre-microbiological times, these theories were shaped by a need to explain the most important prevailing diseases of the day. It can be easily demonstrated that as the prevailing epidemic diseases of the times changed, theories of epidemic diseases changed with them, not evolving in any forward or consolidating direction, but back and forth between what ultimately became the "poles" of contagionism and miasmatism. When diseases that arose from the environment prevailed (e.g., malaria in ancient times; plague in the 14th century; cholera in the 1830s) theories of disease causation swung forcefully in the direction of miasmatism; when diseases that could easily be traced to human contact prevailed (e.g., smallpox, measles and leprosy before the Middle Ages; syphilis in Europe in the 1490s) disease causation theories moved aggressively toward contagionism. A central problem became that any theory that satisfactorily explained the prevailing disease of the day failed completely to explain many other important diseases. Moreover, for reasons that are not entirely clear, almost all observers on either side of the equation rejected any theory that was unable to explain all epidemic diseases. Disease ecology seems to have arisen when microbiology provided a rational way out of this standoff by explaining both contagious and miasmatic concepts. The old term "miasmatism" is today fully represented by infectious diseases that are acquired from man's environment, e.g., cholera from water, or malaria, plague and yellow fever from (insects borne upon) the air. The concept of disease ecology thus has ancient origins and reflects the modern understanding that all infectious diseases either come from an environment representing the ecologic niche of the particular microbe or, in the case of contagious diseases that spread only between humans (e.g., smallpox, measles, rubella), came from another environment in the recent past. Contagious diseases are thus only one-time miasmatic diseases that became highly and specifically adapted to the environment of man, and the ecology of all such diseases is essentially the necessarily complicated relationships between microbial agents, hosts and environments.