Created in 2000 in the heart of Namur, the URBM is made up of 5 teams from UNamur and one from ULB. It employs 50 researchers and has privileged access to a BL3 platform. Its basic research activities will generate applications for therapeutic and vaccine purposes.

The URBM focuses its research activities on molecular bacteriology. *Caulobacter crescentus*, *Capnocytophaga canimorsus* and *Brucella* sp. are used as working models to study the functions, structure and interactions of proteins involved in processes associated with the cell cycle, the regulation of gene expression, metabolism and, more specifically for *Brucella, Capnocytophaga canimorsus*, *Acinetobacter baumanii* and *Escherichia coli*, interactions with host cells and the modulation of the host's innate immune response. Two groups are also involved in applied research into enzymatic engineering, dietary fiber production and environmental detoxification. More specifically, the URBM studies the functioning of bacteria and phages at the molecular level: their adaptation to starvation and heavy metals, the homeostasis of the bacterial envelope in pathogens and that of environmental bacteria. The unit is also working on the discovery of new defense mechanisms against viruses that infect bacteria: phages.



Xavier De Bolle, Professor at University of Namur and WEL Research Institute Investigator, Department of Biology - URBM. © URBM



Prof. Xavier De Bolle's research group. © URBM

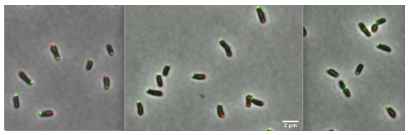
Several research themes are currently being developed within 6 teams: Bioinformatics and Bacteriophages (Prof. Gipsi Lima Mendez); *Brucella* envelope and infection (Prof. Xavier De Bolle); Heavy metals and response to oxidative stress (Prof. Jean-Yves Matroule); Bacterial stress response (Prof. Régis Hallez); Envelope biogenesis and

homeostasis in Bacteroidetes (Prof. Francesco Renzi); Host-pathogen relationship (Prof. Eric Muraille).

Focus on *Brucella abortus*

Prof. De Bolle's research group is interested in pathogenic bacteria that use hosts as substrates for their proliferation. Over the course of evolution, they have therefore selected molecular mechanisms that enable them to colonise, feed on and proliferate within host organisms. Some pathogenic bacteria (such as *Salmonella* or *Shigella*) are very well characterised, but some bacteria responsible for global diseases are still poorly understood. This is the case with *Brucella*, a genus responsible for brucellosis, a major zoonosis affecting many mammals, including domestic animals such as sheep, goats and cows. Two research groups are working on *Brucella*, and more specifically on *Brucella abortus* (*B. abortus*), a species found mainly in infections of cows.

Important discoveries have been made in this context. *B. abortus* shares many cell cycle regulators with *C. crescentus* and other alpha-proteobacteria. *B. abortus* cells are asymmetric, with the two poles (new pole and old pole) able to recruit different proteins. When *B. abortus* enters a host cell in a simplified model of infection, one stage of the bacterial cell cycle (G1) is favored for internalization, and the bacteria can remain in a non-growing, non-replicating state for several hours. During intracellular trafficking, *B. abortus* undergoes starvation, acid shock and alkylation stress. The outer membrane of *B. abortus* contains beta-barrel proteins that are covalently attached to the peptidoglycan by their N-terminal extension. The *B. abortus* envelope (comprising lipopolysaccharide, peptidoglycan and at least two outer membrane proteins) extends across the new pole and into the site of division. Finally, the lipopolysaccharide is decorated with an O chain (or O antigen) by a bifunctional O-antigen ligase in the periplasm and exported to the outer membrane at the new pole or division site by localised Lpt proteins (LptB2CFG) at these specific sites.



Fluorescent bacteria. © URBM



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An integrated approach

The current research of Prof. De Bolle’s group uses an integrated approach, studying the basic molecular biology of the *Brucella abortus* pathogen, including envelope structure, biosynthesis and its regulation during polar growth, but also aggression, feeding and starvation in culture and inside host cells.

To carry out its work, Prof. De Bolle’s research group uses a state-of-the-art research infrastructure: the Biosafety Laboratory Technology Platform at Level 3 (BL3). The BL3 is equipped with a fluorescence microscope that can be used to visualize the location of certain proteins (such as enzymes) inside a bacterium, for example when the bacteria themselves are inside host cells. Two pathogens are studied there: SARS-CoV2 (research carried out by the URVI and URPhyM, UNamur) and two *Brucella* species: *B. melitensis* and *B. abortus*. What is more, URBM researchers have the capacity to infect cells in culture to study the intracellular behavior of *B. abortus* inside human or animal cells. They also use mice to test potential vaccine strains and to develop a rational design of new vaccinal strains using a genetic approach.

Fundamental and applied research questions

Prof. De Bolle’s group is currently focusing on the main component of the outermost layer of the *B. abortus* envelope: lipopolysaccharide, or LPS. LPS is a complex molecule, with a lipid part and a polysaccharide part. We still don’t know which enzymes catalyze which stages in the biosynthesis of the longest polysaccharidic part, called the O chain. Not only is LPS of interest for understanding the fundamental biology of all bacteria, but it is also a key molecule in the interaction with the host infected by a pathogen, which is of interest from the point of view of vaccines. These are fundamental and applied research questions that benefit from numerous collaborations with groups in the USA (Wisconsin, Virginia and North Carolina), Spain (Madrid and Pamplona) and Singapore.



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For Prof. De Bolle, the main challenge is to enable researchers, after their time in a basic research laboratory, to move on to applied research in synthetic microbiology: just as enzymes naturally produce different molecular conformations, genetic engineers could use their talents to create complex molecules for vaccines or therapeutics (e.g. complex polysaccharides or precursors for the manufacture of drugs). In the longer term, establishing a base of expertise in synthetic microbiology will open up new fields of investigation. New materials could also be developed in this context. Even if we look 20 or 30 years ahead, these are exciting challenges for researchers in synthetic microbiology and for engineers keen to make the most of promising applied research.

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