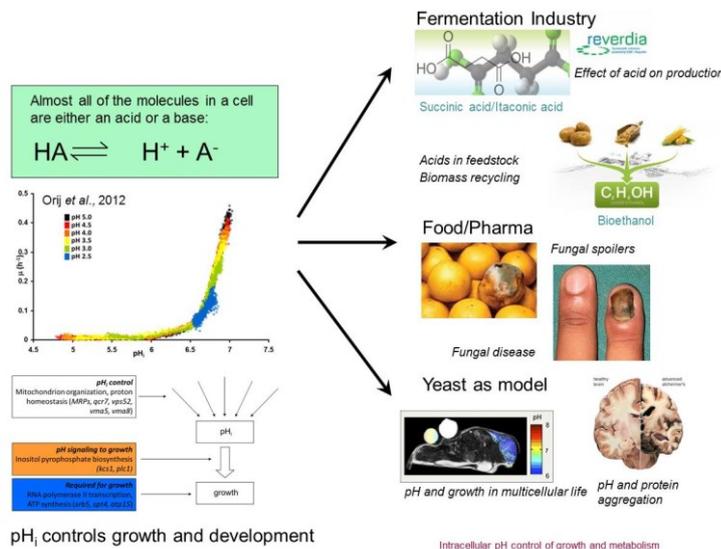


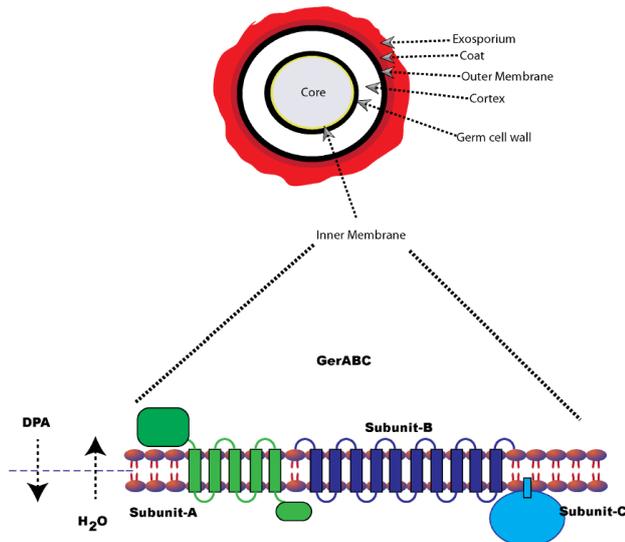
Molecular Biology and Microbial Food Safety

Group leader Stanley Brul

The mission of the 'Molecular Biology and Microbial Food Safety' group is to understand the interaction of microbes and their environment. We focus on the bioenergetics and importance of the intracellular pH as a signal in growth, survival and death. We deploy our insights with partners in SILS (Microbiology, Mass Spectrometry, Omics and Advanced Microscopy) and partners outside (Unilever, FrieslandCampina, TNO, NVWA, AMC) in fundamental and application oriented research that is of importance to health and disease. The group uses several modelsystems and is equipped to do in vivo studies in *Caenorhabditis elegans*.



Bacterial Spores and Spore germination

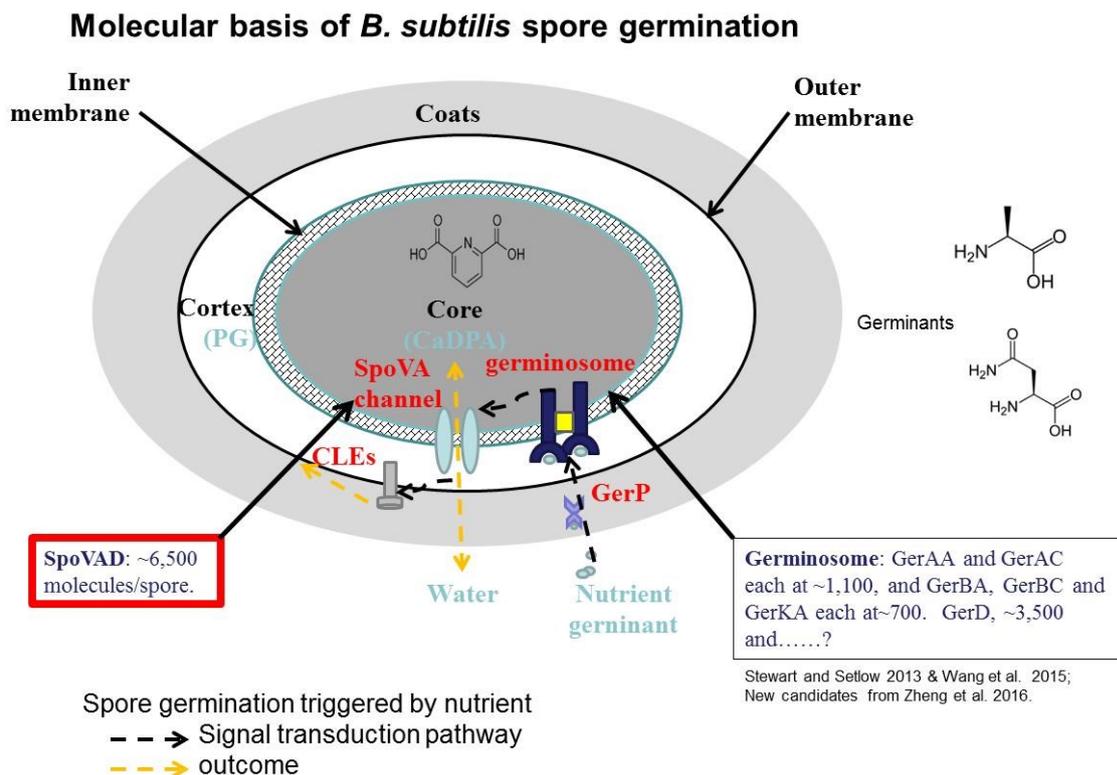


Stress response in microbial systems

An overriding issue in biology is stress response to environmental challenge. We study this response at the level of cellular bioenergetics and pH homeostasis in the context of challenges with antimicrobials and antibiotics. As modelsystems both *Escherichia coli* (antibiotic resistance in the food chain), *Bacillus subtilis* (germination mechanisms and antimicrobial resistance in food and man), and *Saccharomyces cerevisiae* (antimicrobial resistance in food and man) are used. Spin-off also involves industrial biotechnology. In vivo tests are done in *Caenorhabditis elegans*, as a simple multicellular model. In our studies we address the hierarchy in decision making focussing on genome, transcript and proteome analyses as well as quantitative physiology.

Funded by NWO, EU, Erasmus Mundus programs, Chinese Scholarship Council, NWWA, TNO and companies.

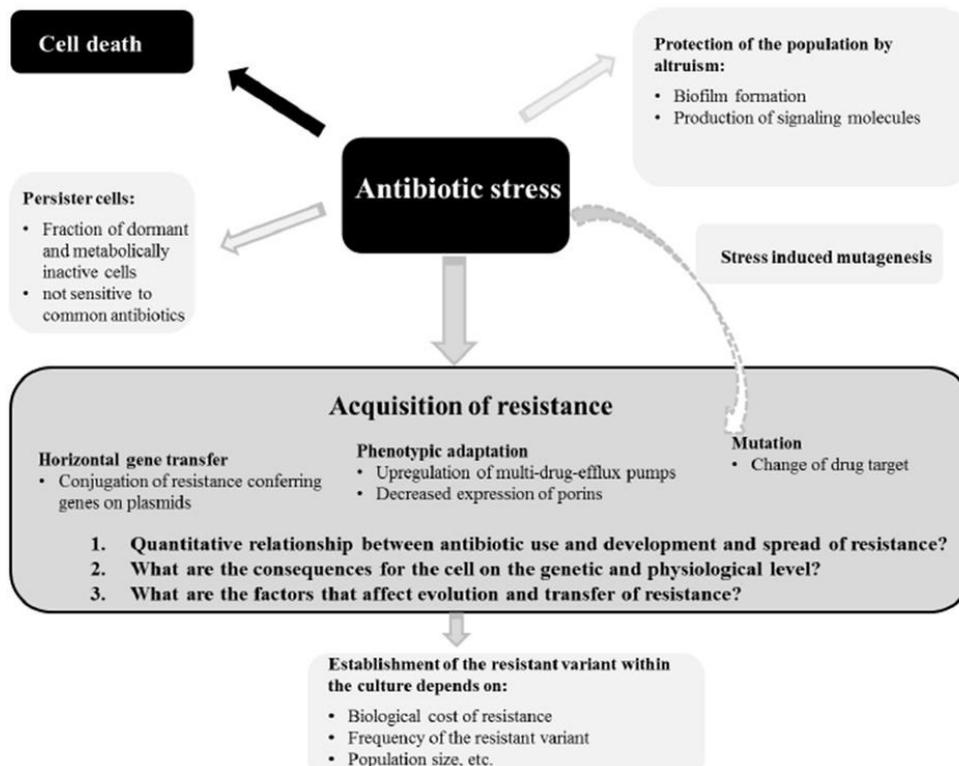
Food spoilage & pathogenic bacteria



(i) Bacterial spore formers

The behaviour of aerobic spore formers is studied in the model *Bacillus subtilis*. Spore forming organisms are spoilage organisms of prime-importance to the food industry due to their highly stress resistant endospores. Their occurrence necessitates the application of harsh food preservation processes such as high thermal treatments. The mechanistic basis of their extreme high thermal resistance (some for various minutes at 121°C) as

well as the molecular mechanisms involved in the early phases of spore germination and outgrowth under optimal and sub-optimal environmental conditions, are still far from mechanistically understood. We focus on analysis of thermally stressed spores growing out under weak-organic acid preservative stress. The data provide new targets for the enhancement of the efficacy of weak-organic acids as food preservative. For proteomic analyses of the spore coat we collaborate extensively with the department of 'Mass Spectrometry of Bio-macromolecules' at SILS. The analyses are extended to include (validation in) *Bacillus cereus* and *Clostridium difficile*.



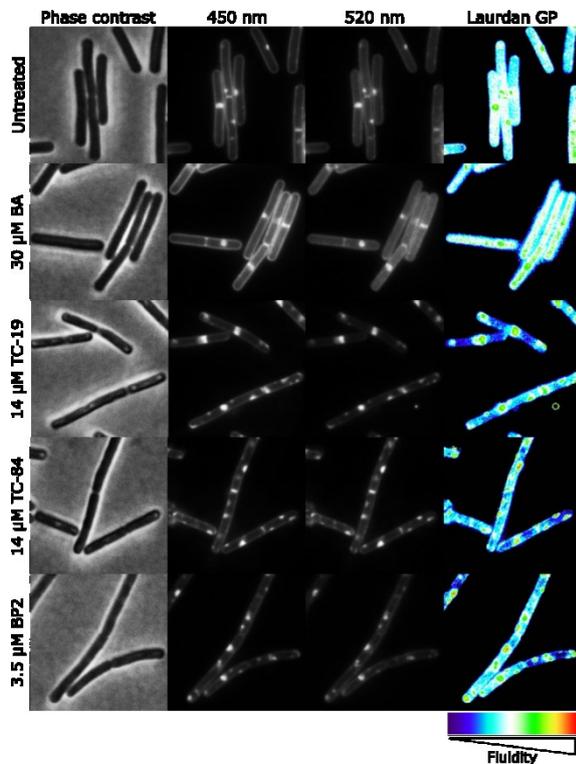
(ii) Antibiotic resistance development in the food chain

Bacteria of relevance to microbial food safety are prone to acquire resistance towards environmental conditions such as the use of antibiotics in animal feed practices. Such events create potentially harmful situations to the medical field as multiple antibiotic resistance development may occur and could well harm the effective use of these antibacterial agents in treating infection. Our group focuses on the development of systems to study (1) acquisition of antibiotic resistance, (2) transmission of antibiotic resistance, (3) loss of antibiotic resistance. For all scientific questions we make use of well accessible model systems (primarily *Escherichia coli*) and controlled culture conditions (fermentors and chemostats). This research is led by Dr. Benno Ter Kuile of the Dutch [Food Safety Authority](#) (NVWA) who holds a part-time research position at our department.

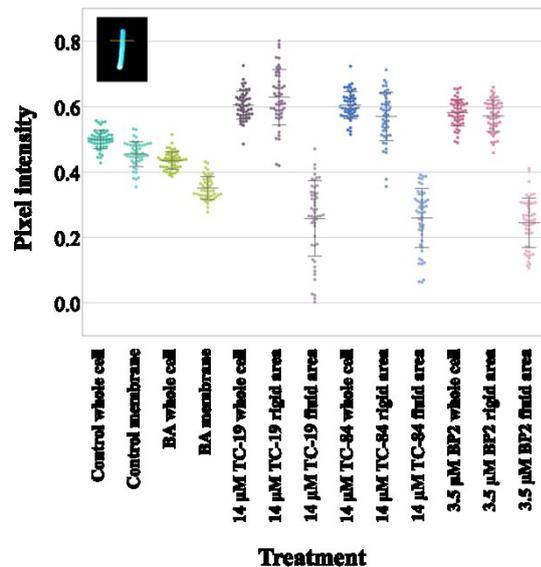
Funded by NWO, EU Erasmus Mundus, Chinese Scholarship Council & NVWA

Studies on antimicrobial peptides with Medical Microbiology (AMC)

Laurdan GP microscopy images



Laurdan GP quantification of microscopy images



Membrane Domains are Formed with Thrombocidin-derived TC peptides and BP2

Medical Microbiology is the field of research in which molecular and physiological tools are used to unravel the behaviour of disease causing microorganisms. We focus on the response of the organisms to antimicrobial peptides of natural origin (i.e. Thrombocidin derived). The studies have both a fundamental and an applied angle. At MBMFS our focus is primarily on the fundamental aspects of the behaviour under antimicrobial peptide stress using *Bacillus subtilis* as a model. Validation is done in *Bacillus cereus* and *Clostridium difficile*. We identified that antimicrobial peptides act upon the membrane of cells and lead to a perturbation of membrane fluidity homeostasis. In collaboration with and funded by TNO, data were also gathered on alternative non proteinaceous compounds. Together with the department for Medical Microbiology at the Academic Medical Centre (AMC) we provide studies to understand the molecular basis of damage and response to novel antimicrobial compounds with potential for medical application.

Funded by : EU Erasmus Mundus Action 2 program (EMA 2)

Fungi and response to environmental stress



Fermentor

The interaction of bakers yeast (*Saccharomyces cerevisiae*) with weak organic acids, prominent in the food industry is studied. Together with the group of prof. Teun Boekhout at IBED we aim at capitalizing on our gathered understanding of pathogenic yeast behaviour (*Candida albicans*). Prime focal points are thermal and weak-organic acid stress response as well as a basic understanding of effects of intracellular pH on growth. We deploy our knowledge for the understanding of the behaviour of Aspergilli in the production of organic acids. A project focussing on itaconic acid is sponsored by Dutch DNA Biotech and TNO. In our experimental set-up we focus on analysing and subsequently providing targets for interfering with stress (cross-)tolerance mechanisms. For proteomic analyses of the response to environmental stress we collaborate extensively with the department of Mass Spectrometry of Biomacromolecules at SILS.

Funded by University funds, TNO, Dutch DNA Biotech.