BACTERIAL STRESS RESPONSES
Second Edition

Edited by

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Cover image: The two panels show the same area of false-color fluorescence images of a single microarray spotted with 50-nucleotide oligomers specific for all open reading frames in the *E. coli* K-12 genome that was hybridized with a mixture of Cy3-/Cy5-labeled cDNA obtained with RNA extracted from strain W3110. The cells were grown in defined rich medium and harvested for RNA preparation during growth (at an OD$_{578}$ of 1.0) at 37°C or 5 min after a shift from 37°C to 42°C (preparations labeled with Cy3 or Cy5, respectively). These cells were treated exactly as the cells used by Roth van Bogelen and Fred Neidhardt for the “historic” proteomic analysis of heat-shocked *E. coli* cells shown on the cover of the first edition of *Bacterial Stress Responses* in 2000. The upper panel shows fluorescent signals derived from non-heat-shocked cells. The lower panel shows fluorescent signals derived from heat-shocked cells. Spots representing heat-shock-inducible genes are circled, and gene designations are given. Microarray analysis was performed by Nicole Sommerfeldt and R. Hengge.
To Ella, Toby, Felix, Lisa-Maria, and Manolis
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A decade has passed since the first edition of the *Bacterial Stress Responses* book was published, and the time has come for a new edition.

Reflecting back, an astonishing amount has been learned about bacterial stress responses in the past ten years. Major developments include new ways of thinking about regulation. It has become clear that there is far more posttranscriptional regulation than initially imagined, by regulatory small RNAs and riboswitches as well as by proteolysis. The genome-wide identification of transcription regulators and their target genes in a broad range of organisms has also allowed scientists to think about regulatory networks on a much larger scale. General regulatory principles, which have come to be better understood and underlie all stress responses, are the focus of the first section of the new edition.

The second and third sections of this edition illustrate how much more we now know about both the specific and general stress responses. Many more regulators and target genes and connections between different responses have been identified. In addition, the physiological roles of many of the target genes are better understood. The research on extremely complex general stress responses, which encompass hundreds, if not thousands of genes, has revealed how general stress responses are comprised of highly integrated regulatory networks, modulated at the levels of transcription, transcript stability, translation, protein activity, protein degradation and by the production or decay of small signaling molecules. Significant insights into how bacteria survive stress conditions by undergoing changes of their state or morphology or cell surface have also been obtained. These topics discussed in the first three sections provide background for the last three sections, including the fourth part of the book focused on how stress responses affect the interactions between bacteria and host cells.

The accumulating knowledge of the molecular mechanisms of stress responses illustrates the power of studying model organisms. The many years of research on *Escherichia coli* and *Bacillus subtilis* have been critical in setting the stage for the analyses of other species. However, in this edition as in the first edition, there is an emphasis on what has been learned across species. In the past ten years we have come to have an even greater appreciation of the diversity of bacteria and the diversity of responses to different environments, in part due to significant advances in sequencing. The fifth section of the book describes the study of bacterial stress responses in different niches and communities, particularly in extreme environments.

It has also become increasingly clear that in order to combat bacterial infection with antibiotics or to exploit bacteria for biofuel production or bioremediation, topics of significant medical and commercial importance, there is a need to understand the stress responses. The connections between stress and antibiotic action, as well as the stresses encountered during biofuel production and bioremediation, are discussed in the last chapters.

The review of what we have learned, as covered in the chapters of this edition, has also pointed out what is still less well understood:

- Many aspects of regulation by RNAs as well as the role of proteolysis in shutting off responses or in molecular switches have not yet been fully explored. There also are hints that largely-ignored small proteins modulate the activities of sigma factors and two-component systems and may comprise yet another unexplored level of regulation.
- Current studies have led to a revival of research on second messengers, both long-known and newly-identified, which seem to operate in
far more complex ways than imagined only a few years ago; however, much remains to be learned about the production and sensing of these molecules.

- Environmental signal perception and transduction are still the most poorly characterized steps of stress response pathways.
- A remaining challenge is how to integrate and synthesize the increasing amounts of data from different lines of experimentation. As interesting as any one approach to a problem may be, whether it be mechanistic details or a whole genome survey, full understanding of an entire response requires that we be able to integrate information obtained at all levels and from multiple perspectives, including quantitative analyses of the response dynamics.
- Finally, despite significant advances in recent years, our knowledge regarding bacterial communities such as biofilms (including aspects such as bistability of genetically identical cells and mixed species communities) as well as entire ecosystems is still limited.

We look forward to seeing what is learned in the next ten years.

Gisela Storz
Regine Hengge
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