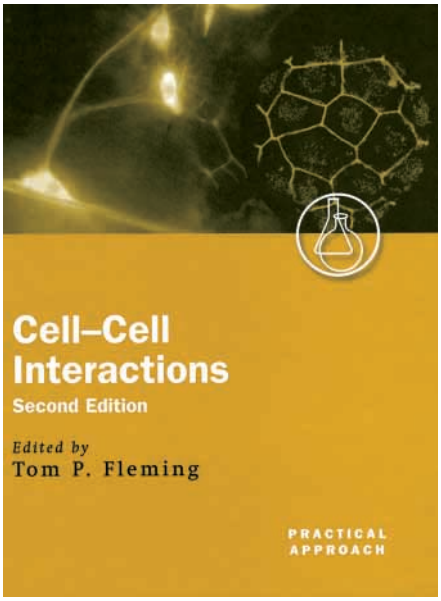
Protocols that stick



Cell-Cell Interactions, 2nd edn

edited by Tom P. Fleming

Oxford University Press (2002) 268 pages. 0-19-963863-2
£35

Ever since the pioneers of cell biology first used electron microscopy to reveal the structures that hold us together at the cellular level, cell biologists have recognized the important role that cell-cell interactions play in development and disease. This appreciation for structure forms the foundation of modern cell biology, and it has evolved into a broad effort to understand the mechanisms by which cell adhesion and communication are established and regulated. In *Cell-Cell Interactions*, Fleming has drawn on an international field of experts who have made major contributions to this important area of cell biology. The end result is an outstanding collection of protocols and approaches that could be a resource for any laboratory addressing questions that involve an assessment of cell-cell contact.

Cell-Cell Interactions is part of the 'Practical Approach' series published by Oxford University Press. This series includes books that focus either on technical approaches, such as *Epithelial Cell Culture*, or on a particular subject area, such as *The Cytoskeleton*. In the preface to *Cell-Cell Interactions*, Fleming writes that the 10 chapters and 105 protocols are "written in sufficient detail for investigators of cell-cell interactions to follow and repeat for their own system." This somewhat lofty goal leads one to ask, who is this book for? Do you really need this kind of book if you are an expert in cell adhesion? And if not, would it really be possible to use this book to get started? We will return to these questions later.

The first chapters of the book focus on cell culture systems that are used to study keratinocyte and endothelial cell-cell adhesion. These are followed by chapters on leukocyte adhesive interactions, gap junctions and tight junctions. The book approaches the subject area in two ways: first, by examining different cell types that assemble functionally similar structures, and second, by examining different types of cell-cell interactions that assemble in various tissues. The duality of this organization is amplified by the dramatically different styles apparent in some of the chapters. This contrast is perhaps most obvious in the first few chapters, with a very brief but useful chapter on endothelial cells sandwiched between much more extensive chapters on keratinocytes and gap junctions. The second half of the book explores protocols that can be used to study interactions that occur in developmental or genetic models, including *Drosophila*, *Xenopus* and mammalian systems. Certainly, a novice would need help from a collaborator or consultant before using some of the model systems outlined in these sections. However, the inclusion of these chapters, and the emphasis on developmental model systems, provides the reader with an appreciation for the range of experimental approaches that can be undertaken to address questions involving cell contact.

By the end of the book, most of the key structures that assemble at cell interfaces are covered in detail except for the desmosome, which is only mentioned in passing. Overall, the quality of the writing, diagrams and photographs is excellent and most images are clear and well labeled. One notable exception is the color plates. In Chapter 4, the authors refer to their figure as Plate 1 but no page number for Plate 1 is given, and it is not until the middle of Chapter 6 that the color plate appears. In addition, the plates themselves lack references back to the chapter that discusses them, making the utility of the images questionable. However, most of the line drawings and models are exceptionally helpful, although additional diagrams of the various proteins and junctional complexes referred to in each chapter would be welcome, such as those provided by Gahmberg et al. on page 95. Also useful are the examples of real data that were generated using some of the protocols, such as immunofluorescence images, gels, immunoblots and graphs. These examples could prove invaluable for the newcomer attempting a protocol for the first time. For the adviser trying to convince a student that a particular protocol can in fact be done successfully, the examples provide direct evidence of feasibility.

In many ways, the approach that Fleming takes seems to lie at the junction between a review and a protocol. Most of the contributors do an excellent job of weaving together protocols with background information that provides context, allowing the reader to appreciate both the question and the method. Several authors, particularly Citi and Shepherd, do a wonderful job describing the kinds of biological problems that can be addressed with each protocol. I must admit that, while reviewing the volume, I found myself making notes of useful protocols and approaches – not for the purposes of this critique but for the people in my own lab! So, who is this book for? Clearly, it is an outstanding volume for the postdoc or graduate student setting out to tackle a sticky problem. And, maybe it is for the skeptical critic too, who answered his own question while writing this review.

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Homeostasis, that's the rule…

Apoptosis: the molecular biology of programmed cell death

edited by Michael D. Jacobson and Nicola McCarthy

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£35

Life for cells in an organism is not as easy as you might think. Every cell that has a job and lives in harmony with its neighbours will receive its daily supply of vittles and other goodies to keep going until… homeostasis, that's the rule. Cells who do not want to follow the rule and have ideas of rebellion, beware: Big Brother is watching and will make sure that any offenders are quickly and silently removed. Apoptosis, they call it, and the offender will be required to participate. You need strong rules to maintain homeostasis, but the system has proved its worth.

Too little apoptosis is a cause of, or an aggravating factor in, cancer and autoimmune diseases. Too much apoptosis is not good either, as it may permanently inactivate a vital organ and lead to the collapse of a whole edifice, as is seen in degenerative diseases. However harsh the rule may seem, it is probably very important because it has been conserved and refined during evolution.

Although programmed cell death was first identified in the 1800s, its importance has been recognized only recently. Apoptosis has now become one of the most popular and prolific subjects of biomedical research. In this book, Jacobson and McCarthy have assembled a series of reviews in an attempt to capture the relevant and lasting ideas emanating from more than 100,000 scientific publications on the subject.

The chapter by McCarthy recapitulates the main facts about apoptosis, such as the morphological features, the different phases and the main players in that deadly game. The delineation of the molecular mechanisms of apoptosis owes much to genetic studies of the development of the *C. elegans*. Xue, Wu and Shah review the advantages of this system and how this simple worm has helped unravel most aspects of the apoptotic process, from the commitment point to the disposal of the corpses. Bergmann and Steller explain why *Drosophila* has been useful in the study of apoptosis: *Drosophila* are genetically accessible, like *C. elegans*, yet have developmental plasticity, like vertebrates. The death sentence is carried out by special proteases called caspases. Roy and Cardone recapitulate the many different aspects of caspase activation, and the different roles each individual caspase might play in this proteolytic cascade.

Two of the most fiercely debated issues in the study of apoptosis are the role that mitochondria may play and how the Bcl-2 family of proteins regulate the activation of caspases. It is widely accepted that the mitochondrial intermembrane space houses a number of extremely dangerous molecules (cytochrome c, caspases, Smac/Diablo, AIF) that are released into the cytoplasm at some point during the apoptotic process. The anti-apoptotic proteins of the Bcl-2 family inhibit this release, whereas the pro-apoptotic members favour it. Tsujimoto, Kroemer and Clarke have had the difficult task of extracting some definitive ideas out of a sea of condradictory results. What will remain of it in the long term is not clear. Such is the intensity of the research in this area that we could already write an addendum to supplement Tsujimoto's addendum. McCarthy and Bennet review the death pathway initiated by death receptors and their ligands, and Franke shows us how many different apoptotic and survival signals may be integrated by kinases and phosphatases.

Finally, and to justify all that frantic research on apoptosis, Vaux explains how the ongoing battle between cells and viruses has provided much insight into the molecular mechanisms of apoptosis, whereas Jacobson and Bergeron review the importance of apoptosis in the development of the nervous system and in neurodegenerative disorders, such as stroke or Alzheimer's disease. I would probably have welcomed a special chapter about the different diseases that are believed to be in part caused by the deregulation of an apoptotic pathway.

Overall, this book clearly meets the goals that were set by the editors, and recapitulates the fundamental findings about the general cell death machinery. It is definitely a valuable addition to the library of any newcomer to the field, and I would certainly recommend it to any undergraduate students joining our lab. However, this field is an extremely fast-moving one, and some ideas have a very short life. Thus, a warning should be issued that the content of this book should not be considered as the definitive truth in all regards, but rather as a collection of beliefs that are awaiting confirmation. This is quite normal after all, because an understanding of cell death is still very much in development. As for cells, death is the default pathway of scientific hypotheses. They need permanent input to stay alive, and most of the wrong ones contain the reasons for their own silent removal and oblivion. No doubt, with time, many of the now popular beliefs will undergo apoptosis and a more mature and stable consensus will remain. Homeostasis, at last…

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