# NMR of Biomolecules

## Towards Mechanistic Systems Biology

Edited by Ivano Bertini,
Kathleen S. McGreevy,
and Giacomo Parigi

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**NMR of Biomolecules**

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# NMR of Biomolecules

**Towards Mechanistic Systems Biology**

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**Cover**
The artwork on the cover attempts to convey the idea of the systems of interacting biomolecules that are at the basis of Life. The Birth of Venus, which has been reimagined for the cover in this spirit, was painted by Sandro Botticelli in the late 15th century and is held by the Uffizi Gallery in Florence. His painting depicts the birth of the goddess of love as she emerges as a fully grown adult from the sea.

Acording to Plato, as well as members of the Florentine Platonic Academy, Venus had two aspects: an earthly goddess who aroused humans to physical love, and a heavenly goddess that inspired intellectual love. Who better than she to represent our passion for the study of biomolecular structures and mechanisms, and the physical-intellectual duality that leads us to learn more about the living world around and within each of us? Actually Venus has already been used as the logo by the Society of Biological Inorganic Chemistry for the Journal of Biological Inorganic Chemistry (JBIC).



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## Preface

The use of NMR to solve protein structures has a tradition that dates back to 1984 (M.P. Williamson, T.F. Havel, and K. Wüthrich (1985) *J. Mol. Biol.* **182**, 295). Since that time, the role of NMR in structural biology has constantly increased in terms of the number of researchers involved and the scientific relevance of the results. Spectrometers are becoming more and more powerful, with magnetic fields that currently reach 22 T, and high-temperature superconducting materials raise the possibility that this value can be surpassed. The investment required for a magnet of the above intensity is currently around €10 million (US$14.3 million) and an estimate of €18 million (US$25.7 million) is reasonable for new-generation magnets. It is clear that NMR is a technology that deserves a special place in research infrastructures, as individual schools may find it difficult to have a battery of machines, all at the forefront of the technology, dedicated to various types of experiments. In 1994, the European Commission (EC) began financing transnational access to NMR instrumentation at some research infrastructures, which have continued and grown in number until the present with the EC-funded Bio-NMR[1] project. In Europe, the recent European Strategy Forum for Research Infrastructures (ESFRI) Roadmap identifies NMR as a fundamental node in the Integrated Structural Biology Infrastructure (INSTRUCT),[2] while it also plays a role in the EU-OPEN-SCREEN (European Infrastructure of Open Screening Platforms for Chemical Biology)[3] infrastructure, Euro-BioImaging,[4] and Biobanking and Biomolecular Resources Research Infrastructure (BBMRI).[5]

The EC-funded electronic infrastructures (e-NMR[6] and WeNMR[7]) provide nonspecialists with tools for automatic data handling, structure calculations, molecular dynamics simulations, and the creation of interaction models in such a way that the potential of the NMR technology can blossom in favor of the progress of science.

Much of this reasoning was debated during the FP6-funded Coordination Action NMR-Life[8] and resulted in a booklet entitled *NMR in Mechanistic Systems Biology*,[9] which ultimately served as the spark for this volume. We were pleased when Gregor

1) http://www.bio-nmr.net.

2) http://www.structuralbiology.eu.

3) http://www.eu-openscreen.eu.

4) http://www.eurobioimaging.eu.

5) http://www.bbmri.eu.

6) http://www.enmr.eu.

7) http://www.wenmr.eu.

8) http://www.postgenomicnmr.net.

9) http://www.postgenomicnmr.net/NMRLife/docs/NMR_in_MSB.pdf.

Cicchetti from Wiley-VCH noticed this booklet and proposed that we edit a book on the very same subject, and we gathered a number of outstanding contributors to fulfill the task.

Our intention, which we hope pervades the book, was to provide a text for graduate students, junior post-docs, and other newcomers that would serve as an introduction to the field, addressing classical NMR approaches from solution to the solid state, providing some tips and tricks not available in journal articles, and providing perspectives on future developments. It is our hope that the Protocols and Troubleshooting sections will be of assistance and guidance when choosing experiments and overcoming difficulties.

However, everyone who has experience in editing books knows how difficult a task it is – obtaining the manuscripts on time, convincing everyone to adhere to a template and write for students and not for their fellow professors, and even drawing the line on what content to include and when to call an end to the editorial process, including substitution of recalcitrant contributors. We editors have tried our best to overcome these difficulties, but we are aware that much more could have been done. For example, the development of isotopic labeling has been fundamental for the development of NMR, but we decided not to address it here. The reader should therefore be aware that the field of NMR is even broader and more exciting than it appears from our efforts!

Part I of the book (Introduction) explains NMR's role in Mechanistic Systems Biology and provides a broad overview of biomolecular structure before identifying what NMR can teach us about the structure and dynamics of biomolecules. Parts II–VII address a series of relevant topics in NMR-driven biological research: the role of NMR in the study of the structure and dynamics of biomolecules, its role in the study of the structure and dynamics of biomolecular interactions, NMR in drug discovery, solid-state NMR, frontiers in NMR spectroscopy, and computational aspects.

We would like to take the opportunity to thank, in addition to Gregor, Dr. Marco Fragai of the Center for Magnetic Resonance (CERM) at the University of Florence for his assistance in editing some chapters of the book, and Professor Claudio Luchinat, who consistently demonstrates his friendship and his willingness to support any initiative of CERM, and the scientific personnel of CERM who have contributed to discussions and sustained the work.

It is our sincere hope that this book will find a home not only in NMR facilities, but also in biomedical laboratories around the world, where it can be of use to the broader scientific community and help diffuse NMR as a technique for the study of biological systems.

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Florence, January 2012

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