Foreword

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The molecular universe is one of the final frontiers for human exploration. Inaccessible until recently due to the limitations of our senses, this world of nanometer-sized objects is now becoming more accessible through increasingly sophisticated instrumentation and theories that extend our senses and bring understanding to structure and events at the molecular level. Like its cosmic counterpart, the molecular frontier is rich with information, much still unknown, that will profoundly advance our fundamental knowledge of our world, provide the basis for the major discoveries and inventions of the XXIst century, drive global economies and determine our collective and individual well-being. From new materials and medicines to an understanding of how we think and the origins of life itself, the molecular frontier promises to provide an enormous return for those who invest in its exploration.

Chemistry represents the quintessential discipline for the exploration of the molecular universe. This point is reflected in the increasing number of disciplines that have prospered through fusion with chemistry, from chemical physics to chemical biology and the growing list of disciplines that have come to the molecular world to seek insights and opportunities for advancement. From molecular biology, molecular medicine, and molecular pharmacology to molecular paleontology and nanotechnology, *molecular science* is becoming the dominant integrated discipline of this century. We are indeed at the beginning of what can be called a molecular revolution, a time of major change that will more profoundly shape our world than the industrial revolution did one hundred years ago. It is an exciting time for our global community and for science and an unprecedented opportunity for chemistry.

Chemistry enables us to understand the connections between molecular structure, properties and transformations, and macroscopic consequences. With increasing frequency, these connections are being exploited to produce new knowledge, medicines and materials that drive new technologies and determine our well-being. Many human diseases, for example, are associated with molecular « defects » which in turn become the targets for the design of new therapeutic agents or prevention strategies. The world of materials science and nanotechnology is similarly impacted as molecular science seeks to develop devices and materials that exceed the capabilities of living systems and current materials. From molecular « noses », molecular computers and molecular sensors to plastics stronger than steel, organic conductors and « smart » materials, chemistry is not only providing new materials but also materials with new functions.

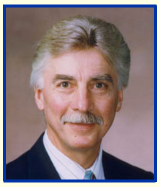
Driving many of the advances in chemistry is synthesis, the science and often art of making molecules, a central theme of this issue of *L'Actualité Chimique*. Synthesis allows for the practical supply of materials and medicinals that would otherwise be difficult or impossible to acquire. More importantly, it allows us to create and access new compounds that open new opportunities in research, with profound consequences for human health and our standard of living. One need only to consider the transformation of materials science research that has been enabled by the synthesis of fullerenes, nanotubes, conducting polymers and self-assembled materials to appreciate the enormous impact of basic research on the generation of new product opportunities. Here we see what can be considered a *silent* revolution that in the fullness of time will transform our world at both the fundamental and applied levels. Like the discovery of plastics almost a century ago, the silent revolution in materials research is creating XXIst century materials that will provide the basis for smart materials, devices, sensors and even therapeutic agents of the future. Like all silent revolutions, whether in computers, aviation, health or other fields, the realization of this potential will take time and a serious investment of national and global resources. Those who make these investments will benefit enormously. It is clear, moreover, that only through such investment will our global community be able to reach a higher standard of living and realize the full potential of science. Exciting examples of such materials research are elegantly presented in the final section of this overview.

In addition to materials research, synthesis has also had a close and exceptionally productive association with medicine. Indeed most of the therapeutic agents now in human use are the products of organic synthesis. At one point the role of synthesis was principally to supply therapeutic agents that would be otherwise difficult to obtain from natural sources. Increasingly, synthesis is involved in the creation of new agents, often inspired by Nature but designed and prepared in the laboratory. Taxotère is but one example of such synthetic agents created through synthesis that is now in use to treat cancer. As we learn more about biochemical pathways and therapeutic targets, synthetic chemists are increasingly able to design and, through biased combinatorial approaches, discover molecules with exquisite therapeutic function. While we will continue to use natural sources for structural inspiration, medicinal leads, and drugs, this century will also witness a revolution in the invention and discovery of new therapeutic agents with exceptional functional selectivity. We have already seen, for example, the first agents that selectively target one human kinase out of hundreds in the genome. Such smart drugs will be increasingly encountered through the fusion of synthetic and medicinal chemistry. This, too, is a silent revolution, in this case one that will transform the future of medicine. Representative examples of the powerful interplay of synthesis, drug design and medicine are beautifully presented in this issue in the section on new drugs and targeted synthesis.

Our ability to address opportunities in materials science and medicine depends critically on the advancement of synthesis. While the field has come a long way over the past two centuries, we have much work to do if we are to realize the full potential of synthesis. Investment in green chemistry is critical to progress. Our ability to extend the range of solvents for chemical reactions and even to develop solvent-less reactions are other areas of opportunity that will greatly expand the reach and efficiency of chemistry. Equally important will be our ability to address separation science in ways beyond what has been possible traditionally. Phase separation of reagents and substrates offers tremendous advantages in accelerating the separation and purification process accompanying most chemical reactions. The introduction of environmentally benign reagents and processes will also have a profound impact on synthesis in this century. Opportunities and research in the green chemistry of solvents, reaction conditions, reagents and separations are impressively addressed by several authors in section « La synthèse propre » of this overview.

The success of synthesis can be measured by our ability to approach the ideal synthesis in which a target molecule, whether it be a medicinal, material or structure of theoretical interest, would be assembled from readily available starting materials in one step that proceeds in 100% yield in a simple, safe, efficient and environmentally acceptable fashion. Much work is needed to approach this goal. In particular, it is critical to improve existing reactions, reagents and strategies and, more significantly, to invent new ones. Of exceptional importance is the goal of step economy. Step economy can be achieved only through the use of reactions that allow a great increase in complexity or through operations that incorporate many steps that collectively achieve the same high complexity increase. The advancement of existing reactions and the invention of new reactions, reaction sequences, reagents and strategies are critical to the realization of step economical syntheses. In the first three sections of this issue, an impressive group of thought leaders in the field of reaction science insightfully address these issues of critical importance in synthesis and the science and technologies that they enable.

Collectively, the reviews, perspectives and studies reported in this issue beautifully illustrate the rich and exciting palette of molecular science that has been enabled by chemistry and synthesis. Over the past two centuries, chemistry and synthesis have evolved from relatively pure disciplinary pursuits to positions of central importance in the physical and life sciences. More generally, they have provided the language and methodology that have unified the sciences, shaping our understanding of our molecular world and the direction, development and destiny of scientific research. From new reagents, reactions, strategies and processes to materials, medicinals and machines, the investment in molecular science has provided returns of fundamental and technological significance, profoundly impacting all facets of our global economy and our global community. This issue of *L'Actualité Chimique* provides a most exciting perspective on the state of the science and an inspirational assessment of where the field is headed.



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