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EDITORIAL

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A Man for Single Molecules

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Single-molecule methods have developed into a mature and powerful research approach that is adding new insights into many different areas within the physical and life sciences. The ability to detect and perform experiments on single molecules opens up new experimental approaches to investigating the physical world. One is no longer limited by ensemble averaging, making it possible to detect subpopulations directly, to measure dynamic processes without synchronization of the sample, to visualize rare events and to gather information over the heterogeneity of the sample. Single molecules can be detected and investigated using electrophysiological approaches, force microscopy, electron microscopy or fluorescence microscopy. Pioneering work in the fluorescence-based detection of single molecules was performed by Rotman in the 1960's and 1970's,[1] where he trapped individual enzymes in microdroplets and watched the generation of the fluorescent product. Hirschfeld was the first to directly detect fluorescently labeled molecules diffusing in solution, using antibodies labeled with 80–100 fluorophores. In 1989 and 1990, individual fluorophores were detected for the first time using low-temperature optical spectroscopy, initially with absorption spectroscopy,[2] shortly thereafter with fluorescence spectroscopy[3] and at room temperature.[4] Historical accounts of the development of single-molecule detection can be found in refs. [5,6].

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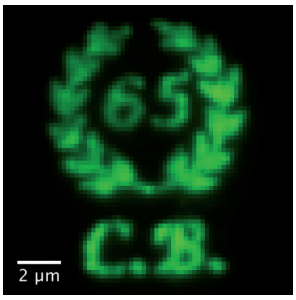
Shortly after the detection of single fluorophores, Christoph Bräuchle saw the potential of this method and began working in the area of single-molecule spectroscopy with his first publication in 1992.[7] Combining his expertise in low-temperature spectroscopy with single-molecule methods, he was able to observe for the first time quantum transitions in the electronic states of a single molecule and could optically switch the fluorescence of terrylene in p-terphenyl.[8,9] As the field warmed up to room temperature, Christoph used single-molecule methods to follow the entry pathway of individual viruses in living cells in real time.[10] He has become an expert on the diffusional motion of molecules and has used single molecules as fluorescent beacons to map out structures of nanoporous systems with an accuracy of better than 5 nm. This elegant method allows one to visualize the molecular dynamics in and the structural details of pore systems with pore sizes at the nanometer scale including the formation of domains, accessibility of the channels and connectivity of the network.[11,12]

On the occasion of Christoph Bräuchle's 65th birthday, we dedicate this issue of *ChemPhysChem* to his honor and to the exemplary research he has performed. In this issue, several authors from different countries have contributed groundbreaking research articles, giving an overview of the current status of single-molecule research. Many of the articles touch upon topics where Christoph has made significant contributions. **Spectroscopy:** Spectroscopy has been used extensively in the research of Christoph. This issue of *ChemPhysChem* contains many examples of spectroscopy with different applications ranging from nonlinear optical applications for modern microscopy techniques, investigations on the photophysics of dye molecules towards the use of single-molecule approaches for the development of ultrasensitive bioanalytical tools. **Method Development:** Christoph has always pushed and supported method development to perform more accurate and sensitive experiments. In this issue, several groups report on different novel methodological approaches with the general idea of combining different spectroscopic tools as well as rigorous mathematical and statistical treatment of the recorded data to maximize the information obtained in the single-molecule experiments. **Diffusion and Tracking:** Through his experiments on the entry of single viruses into living cells and on the diffusion of single molecules in mesoporous systems, Christoph has shown how important insights into complex biological as well as nanotechnological systems can be obtained by following the movement of single molecules or particles in real time. In this issue, several papers will report on novel developments in this very active research area. **Nanoscience:** In his professional career, Christoph has been strongly engaged in the advancement of nanoscience, for example, by serving several years on the board of Munich's Center for NanoScience (CeNS). Nanoscience is also very visible in a number of contributions in this issue of *ChemPhysChem*, with topics ranging from the investigation of carbon nanotubes to novel techniques for the programmed manipulation of matter on the nanometer scale.



Fluorescence micrograph of a micron-sized laurel wreath honoring the 65th birthday of Christoph Bräuchle. The pattern was assembled by Single-Molecule Cut&Paste from roughly 1000 Atto 647N labeled DNA molecules. For details, see H. E. Gaub et al. on page 914.

In light of the current exciting developments in single-molecule methods, it is interesting to speculate on the future of single-molecule research. One exciting and exemplary development here is the controlled switching of individual molecules, which was already investigated in Christoph's early single-molecule contributions.[8, 9] Using different strategies, it has been shown that the switching of fluorescent molecules allows for the development of microscopy techniques capable of resolving objects far smaller than the diffraction limit of optical microscopy. By bypassing the diffraction limit, it opens the possibility of using optical microscopy to visualize processes that occur on the length scale of individual proteins and nanodevices. It is quite clear that such capabilities will revolutionize many areas of current research in the life sciences as well as in nanoscience.

For many of the contributors to this special issue, Christoph Bräuchle has been a collaborator, colleague and/or mentor. His enthusiasm, insights and passion for single molecules in particular and science in general have been an inspiration and an example to us. We thank Christoph for his excellent contributions to physical chemistry and look forward to learning of his latest results in the future. Christoph, we wish you a happy 65th birthday and dedicate our newest research results to you in this special issue of *ChemPhysChem*. What birthday gift would be more appropriate for a man with such a passion for single molecules?

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