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Application of the high-sensitivity pulsed dipolar ESR spectroscopy to membrane protein structure and function

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Pulsed dipolar ESR spectroscopy (PDS) is a rapidly developing technique with significant potential to study functionally related conformational changes in proteins, oligonucleotides, and a variety of biomolecular complexes. In our research we apply PDS to large membrane proteins reconstituted into lipid membranes and detergents, to find details that currently are not readily (or at all) accessible by using other methods, such as NMR or X-ray crystallography. Particularly, we benefit from the high sensitivity of our unique pulsed EPR spectrometers and methods, which expand our research base by giving us the opportunity to study biomolecule structure/function in a broad range of physiologically relevant concentrations and conditions by accurately measuring the distances spanning the range from 10 to nearly 90 Å. We illustrate the applications of PDS with two examples. (i) We studied structural conformations of membrane-associated α-Synuclein. By measuring long distances of up to ca. 90 Å in this intrinsically unstructured eukaryotic protein, we provided direct proof of forming an extended helix, when it is bound to the surface of lipid membrane. Also, we characterized its transition between broken and extended helix in detergents. This essential knowledge about physiologically relevant structures of α-Synuclein helps us to learn the mechanisms that govern its assembly into fibrils causing neurodegenerative diseases. (ii) In our study on glutamate transporters, using a prokaryotic homologue, GltPh, we reveal molecular rearrangements, which are deemed to underlay their function. Of particular interest is populating of outward and inward facing states of GltPh in detergent-reconstituted protein and in lipid membranes.

Biography

Elka Georgieva received Ph.D. from Bulgarian Academy of Sciences in December 2005. Her research focus was on radiation dosimetry. From January 2006 to October 2007 she was a postdoctoral fellow in the Department of Biochemistry and Biophysics, Stockholm University, where she studied RNR from Mycobacterium tuberculosis. In October 2007 she joined ACERT at Cornell University as a postdoctoral associate. Her current position there is Research Associate. At ACERT E. Georgieva carried out several research projects, most of which collaborative, on protein structure and function, using advanced Pulsed Dipolar ESR spectroscopy. E. Georgieva was fortunate to work with and learn from scientists with high levels of expertise in different areas. She contributed several papers to reputed journals.

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