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Sommario/riassunto	What is life? How, where, and when did life arise? These questions have remained most fascinating over the last hundred years. Systems chemistry is the way to go to better understand this problem and to try and answer the unsolved question regarding the origin of Life. Self-organization, thanks to the role of lipid boundaries, made possible the rise of protocells. The role of these boundaries is to separate and co-locate micro-environments, and make them spatially distinct; to protect and keep them at defined concentrations; and to enable a multitude of often competing and interfering biochemical reactions to occur simultaneously. The aim of this Special Issue is to summarize the latest discoveries in the field of the prebiotic chemistry of biomolecules, self-organization, protocells and the origin of life. In recent years, thousands of excellent reviews and articles have appeared in the literature and some breakthroughs have already been achieved. However, a great deal of work remains to be carried out. Beyond the borders of the traditional domains of scientific activity, the multidisciplinary character of the present Special Issue leaves space for anyone to creatively contribute to any aspect of these and related relevant topics. We hope that the presented works will be stimulating for a new generation of scientists that are taking their first steps in this fascinating field.