Research summary

The Rapaport lab is engaged in various projects related to the design, characterization and applications of biological molecules, mostly amphiphilic peptides. The research involves the de-novo (from scratch) design of peptides based on physicochemical principles and on structural motifs appearing in natural proteins, with the aid of molecular modeling tools. The peptides are designed to exhibit amphiphilic properties which promote molecular self-assembly in forms of monolayers, fibrils or hydrogels (Fig.1). We aim at acquiring control over these structures to construct systems with varied biological, chemical and physical functionalities.

Amphiphilic and acidic peptides designed in our lab generate hydrogels which may be utilized in applications related to tissue regeneration, drug delivery and diagnostics.

Our studies are carried at various levels, from fundamental molecular structure characterizations to demonstrating the functional properties, usually following these stages:
a) Peptides are designed to form certain ordered molecular systems
b) Structural characterizations are carried by a variety of analytical techniques
c) Biological tests are performed by in-vitro cell cultures or in-vivo

Various surface sensitive techniques are employed in studying the structure of these systems including: grazing incidence X-ray diffraction on liquid interfaces at synchrotron sources, Brewster angle microscopy, thin film X-ray diffraction, atomic force microscopy, FTIR and other spectroscopies.

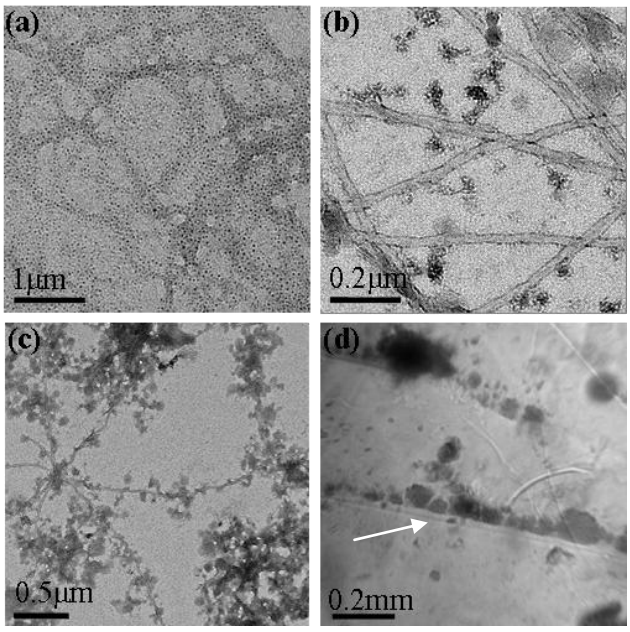

Figure 1: TEM images of amorphous calcium phosphate particulates adhered to P_{FD}-5 hydrogel fibers. a) Unstained sample showing dark dots that appear more abundant on the peptide fibers than in the background. b) - c) Negatively stained hydrogel fibers that are ~30 nm wide decorated by calcium phosphate spherical particulates. d) An optical microscope image of peptide fibers aligned by spherical calcium phosphate particulates. The fiber marked by the white arrow reaches more than 1 mm in length

The acidic rich peptides serve as template matrices for calcium adsorption and hydroxyapatite formation (Figure 1). [1] The peptides can be assembled into hydrogel structures at physiological pH's with the addition of calcium and/or calcium minerals. [2] Currently, the peptides matrices are being exploited for bone tissue engineering applications (Rapaport, 2006 PCT). Together with the company curasan AG

(Germany), which develops various minerals for bone tissue regeneration, products that combine our peptides with curasan's minerals are being studied.

In context of calcium phosphate mineralization we have established collaboration with Prof. Yoram Oren and Dr. Roni Kasher from Department of Desalination & Water Treatment, The Blaustein Institutes for Desert Research Sede Boker BGU, regarding mineralization in water filtration systems, especially in biofilms.

Recently we found that amphiphilic peptides exhibit crystalline elasticity at the molecular level. These findings may have relevance to the understanding of structure-function activity of natural proteins such as apolipoproteins (in collaboration with Prof. D. Small, Boston University), in stress induced activity in proteins and more. We are exploring various molecular aspects and their affects on the β-sheet molecular compressibility. [3]

We are also carrying a research in collaboration with Prof. Sam Gellman, (UW, Madison), that was supported by the Israel-US binational science foundation. β-sheet like peptidomimetic foldamers based on β-peptides synthesized in Gellman's lab, were designed and characterized by grazing incidence X-ray diffraction (GIXD) and other techniques at interfaces and in bulk. [4]

References:

[1] Segman-Magidovich, S., Grisaru, H., Gitli, T., Levi-Kalisman, Y. and **H**. **Rapaport** (2008) Matrices of acidic β-sheet peptides as templates for calcium phosphate mineralization. Advanced Materials 20, 2156-2161 .
[2] **Rapaport**, **H**. Grisaru, H. and T. Silberstein (2008) Hydrogel formation by matrices of acidic β-sheet peptides at neutral pH values. Advanced Functional Materials 19, 2889-2896.
[3] Isenberg, H., Kjaer, K. and **H. Rapaport** (2006) Elasticity of crystalline β-sheet monolayers, J. Am. Chem. Soc. 128, 12468-12472.
[4] Segman, S., Lee, M-r., Vaiser, V., Gellman, H. S.* and **H. Rapaport*** (2009) Angew. Chem., 49, 716-719.