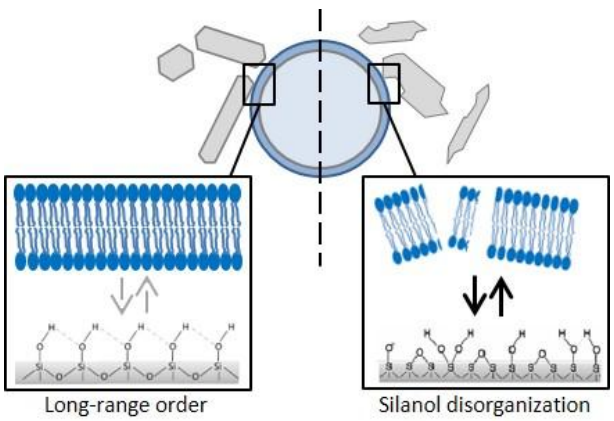
Interfacial molecular recognition in complex systems: chemical investigation of the interaction between silica surfaces and cell membranes

Riccardo Leinardi
Department of Chemistry - Interdepartmental Centre "G. Scansetti" for Studies on Asbestos and Other Toxic Particulates – University of Torino
riccardo.leinardi@unito.it
Tutors: Prof. Gianmario Martra – Dott. Francesco Turci

An impressive body of scientific reviews and experimental works,[1-2] has evidenced two key aspects in the interaction between crystalline silica and cells: i) the crucial role played by the particle surface in triggering the adverse biological response, and ii) the extreme variability in the pathogenic potential among different sources of particulate silica.[3] Such a variability is the consequence of differences in silica bulk and surface chemistry, including the occurrence of free radical generation centers ($Si^{\bullet}$ and $SiO^{\bullet}$ as well as redox-reactive metal impurities) and the nature, abundance, and spatial disposition of silanol (–Si-OH) families. Silanols, acidic moieties with a potential for H-bonding, have a key role in defining silica interaction with cells: silica surface is characterized by different families of –Si-OH groups, including isolated (the most common), geminal, and vicinal silanols. The long-range order and distribution of silanol patches on silica surface impart specific characteristics to different silica specimen. Quartz dusts used so far in particle toxicology assays have been obtained by grinding rock containing natural quartz, a process that affects crystallinity and yields samples with extreme variable and complex surface states. To overcome such a variability, we have developed an innovative method to grow highly-pure quartz crystals in respirable size (< 4 µm) with controlled surfaces: such crystals allow us to investigate, at the molecular level, the mechanisms related to quartz toxicity. Surprisingly, the as-grown synthetic quartz crystals with regular faces, characterized by silanol patches with a long-range order, did not show any cellular toxicity on human and murine macrophages, and did not induce rupture/leakage of membrane models (liposome and red blood cells). After inducing the loss of the long-range order of silanol patches by ball milling, synthetic quartz elicited cellular toxicity and strong membranolytic activity. Crystal milling also led to the formation of surface radical species,[4] which are held to be involved in the alteration of the ROS metabolism of cells. Overall, data are consistent with the hypothesis that most of the biological reactivity of quartz dusts is not due to crystallinity *per se,* but it is originated via fragmentation, which entails the formation of conchoidal fractures and new faces. Thus, fracturing upsets the expected long-range spatial order of non-radical surface moieties (silanols, silanolates, siloxanes) and, probably, creates highly-reactive surface silanol patches; accordingly, biological reactivity, and possibly toxicity, appears to be related with the spatial disorganization of surface functionalities.



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