UNIVERSAL TOOLS FOR BIOMOLECULAR ATTACHMENT TO SURFACES

To the editor — As I regularly encounter many scientists and program managers who ask when the myriad autonomous sensors and devices promised by nanotechnology will be delivered, I read with interest the stimulating commentary by Byrne and Diamond on chemo/biosensor networks[1]. I strongly concur with the authors that in order to develop the sensing networks they postulate "considerable advances in materials science are needed". However, they argue that the key is "the fundamental issue of how to predict surface characteristics at the interface between the device and the real world…" and "the answer lies in knowing the sensor response characteristics…". Here, I wish to address in more depth a very fundamental point that perhaps they have missed. Biological molecules will be crucial components of these devices, and so for the transition to autonomous chemo/biosensor networks the problem is more fundamental; namely interfacing biological molecules (dominated by proteins) and biosensing molecules with what in the end will probably be the solid-state components of any device. This is a true materials problem. Clearly, sensor and surface characteristics are important, however, the overarching problem will be in creating a biosensor that can be integrated with the rest of the device on a nanoscale, in a generally applicable manner that can be easily transferred to almost any other sensor design.

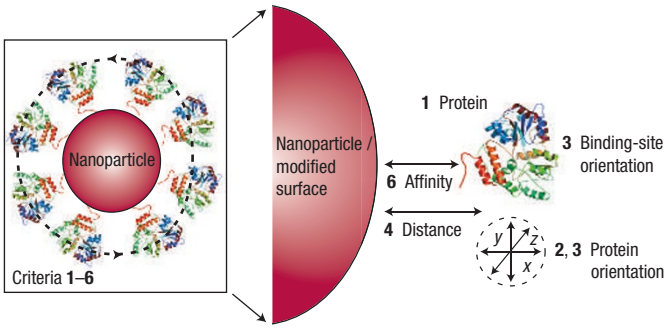

Figure 1 Schematic representation of the six criteria (see text) for a universal 'toolset' that would allow controlled attachment of any protein to any nanoparticle or surface. In this example, the proteins would cover the nanoparticle surface in three dimensions and could still have some rotational freedom around the axis connecting them to the nanoparticle while still fulfilling the criteria. These criteria can be extended to the interaction of any biosensing molecule with the solid-state components of any biosensing device.

I believe that one possible solution lies in developing a 'universal' set of tools to systematically attach almost any biomolecule to any surface in a manner that satisfies several important criteria. I find the criteria are easily visualized if we use as an example the attachment of proteins to surfaces or nanoparticles (Fig. 1). An ideal set of such tools would allow: (1) any protein to be attached to any nanoparticle/surface material, (2) in a homogenous manner, (3) with control over the final orientation of the protein, (4) control over its distance from the surface, (5) control over its density on the nanoparticle/surface and (6) control over its affinity to that surface. Although relatively simple conceptually, these criteria are not easily attainable individually let alone cumulatively. If achieved, then the confounding sensor issues that the authors mention including stability, sensitivity, regenerability, energy consumption and so on, can all be systematically addressed by using optimized protein–surface or protein–nanoparticle conjugates as universal test platforms. Success here may also be applicable to other biomolecules such as DNA aptamers, and may further allow researchers to work on nearly comparable platforms, something that would greatly accelerate research.

There are avenues of research addressing some of the criteria and sensor issues, but these seem to be in parallel with separate goals rather than cumulative and focused approaches. These include, for example, the evolution of peptide-driven binding motifs targeting almost any desired material[2,3], developing new recognition elements such as temperature-stable antibody fragments[4], new signal transduction modalities for biosensors[5], and new chemistries for protein modification[6]. Creating a fully autonomous, integrated chemo/bio(nano)sensor network will be a major achievement, but this will be significantly diminished if we have to start from scratch to build another. I realize the difficulties of this endeavour, but perhaps it is time we stepped back from the goals and focus more on concerted means to achieve them.

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