Implant integration: Problems at the interface

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The history of glues (adhesives) goes back tens, if not hundreds, of thousands of years.[1,2] Over an extended period of time, humans learned how to bind together a wide variety of materials: wood, metals, ceramics (in the form of bricks and crockery), concrete, and plastic.[3] These materials are "hard:" their constituents rearrange on timescales that are rather long. Concrete, for example, sets in a few hours, cures over a period of about a month, but then retains stability over the course of decades (note, however, very interesting creep phenomena[4]). Adhesives work either by softening interfaces, temporarily decreasing the rearrangement times to allow interdiffusion, or by wetting the rough surfaces of the materials. Subsequent hardening, through solvent evaporation, cooling, or cross-linking, joins the interfaces together.[3]

Mineralized human tissues found in teeth and bone are the closest to hard materials. The vast experience gained with adhesives has been successfully adapted to osteoimplants: for example, artificial hip and knee joints are cemented into the bone. Cementless implants also exist.[5] They have porous interfaces that rely on bone tissue ingrowth (compare with the adhesion between rough surfaces mentioned above). Healing times of cementless implants—several weeks—give an idea of the relevant timescales.[6] This timescale is comparable with that on which bone remodeling occurs.[7]

Artificial joint replacement enjoys considerable success.[8] Modern artificial hip joints can withstand significant loads associated with athletic activities.[9,10] However, problems remain: implant loosening, loss of bone mass around the implant, and the need for repeated interventions.[9] These problems occur because bone tissue is not like metal, plastic, or concrete. However slowly, the bone tissue rearranges; the re-arrangement has functional significance.[6,7] An implant is unable to match or support these rearrangements. The approach rooted in gluing fails. In this context it is noteworthy that the improvement in durability of cementless implants (as compared to cemented implants) is questionable.[5] Other causes of osteoimplant failure include recalcitrant infections, which is another biointerfacial problem,[11] and wear of the working surfaces of the artificial joints, reviewed in detail by Sullivan and Topoleski.[8]

The consequences of our limited ability to control interfacial phenomena are far more readily apparent with vascular implants such as stents and mechanical heart valves that interact with soft tissues and fluids. Here, the relevant timescales are significantly shorter: protein adsorption and platelet activation at implant surfaces take seconds to minutes.[12,13] (Platelet activation is thought to be induced by the adsorbed proteins and underlies thrombotic and inflammatory responses to foreign materials, as reviewed in Ref. 14.) Consequently, the experience with gluing is not very helpful. Instead, the success of vascular implants is due to the application of antiplatelet and anticoagulation therapy,[15,16] while the materials currently used in vascular implants—all of them, without exception—induce thrombosis and inflammation.[17]

Initial biological responses to the two types of implants are also more similar than one would, perhaps naively, expect. Both implants interact with blood—vascular implants for the duration of their lifetime, osteoimplants—initially. This initial interaction is as important for the eventual integration of the osteoimplants[18] as it is in adverse thrombotic and inflammatory reactions to the vascular ones. Also well-recognized is the general role of platelets in these processes—both the adverse reactions and wound healing.[19,20] Although the latter remains poorly understood, there is the relatively recent interest in platelet-rich plasma (PrP) formulations to aid osteoimplant integration.[21] [The irony of fibrin gels being used as surgical glues (that gluing approach again!),[22] which led to the development of PrP-based approaches,[19,21] should not be wasted here.]

In summary, similar interfacial phenomena contribute to implant failure in different physiological contexts. Failure becomes apparent at different times because of the difference in the relevant rearrangement timescales, and is ultimately rooted in the inability of the existing artificial materials to match these rearrangements. Integrating the capacity to rearrange into artificial bio/non-biointerfaces is a formidable bioengineering challenge. Interfaces between systems that rearrange on different timescales are also interesting from a fundamental perspective. In both aspects, inspiration might be drawn from the field of biomineralization that is concerned with a variety of mechanisms evolved by organisms for design and repair of interfaces between biological and inorganic structures.[23–25] Appreciation of the notions presented in this Letter can help focus the basic and translational research efforts in the field of biological surfaces and interfaces.

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