The "Theta Surface" for Biocompatibility: Minimizing Protein Denaturation

Robert E. Baier
University at Buffalo

How to Choose a Biomaterial: What is your best choice for a biomaterial that will display long-term, passive, minimally bioadhesive interactions with flowing blood or any other biological phase? Choose a material that will least denature the inevitably deposited (glyco)proteins arriving at its surface, so this mandatory "conditioning" film is least-retentive of subsequently arriving matter, living or dead! Materials that present such "easy-release" properties are those with "theta surfaces", so-named in analogy with "theta solvents" which have long been defined as solvents for macromolecules in their most thermodynamically stable forms, or ideal three-dimensional conformations. This is simple to remember, since the "theta surface" is defined by a particular set of contact angle measurements, and contact angles—as determinants of relative surface energies--have been historically characterized with the symbol "theta" (θ).[1] *The "theta surface" is that surface quality associated with maintenance of attached proteins in their most solution-like conformations.* If you desire strong bioadhesion, as for osseointegrated dental implants, stay away from the "theta surface" so that Nature's protein-primer "glue" will better sustain mechanical challenge!

Empirical and Theoretical Justification: When diverse pure liquids have their directly measured contact angle values plotted against their carefully controlled surface tensions, extrapolation of those plots to the Zero contact angle (full spreading) defines each material's Critical Surface Tension (CST).[2] CST values between 20 and 30 mN/m, preferably between 22 and 24 mN/m, define the "theta surface" condition for biological interactions.[3] Although CST is an empirical construct for actual materials, and not always equated to surface free energy of an ideal system at equilibrium, there is good theoretical justification for the observation that *excess interfacial energies (during macromolecular adsorption at water-material boundaries) are minimized in this CST range* as a consequence of the distribution of water's surface energy into dispersive versus polar components.[4]

Lessons Learned and Mistakes Overcome: It was not correct to assume there was a linear relationship between surface energy and adhesive strength of biological substances to materials underwater, as there is for adhesion of contacting phases in air [5], or that hydrophobicity was a main factor. Rather, blood coagulation and thrombotic deposits are equally well-triggered by hydrophobic low-CST PTFE and hydrophobic higher-CST LDPE, but least of all by hydrophobic "theta surface" intermediate-CST PDMS, and hydrophilic "theta surface" umbilical cord vein graft intima. It is not correct that cells come into direct contact with biomaterials in natural systems. Rather, there is first spontaneous and universal deposition (and then selective retention) of protein-dominated conditioning films before arriving particles attach.[6] The weakest attachment of particulate in all natural biological systems is found to be to materials showing the "theta surface".[7] It is not correct that different materials become coated with different proteins from the same complex biological systems. Rather, the dominant deposited and retained constituent from a given biological fluid is the same (usually highly-hydrated glycoprotein) macromolecule in about the same amount and time to all materials. Differences in conditioning films are in bound protein conformation rather than composition [8]. It is not correct that different cells or particles are the first or most abundant to attach to different biomaterials in different natural systems. Rather, within a given system, a primary type of particulate (e.g. platelets) is the first to attach over the same times and in the same numbers to the pre-deposited conditioning films on all materials. Material-related differences are displayed in varying deposition patterns and degrees of (spreading) interactions.[9] Differences in material-biosystem interactions are determined by post-deposition retention strength differences of the primary particulate films, rather than by differences in (generally random and uncontrollable) arrival events.[10] Application of relevant mechanical work (e.g. shear rate) is required to reveal substratum-dependent differences in bioadhesive strengths; never zero but always minimized at the "theta surface" in every natural biological system.[11]

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