Solute exclusion from cells, gels and proteins: relevance to drug delivery

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A vital dye exclusion test is the most commonly used method for determination of living vs. dead cells. Cell death is thought to disrupt the vital dye (i.e. methylene blue, trypan blue, nigosin, propidium iodide and others) exclusion function of the cell membrane and this allows the dye to enter and stain the intracellular contents. An alternate dye excluding mechanism is that most if not all of the water in the cytoplasm of a living cell is structured in such a way as to be non-solvent for the vital dye. As proteins are, by dry mass, the most abundant material in the cell it seems logical to think that proteins are the likely source of water structure. According to this idea, death of the cell causes decrease in water structure and its dye excluding properties.

It is difficult to get enough cytoplasm to study its solute exclusion and other physical properties. As reported here, hen egg white has provided a useful surrogate for cytoplasm and can be separated into thin and thick albumen fractions that remain non-miscible. Thick albumen without a membrane is vital dye excluding, demonstrates osmotic behavior and has the ability to transform from a dye excluding gel to a non-dye excluding more fluid sol by pressure agitation a gentle shear force. The sol phase does, with time, transform back to a dye excluding gel. Thin albumen is also shown to have a dye excluding shell of water that can be removed by centrifugal pressure.

It seems likely that protein rich living cells, like thick albumen, would have a proclivity to exist in a vital dye excluding gel state that can transform to a more fluid non-dye excluding sol state upon physical perturbations or death.

It may be that structured cell water excludes drugs from interaction with their cellular target molecules and that physical means could be used to help destructure water and therefore allow access of drugs to their target molecules at specific sites in the body.