



Feature Article

The Biological/Physical Sciences Divide, and the Age of Unreason

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Abstract. D'Arcy Thompson in *On Growth and Form* tells us that the early founders of the cell theory of biology, and the physiologists believed that progress in their sciences depended critically on our knowledge of molecular forces. The hubris of a new science that followed the application of X-rays and other techniques to the structure of proteins, the focus on DNA, transport in neurophysiology and ion pumps is understandable. In that progress, the environment, molecular forces and lipids played no role.

Structure and Form took a giant, unifying step forward in the recognition of a key role for hyperbolic (non Euclidean, bicontinuous) geometries, from the self assembly of lipids, surfactants and proteins; to nanostructure in inorganic and solid state chemistry generally.

But the complementary concepts of Function and Growth that depend on molecular forces remained poor cousins. The reasons are becoming clear. Changes in the foundations of colloid and physical science took place over the last 70 years since the theory of Deryaguin, Landau, Verwey and Overbeek took center stage.

A number of related advances occurred.

The first is in the conceptualisation and quantification, and understanding of recognition built into Lifshitz theory, its many body, temperature and frequency dependencies. The second lay in the quantification of Hofmeister (specific ion) effects. These, due to dispersion and related hydration forces, had been inaccessible to classical theories of electrolytes and molecular forces. This defect rendered theory impotent for prediction. The third has to do with the startling recognition that dissolved atmospheric gas, at a molecular level has qualitative effects which have been ignored.

Also ion specific, the effects are ubiquitous and range over enzyme activities to protein structure, catalysis and emulsion stability – “Hydrophobic interactions” apparently disappear when gas is removed.

The fourth is a new “non- Hofmeister” universal ion specificity that occurs for bubble bubble interactions. Inhomogeneity in temperature between bubbles and solvent can be used to catalyse high temperature reactions at low temperatures. These so far inexplicable effects open up other new technologies unimagined., in e.g., desalination, water purification and sterilisation and others.

In other words the classical theories of physical chemistry that inform our intuition had become rigid and inhibiting to progress. Application of fundamentally wrong theories of molecular forces based on electrostatic forces to many areas of biology like has produced an unhappy muddle.

An account is given of these complexities that are missing from classical theories of physical chemistry. Essentially although the Greeks told us that the elements were water, earth, fire and air, we forgot the last two.

When we include them, a different intuition and a new vistas emerge.

The paper is complemented by two other relevant manuscripts: one is published in *Colloids and Surfaces Science B: Biointerfaces* 2017, vol. 152, 326-338. *Two sides of the coin. Part 1. Lipid and surfactant self-assembly revisited*. The second has appeared in *Current Opinion in Colloid & Interface Science* 2016, vol. 27, 25-32, *Surface forces: Changing concepts and complexity with dissolved gas, bubbles, salt and heat*.

Keywords. progress of sciences, molecular forces, surface forces, specific ion effects, bubble-bubble interactions, dissolved gas.

1. INTRODUCTION

This essay has a precedent in and pays homage to the magnificent book *Mathematics: The Loss of Certainty* by Morris Kline.¹ Kline relates the calamities that have befallen Mathematics. The realisation that the foundations were insecure, and did not as we thought, represent absolute truth led to a widening gap between Mathematics and Science. They are both poorer for it. Mathematics, once the Queen of the Sciences, and Science are hardly on speaking terms.

Our essay mirrors Kline and explores a similar calamity that has befallen Physical Chemistry. That subject is the enabling discipline that underpins subjects as diverse as Chemical Engineering to Soil Science to Molecular Biology and Physiology.

The discipline of chemistry, whose name, from Khemia, the black soil of Egypt that gave it life, is the most venerable of the tribes of the physical sciences. It has failed to contribute to biology as it ought to have done. The reasons lie deep. We will show that the foundations were flawed. And that when they are repaired, a wall of non communication between biological and physical sciences begins to come down.

2. JOHN W. DRAPER AND CELEBRATION OF THE ENLIGHTENMENT

In the heyday of the Age of Reason in the 19th century there was an unlimited confidence in reductionism. Let us hear from the American polymath and Professor of Chemistry at New York University, J.W. Draper in the peroration to his encyclopaedic *History of the Intellectual Development of Europe* published in 1876 by Harper Brothers.²

Here is his peroration:

In such things are manifested the essential differences between the Age of Faith and the Age of Reason.

In the former, if life was enjoyed in calmness, it was enjoyed in stagnation, in unproductiveness and in a worthless way. But how different is the latter! Everything is in movement. So many are the changes we witness even in the course of a very

brief period, that no one, though of the largest intellect, or in the most favourable position, can predict the future of only a few years hence. We see that ideas which yesterday served us as a guide, die today and will be replaced by others, we know not what, tomorrow.

In this scientific advancement, among the triumphs of which we are living, all the nations of Europe have been engaged. Some, with a venial pride, claim for themselves the glory of having taken the lead.

But perhaps each of them, if it might designate the country - alas - not yet a nation - that should occupy the succeeding post of honour, would inscribe Italy on its ballot.

It was in Italy that Columbus was born; in Venice, destined one day to be restored to Italy, newspapers were first issued. It was in Italy that the laws of the descent of bodies to the earth and of the equilibrium of fluids were first determined by Galileo. In the Cathedral of Pisa that illustrious philosopher watched the swinging of the chandelier, and observing its vibrations, large and small, were made in equal times, left the house of God, his prayers unsaid, but the pendulum clock invented. To the Venetian senators he first showed the satellites of Jupiter, the crescent form of Venus, and, in the Garden of Cardinal Bandini, the spots upon the sun. It was in Italy that Sanctorio invented the thermometer; that Torricelli constructed the barometer and demonstrated the pressure of air. It was there that Castelli laid the foundations of hydraulics and discovered the laws of the flowing of water. There too, the first Christian astronomical observatory was established, and there Stancari counted the number of vibrations of a string emitting musical notes. There Grimaldi discovered the diffraction of light, and the Florentine academicians showed that dark heat may be reflected by mirrors across space. In our own times Melloni furnished the means of proving that it may be polarised. The first philosophical societies were the Italian; the first botanical garden was established at Pisa; the first classification of plants given by Caesalpinus. The first geological museum was founded at Verona; the first who cultivated the study of fossil remains were Leonardo da Vinci and Fracasta. The growth of chemical discoveries of this century were made by instruments which bear the names of Galvani and Volta.

Why need to speak of science alone? Who will dispute with that illustrious people the palm of music and painting, of statuary and architecture? The dark cloud which for a thousand years has hung over that beautiful peninsular is fringed with irradiations of light. There is no a department of human knowledge from which Italy has not extracted glory, no art she has not adorned.

Draper's book was written first in 1859 before Italy became a nation; when the industrial revolution was coming into its apogee. It was reissued in 1876 America was still young and had recovered its confidence. Hubris abounded in the emerging empires. It was as if, quoth General Smuts, statesman of the British empire: "Mankind has struck its tents and is on the march" .

We can forgive Draper's naivete on an apparently boundless future driven by science and too easy dismissal of the Age of Faith.

If we imagined that the core of what he says still rings true today, we face a rude shock. In the 19th century it was possible for one man to understand all science. The meetings of the British Association for the Advancement of Science of the 19th century were attended and followed with much interest by the Press and "Gentlemen", products of greater Public Schools who knew Latin and Greek. Huxley argued with Bishop Wilberforce in defense of Darwin. They followed Burton and Speke's dispute over priority on the sources of the Nile. They waited on the translation of the Rosetta stone and Layard's and the French and German archeologists in Nineveh, were excited by Adams and Le Verrier's prediction and observation of Neptune in 1846. They were excited by the fossil record. They rejoiced with Queen Victoria when Stanley greeted the lost hero missionary in darkest Africa with: *Dr. Livingston I presume*. They rejoiced with the expansion of the railroads and even more when Kitchener avenged General Gordon with the systematic massacre of the Mahdi's large part of army with the new machine guns in Khartoum.

It has changed now. There is now fragmentation into a multitude of disciplines. Each is surrounded by firewalls, and there is little intercommunication.

Hubris now attends modern science, biology, and quantum mechanics. Mindless replacement of thought by computers is our century's equivalent of the Age of Faith.

To computers are imputed all wisdom just like the Church in the worst of pre-reformation times. This is a reflection of the tides of fashion or a gestalt, the periodic emergence and dominance of which we are hardly aware.

Just a time when science seems dominant, triumphant even, the new age of Reason has disappeared, again. A new Age of Unreason is upon us.

3. D'ARCY THOMPSON'S PLEA

It is exactly 100 years since D'Arcy Thompson (1860-1948) published his book on *Growth and Form*.³ He told us that the early founders of the cell theory of biology and the physiologists emphasised that progress in their disciplines had to wait on advances in our understanding

of molecular forces and what even then we called colloid science. Immanuel Kant (1724-1804) had much the same to say, reported D'Arcy. He said "of the chemistry of his day and age that it was a science but not a Science – *eine wissenschaft aber nicht Wissenschaft*, - for that the criterion of a true science lay in its relation to on Mathematics".³ Curiously, an aside, D'Arcy could not bring himself to mention the great German chemists of the preceding century on the track of what he pleaded for, Fredrik W. Ostwald (1853-1932) who mentored the first four Nobel prizes in chemistry men like Wöhler who synthesised urea to break down the myth of a special life force for biomolecules and Friedrich August Kekulé von Stradonitz (1829-1896). Perhaps this was because Britain was at war with Germany. The same recurs. Witness the furious prejudice attached to "polywater" in Felix Franks' book *Polywater* and the Russians during the cold war.⁴

Lest our thesis be misinterpreted as an unfair attack on orthodoxy, let us remark that the claim that "the science is settled" raises a red alert. It is unique to the science of Climate Change only.

There is no other science for which that claim is made by its acolytes.

Indeed if it were, the "science" would be dead and uninteresting.

Let us go through some of them.

Astronomy: At an international meeting in Kyoto in 2016 the astronomers/cosmologists agreed that they have no idea of how to find dark matter or what it is, after 30 years of looking. (They are missing 98% of the mass of the universe necessary to explain the too rapid motion of spiral arms of galaxies). This is a bit of a problem to practitioners who can nonetheless tell us the age of the universe with great precision.

Solar Physics: We have no idea of the source of solar magnetic field nor of the origin and genesis of sunspots.⁵ These dark spots on the sun's surface are gigantic magnetic storms.

They cause a solar wind of ionised particles that hit the poles of the Earth and ionise the upper atmosphere. Hence ozone. But the sunspots fluctuate and have disappeared in the last few years as they have in the past, coinciding with major weather fluctuations. For that matter the standard solar model lacks conviction.

Quantum Mechanics: Considered possibly the greatest achievement of physics. It is still in a mess.

Particle Physics: It seems in a worse mess. The story of the many species of neutrinos and the Higgs giant boson CERN is as credible to those of us not adepts as the Book of Genesis, but less useful.

Geology. Remember how Samuel W. Carey in Tasmania who pushed the theory of continental drift was exco-

riated? The theory was only accepted in the 1960s. Revolutionary theories of the formation of granite and orogenesis are in the wind with the new book of John Elliston.⁶

Biology of all kinds. These new sciences still very much in the process of big changes. The sex of crocodiles depends on the temperature. Kangaroo sex depends on concerted work between 17 different chromosomes. Hence epigenetics, a word that means imputing all wisdom to DNA is too simplistic. The physico-chemical environment of DNA is important too. As for the source of the energy that drives ubiquitous enzymatic action, most are content with the statement that energy flows downhill.

Agriculture: The practice of planting without ploughing, a previously unheard of idiocy for millenia, is now often de rigueur – we forgot about the soil microbes.

Mathematics: As already remarked, it never recovered from Gödel's theorem that showed 100 years ago too that there was no such thing as absolute proof. In a stunning example of delusions of claims of rationality, the mathematicians not only rejected divergent series, but also rejected the delta function and periodic delta functions and their other generalised function cousins until 1950.

The rejection is of major significance and still uncomprehended. The fact that a periodic delta function is a sum of cosines is both intuitive and profound. It is equivalent to the two forms of Euler's product, to Jacobi's theta function transformations, and the Riemann relation. The latter is also intuitive and its equivalence to the periodic delta function means geometry and arithmetic, shape and that we count, are two sides of the same coin. A finite version of the calculus can be derived from these which also gives analytic continuation automatically. The usual infinitesimal calculus is a special case. The Schrödinger equation of quantum mechanics and the diffusion equation are satisfied by the Jacobi theta functions, which give out the classical, Fermi Dirac and Bose Einstein statistics of statistical mechanics. The uncertainty principle is not necessary in the more physical finite calculus.⁷

Archaeology. A bit closer to the bone: The Old Kingdom in Egypt ground to a big full stop after Pharaoh Pepi I about 4500 years ago. This was discovered only thirty years ago. It turned out that the Blue Nile stopped flooding for thirty years. Egypt was completely destroyed. The Middle Kingdom remerged in bastardised form several hundred years later. And of course they found the same happened to the Euphrates and Tigris rivers in Mesopotamia. We had no idea.

And the climate scientists forget what Herodotus (484-425 BC) and Strabo (65 BC-23 AD) reminded us about the rapid changes that took place in central Asia. A much larger Oxus river used to flow into the Caspi-

an Sea and spill over to the Black Sea before it changed course again to the Aral Sea - so explaining how Alexander went so far so fast.

And so it goes in all these sciences, the Science is definitely not settled. And all are deficient. This is not bad. It means that the challenges make life more interesting.

We can be comfortable, not threatened if physical chemistry has some problems.

To these we now turn.

4. GROWTH AND FORM, STRUCTURE AND FUNCTION, LOCK AND KEY

Structure, form, lock imply visual images, geometry and shape of living things.

Growth, function, key imply forces, dynamics, more than visualisable streaming matter in hydrodynamic movement like the gel interior of an amoeba in chemotactic motion. Forces also implies the aether, the fifth element of the Greeks, mysterious, that cause molecules to signal and recognise each other and come together as a result.

Forces will be our central preoccupation. They depend on all 5 of the elements of the Greeks: earth, water, fire, air, aether (or quintessence). We will take fire to mean temperature.

The secrets of Greek fire which kept the Turks at bay and the Roman Empire alive for 1000 years has been revealed by Marcus Graecus:

Recipe for Greek Fire: (due to Marcus Graecus, 10th century, quoted by John Julius Norwich) "Take pure sulphur, tartar, sarcocolla (Persian gum), pitch, dissolved nitre, petroleum, (obtainable from surface deposits in Mesopotamia and the Caucasus) and pure resin; boil these together, then saturate tow with the result and set fire to it. The conflagration will spread, and can be extinguished only by wine, vinegar or sand."⁸

Further illumination on Greek fire we leave to the to the erudition of Professor Partington.⁹

But first consider.

4.1 Structure

It is self evidently a matter of physics. From bone to DNA, with the discovery of X-rays by Wilhelm Conrad Röntgen (1845-1923) and their deployment in X-ray spectroscopy by the Braggs, father and son around 1912, structure took off, culminating in the structure of haemoglobin by M. Perutz to 2 Å resolution. Although always plagued by the inverse scattering problem, of which more later, biology and physics came together in a productive

synthesis. (After papering over a few problems! The fact that revisiting the original X-ray data of Rosalind Franklin showed 4 stranded not two stranded DNA as interpreted by Watson and Crick was dismissed by Wilkins. He shared their Nobel prize. When confronted with this annoyance he said: “Why reject a good theory because of an experiment!” (told to the author by Sir Ernest Titterton who knew him)).

And then post the 1960s it all went pear shaped. For soft matter like self assembled lipids and microemulsions and colloidal suspensions. Light scattering, sophisticated low angle x-ray scattering, neutron scattering, became possible because of accessibility of more and bigger machines for rent in search of problems and off-the-shelf computer programs. The results have been catastrophic. The non uniqueness of the inverse scattering problem means that the interpretation of an experiment depends on a theory. For example, with light scattering the inference of the zeta potential of a colloidal particle assumes that the theory applies to all particles and for all electrolytes. The theory is wrong and the results meaningless. With lipid-water self assembled structures, for thirty years distinguished physicists like Luzzatti insisted on interpreting data in terms of models involving alternating stacks of rods. This was opposed by Larsson and colleagues who interpreted the data in terms of *bicontinuous* cubic phases (see Figure 1 for an example). The geometries are non Euclidean.

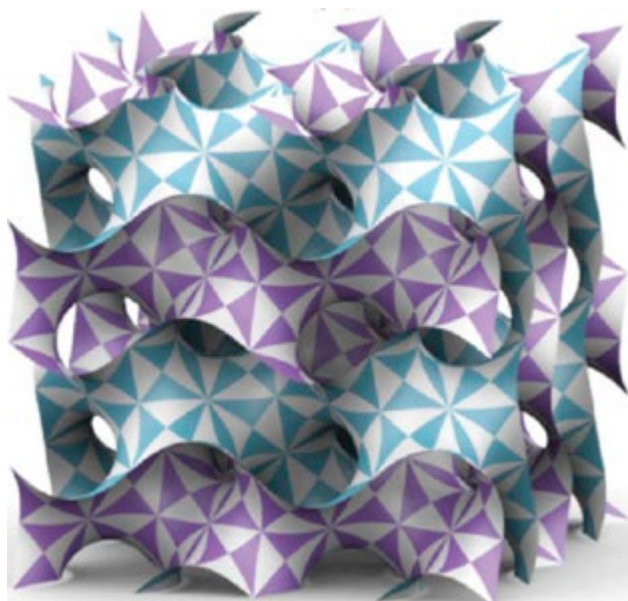


Figure 1. Bicontinuous cubic phases of phospholipids. The average or sum of normal curvatures is everywhere zero, the Gaussian curvatures varies continuously. Reproduced from Ref. 12 with permission of the International Union of Crystallography. <http://journals.iucr.org/>

Invented 200 years ago by Gauss, Lobatchevsky, Bolyai and Riemann, they were first thought to be mathematical anomalies. Not so. The realisation that such geometries are the rule rather than the exception in biological structures was revolutionary.¹⁰⁻¹³

Here then is a classical illustration of Stephen Jay Gould's (1941-2002) maxim: “I have long believed that conceptual locks are far more important barrier to progress in science than factual lacks”.¹⁴

Ironically, Gould's main academic research devoted to the geometry of snail shells, committed the same error. He analysed them in terms of Euclidean geometries when they were in fact non Euclidean shapes.¹⁵

For microemulsions, self assembled soft matter from water or brine, oils and surfactant, the story is much the same. Powerful and expensive scattering data interpreted microstructure in terms of spheres, cylinders and bilayers because that was all the the computer algorithms allowed. Or more often than not, they are random bicontinuous structures as that revealed by cryo-scanning electron microscopy in microemulsion system containing iso-octane, water and DDAB (didodecyl dimethylammonium bromide).¹⁶ A structure – depicted in Figure 2 - that was easily determinable by use of a conductivity meter.¹⁷ Or by taking account of constraints on packing by geometric packing, and volume constraints.¹⁸

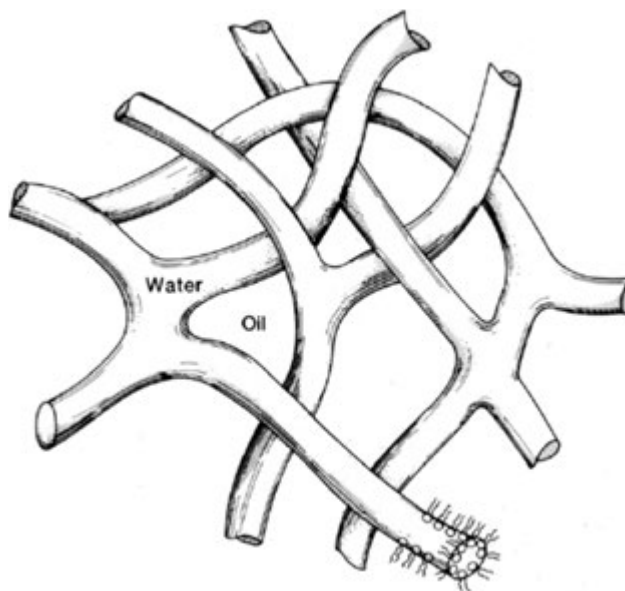


Figure 2. The bicontinuous structure inferred by a conductivity meter 30 years before the cryo-SEM micrographs. The conductivity meter is cheaper than an electron microscope. Such structures were often interpreted as spheres or cylinders from techniques like neutron scattering. Reprinted with permission from Ref. 17. Copyright 1986 American Chemical Society.

4.2 Structure and Simulation

At a Nobel symposium in 1986 devoted principally to simulation in biology the first speaker, a Swiss German working in the pharmaceutical industry began with a slide that said “NMR”. What, said he, does this mean? Not Nuclear Magnetic Resonance. No, quoth this enthusiast. It means: “NO MORE RESEARCH”. He proceeded to explain. With modern computer power and with 30,000 molecular potentials for each possible group – CH₃, –OH, –NH₂ –Cl, etc. (but note, no water molecules) he could simulate the structure of any required drug and enzyme. Game, set and match.

When asked how he would deal with the fact that his model (human) enzyme denatured at 37 degrees centigrade this genius replied. “NO PROBLEMS. WE CHANGE THE PARAMETERS!”

And more, we still can not explain or simulate why ice floats on water.

For more than 40 years this evident insanity has persisted, and does to this day. Much larger programs are bought on NIH grants to “predict” the “structure” of proteins for extravagant amounts of money, by biologists mainly, and cancer research grants. The molecular parameters used have no relation to real molecular interactions, and the key ingredient, water, is missing. When asked if they would please turn off all parameters except that for neon-neon interactions, to test if their program would decide if the ground state energy of solid neon was a face centered or body centered crystal at zero temperature - there is no simpler problem for simulation - they resolutely refuse.

The acceptance by hapless biologist and chemists of such evident charlatism is difficult to comprehend, and arose from frustration and ignorance.

4.3 Structure: The Rise of Computers and Simulation

The story of this deviant science due to misuse of and unquestioning reliance on computers has lessons for the future progression of the Age of Unreason.

One side of this we have already discussed. The easy interpretation of scattering data for structure in self organised soft matter through automated computer programs was clearly a massive and helpful development. But the programs depended on the assignment of structure via Euclidean geometry, restricted to spheres, cylinders and planes. Fitting of data was always possible by allowing an arbitrary parameter that covered “interactions”. The fact that these were impossibly unphysical was ignored.

This can be forgiven. No one was aware that the real geometries of nature were non Euclidean, an example of

Stephen J. Gould’s *conceptual locks* as a barrier to progress in science.¹⁴

This was not a fault of the physical sciences. It was a consequence of ignorance on the art of the life scientists and of chemists.

The more serious issue is how such massive assignment of resources could be devoted to mindless simulation of matter.¹⁹ By simulation we mean for example taking a collection of spherical atoms like argon that interact via hard core repulsion and a two body van der Waals interaction. Program a collection of these in a theoretical box and let them go buzzing around like a bunch of bees until they reach a state of equilibrium. Do this all at different “temperatures” and so construct the whole phase diagram for argon and its thermodynamic properties. The ultimate aim is described by practitioners as the “vision thing”. This is a state of nirvana where all proteins, all states of assembly, micelles, vesicles, membranes can be simulated by big enough computers, and as the German said: NMR.

4.4 Life from Outer Space

In his elegant account on the debate between Galileo and Lodovico Delle Colombe on the question of why ice floats on water, remarked that “Galileo, I will argue, had a scientific style marked by overconfidence. He tended to downplay the importance of obvious contradictory evidence that undermined his claims, and he did this by producing auxiliary hypotheses that sometimes verged on the extravagant. If we focus on this somewhat neglected aspect of his style, some interesting new questions emerge: To what extent did Galileo depend on such auxiliary hypotheses?”²⁰

Very much so it turns out, and so for all of us in ways we do well to recognise.

His thesis on reliance on “auxiliary hypotheses” is, in our parlance, tampering with the truth in support of one’s own prejudice.

Here is a true story that is relevant to our thesis: A professor from California came to my research Department on sabbatical leave with a piece of a chondritic meteorite. These are meteorites containing organic material. The particular meteorite was called the Murchison meteorite after a small rural town in the state of Victoria, Australia where it arrived on a farm. The farmer sold it, illegally, to NASA. NASA divided it up amongst scientists interested in such objects. Their question was since the meteorites contain organic material, could it be that the material contained life-forming molecules. Life might then be considered to have arrived on Earth from outer space. Our expertise was in colloid and surface chemistry,

relevant to the investigation. A very beautiful honours student was assigned this as a research project.

She extracted the organic material and tested it out on a Langmuir trough, a simple apparatus used for examining surface active molecules like proteins, polymers and other molecules. Indeed the pressure-area curves showed all the signatures of biological molecules. This caused great excitement, celebrated by the appearance on a world wide science TV show by the student. The American professor went home happy. The success of his next grant application was guaranteed. Alas, after he left the student and her professor finally got hold of a surface infrared spectrometer from another lab and tested these life forming molecules.

They had all the signature of a protein called bovine serum albumin. The conclusion was obvious: either there are cows flying around in space or the Murchison meteorite arrived at the farm on a piece of cow dung. It was clearly genuinely bullshit.

When I told this story to the NASA chief scientist after his invited lecture to a Gordon conference, he laughed and said – “of course”. But the American Congress like this kind of stuff. It was good for funding.

4.5 Berthollet and Water Structure

Claude Louis Berthollet (1748-1822) was a famous French chemist who went down to Egypt with Napoleon's 1795 expedition.^{21,22}

He observed on dried salt beds of the retreating Nile flood lakes shiny deposits of soda lime, sodium carbonate. (This key observation marks the beginning of physical chemistry). How could it be? Everyone knows that with a solution of sodium carbonate and calcium chloride as the water evaporates calcium carbonate, limestone, is precipitated first with the sodium and chloride ions remaining in solution. The missing factor is temperature. With the midday sun above 60° C the water structure is different, and the reverse happens. In many dried up rivers in Egypt natron sodium carbonate essential for the economy in mummy preservation is the dominant precipitate. Whatever water “structure” means it depends on temperature. Water, H₂O, above 80-90° C, is not hydrogen bonded, at all whatever that means. Above such a temperature it behaves exactly like hydrazine, N₂H₄. The thermodynamics are identical for both water and hydrazine except that hydrazine is explosive.

In solutions of calcium carbonate aragonite is the preferred precipitate above 100° C, calcite that at lower temperatures.

Water structure changes not just with temperature, but also with background solutes.

This can be seen in precipitating nanoparticles. With magnesium or calcium hydroxide particles the size can be varied from microns to zero at will by adding sugars or indifferent salts to change the ambient water structure.

The role of atmospheric dissolved gas is another overlooked and ignored factor that determines these matters. It depends on temperature and background solutes. It is generally considered irrelevant because it is so low. This is absolutely not so, as we shall see below.

4.6 Microfossils and Siderite

Recent debates on the age of life forms and astrobiology occurred with the observation of “microfossils” in very ancient rocks. The microfossils are much smaller than the familiar fossils, too small to represent traces of early life. That conclusion received support from the extraordinary observations in crystallography of Juanma Garcia, Stephen T. Hyde and other collaborators on “microfossils”.¹³ They can be made in the lab with simple experiments. Such inorganic structures probably result from precipitation under double diffusion gradients, and mimic precisely real fossils in form. I leave this challenging new old world to the reader to explore.

Relevant to these matters is the work of McCollom on the formation of meteorite hydrocarbons from thermal decomposition of siderite, FeCO₃.²³

Thermal decomposition of siderite had been proposed as a source of magnetite in martian meteorites. Laboratory experiments were conducted to evaluate the possibility that this process might also result in abiotic synthesis of organic compounds. Siderite decomposition in the presence of water vapor at 300° C generated a variety of organic products dominated by alkylated and hydroxylated aromatic compounds. The results suggest that formation of magnetite by thermal decomposition of siderite on the precursor rock of the martian meteorite ALH84001 would have been accompanied by formation of organic compounds and may represent a source of extraterrestrial organic matter in the meteorite and on Mars. The results also suggest that thermal decomposition of siderite during metamorphism could account for some of the reduced carbon observed in metasedimentary rocks from the early Earth.²³

The important point hardly noticed is that the addition of water to the inorganic iron carbonate rock produced a huge range of complex organic products that occur in oil reservoirs. It had been thought that such “life” product molecules in oil reservoirs had to be the consequence of bacterial activity or forests. It had been postulated by T. Gold in 1990's and other model experiments done in 2004 confirmed that such processes can

indeed be the source of semi infinite as yet untapped sources of natural gas and oil.²⁴

The matter is completely open and of extreme interest. It is connected also to the present interest in “climate change”.

4.7 The Business of Water Structure

The several examples above have been chosen to illustrate something we will continue to emphasise. In the absence of solutes or interfaces we think of water and model it as a Greek element in its own right. Hydrogen bonding is a concept widely used. It derives from a calculation of interactions between two water molecules only. It is elusive and even as an effective quantity a la Pople changes with temperature. Attempts to model water structure cooperatively, imitating a kind of dynamic zeolite that go back to Bernal seem to capture some of it.²⁵

But dissolved atmospheric gas is missing. And that really matters. The tensile strength of water against cavitation is 200 times larger than for gas free water, a matter of profound economic importance for the shipping industry. Even if we were to make a molecular model of pure water correctly, the reality is this business of gas, temperature and salts and other solutes, and of their interdependence.

And of chirality. Is water chiral?²⁶ And of magnetic and electric fields. And of jellyfish, last studied seriously by Gortner²⁷⁻²⁹ in 1933. Jellyfish exist with as little as 2% nonaqueous material. There are some very long range forces that might explain their existence.³⁰ But nobody knows. And And And ...

So much then for Structure and Form.

Let us see how we are placed with Forces and Function.

5. SURFACE FORCES

We have reviewed the state of surface and molecular forces in a number of recent papers, in particular ref. 31.

The situation is evolving. By and large it has been mired in dogma and catastrophic. The entire foundations of the 150 year old venerable field of physical chemistry are flawed. The edifice built on those foundations, has necessarily been built on sand and continually patched up and papered over with more and more effective parameters. The intuition drawn from the theories was wrong and all predictability was lost. Where theory failed, reconciliation was sought by invoking undefined and unquantified words like hydration, hydrophobic, hydrophilic, hydrogen bonds. After a long time, there is

at last a clearer path through the morass. At risk of repetition, but it is so complex that to put our thesis into context, and how to go forward we do so partially and briefly again.

Several missing factors influence real surface forces remarkably. So much that the classical theory is often useless to the real world. Among these factors, we count dissolved atmospheric gas or other sparsely soluble solutes, bubble–bubble interactions. Moreover, inhomogeneity in temperature between bubbles and solvent can be exploited to catalyse endothermic reactions at low temperatures.

Further, the additivity of electrostatic and dispersion forces assumed in the classical theory of forces is wrong. It also ignores ion specificity (Hofmeister effects) due to dispersion forces acting on ions.

We will explain below the complications that we are missing from classical theories of surface forces. Some are explained, most not. Once revealed however, fortunately these phenomena can be exploited for a range of novel technologies as we shall see.

5.1 The Classical Picture of Molecular and Surface Forces: Limitations and Insights

The van der Waals interaction potential between two atoms behaves as $V(r) \sim 1/r^6$, where r is the distance between the centre of the atoms. This was known to Newton. The potential of interaction between two planar surfaces at separation L follows by pairwise addition. It varies as $1/L^2$. Newton tried to quantify this force, but gave up, with the comment (Art. 31 of the Principia): *surface combinations were owing*.

Unlike gravity, surface forces vanish rapidly over very short distances and depend critically on the material properties. And, as for contamination, it will always be with us.

For the opposing electrical double layer forces between two charged surfaces in a continuum electrolyte, the repulsive forces decrease exponentially with distance; asymptotically, $V(L) \sim \exp(-\kappa L)$ where κ^{-1} is the electrolyte Debye length. The pre-factor depends on assumed boundary conditions, constant potential or constant charge. These conditions were relaxed with the extension to allow charge regulation.³² This was a great conceptual advance. The degree of ionisation of surface charges – and therefore surface forces – recognises, and changes in its response to the proximity of, and signalling from, another body.

These few short lines underlie the DLVO (Deryaguin, Landau, Verwey, Overbeek) theory of colloidal particle interactions. The theory has been a core belief to physi-

cal chemists for 50 years. It still is so in spite the fact the theory has severe limitations, already acknowledged by both Deryaguin and Overbeek. These have to do with the assumption that a liquid between interacting bodies keeps its bulk properties up to a molecular distance from an idealised surface. Further, apart from the contamination problem, most surfaces are not molecularly smooth or chemically homogeneous and pure. In addition solvent molecules may interact directly with the surface, for example through hydrophilic or hydrophobic effects in the case of water. Specific ion effects are also ignored. And more, the theory has other amplified problems when the background electrolyte concentration increases, where only very short range surface forces emerge and these other factors can dominate. Especially in the real world.

The DLVO ansatz supposes that van der Waals and electrostatic forces are additive. Sadly they are not.^{33,34} Note that this key ansatz is wrong even for a continuum solvent approximation, and wrong for free energies of transfer (Born energies), interfacial tension, activities of electrolytes and particle interactions. It is deficient in two crucial respects even within the constraints of its own assumptions. The additivity of forces ansatz is wrong. Which implies that the theory can not handle specific ion effects crucial in biology. It is wrong for any problem involving interpretation of experiments on electrolytes at interfaces, zeta potentials, electrochemistry, pH, buffers, ion binding to proteins or lipids, conduction of the nervous impulse and ion transport. The statement is heretical but remains true. Even the IUPAC Committee on pH warns us about the problems of pH and its meaning. And as for buffers, every biologist knows one does not mess with any protocol that accidentally works!

5.2 First Steps Beyond DLVO Theory: Complexities with Double Layer and Oscillatory Forces

A not insignificant aside is that the standard equation to calculate the Debye length for symmetric electrolytes is not valid for asymmetric electrolytes. It has a much more complex form. Direct force measurements for 12:1, 8:1 electrolytes (cytochrome C) and insulin 5:1 and 3:1 give precise agreement with theory.^{35,36}

At small distances, i.e. several molecular sizes, the electrostatic forces are dominated by oscillations. These are sometimes called depletion forces. They act to stabilise emulsions and other systems where e.g. proteins or micelles form part of a fluid that separates two interacting objects.³⁷

This “molecular granularity” emerges in all liquids, from van der Waals hard core fluids³⁸⁻⁴⁰ to micellar suspensions.³⁷ The oscillations decay with separation and merge into the continuum theories after about 6 oscillations.

5.3 Hydration: Surface Induced Liquid Structure

The assumption that a liquid adjoining a surface has its own bulk properties up to contact (at molecular distance) breaks down for reasons other than molecular granularity. The profiles of surface induced liquid order can overlap and originate either repulsive or attractive “hydration” forces. (The terms surface dipole or hydrogen bond ordering are often used and cause much damage. The effects are cooperative not individual molecular properties)

These forces dominate at small separation. For surfaces that are rough at the molecular level, e.g. phospholipid head groups in a bilayer, the oscillations are smoothed out and decay with an exponential form with a range of about a molecular diameter (0.3 nm). They dictate van der Waals interactions up to say 3 nm separations. Correlated fluctuations in the surface dipoles of the head groups can produce other forces. They can appear in force measurements as a hidden contribution that changes effective hydration decay lengths. Thus, for example in the smaller ethanolamine polar head group such contribution is larger than in the bulkier phosphatidylcholine residue. The apparent hydration range is smaller for the former.⁴¹

Maxwell was the first to calculate correctly hydration forces,⁴² followed by Marcelja 100 years later.^{43,44}

5.4 Complexity in van der Waals Forces. Lifshitz Theory: Emerging Concepts of Recognition

Lebedev, the discoverer of light radiation pressure, renovated D'Arcy Thompson's criticism and wrote:⁴⁵

... of special interest and difficulty is the process which takes place in a physical body when many molecules interact simultaneously, the oscillations of the latter being interdependent owing to their proximity. If the solution of this problem ever becomes possible we shall be able to calculate in advance the values of the intermolecular forces due to molecular inter-radiation, deduce the laws of their temperature dependence, solve the fundamental problem of molecular physics whether all the so-called 'molecular forces' are confined to the already known mechanical interaction of light radiation, to electromagnetic forces, or whether forces of hitherto unknown origin are involved.

Lifshitz with theory in 1955, and Abrikosova and Deryaguin with experiments in 1956, confirmed Lebedev's vision on molecular forces. The work was continued also by Dzyaloshinski and Pitaevski who developed – with Lifshitz – a theory of interactions between two planar dielectric surfaces separated by a liquid. Again,

the hydration was neglected, as the liquid in contact with the two surfaces was assumed to retain its bulk properties.⁴⁵⁻⁴⁷

Under these premises, the theory was developed in the framework quantum field theory and was expected to provide the full solution of the problem. It comprised the temperature dependence of the intermolecular interactions, all many body interactions, and contributions from the entire electromagnetic spectrum. The major step was the acknowledgment that the measured dielectric susceptibilities of interacting bodies – that depend on the frequency – include implicitly all many body interactions.^{46,47}

This topic is still an active field of basic research. However, the theory was difficult to test, until the work of Ninham and Parsegian on lipid-water systems.^{48,49} The theory was then extended to include different shapes, layered, conducting and magnetic bodies, and electrolytes.⁵⁰

Again, the crucial point for us here is the fact that the potential is given by all the contributions that derive from the electromagnetic spectrum. Some of these terms are positive, some repulsive, depending on the specific interacting materials, i.e. depending on their dielectric properties. For a planar geometry, the frequency term $F(\omega)$ decreases exponentially as:

$$F(\omega, L) \sim -\frac{A(\omega)}{L^2} \exp\left[-\frac{2\omega L}{c\epsilon(i\omega)}\right] \quad (1)$$

where ω , L , c , and $\epsilon(i\omega)$ are the frequency, the distance between the two bodies, the velocity of light and the imaginary dielectric susceptibility of the medium at frequency ω , respectively. For simplicity I omit the expression of the pre-factor.

The most important result of this model is that two bodies feel and recognise temperature dependent zero frequencies first. As they come closer and closer, then frequencies contribute in order of increasing energy: first the lower energy infrared components (with wavelengths λ between 2 and 5 micron), followed by optical ($\lambda \sim 400$ nm), far ultraviolet ($\lambda \sim 100$ nm), until the two objects come into atomic contact or hydration. This is precisely where chemistry takes over.

Alternatively, two objects sense each other's "specific vibrations", and respond appropriately. In some cases this specific interaction is very strong and extended in space. It is interesting to calculate the interaction potential for two thin parallel rods of a conducting material at a distance L , which is the case of DNA strands:

$$V(L) \sim 1/L \quad \text{for } r \ll \kappa^{-1} \quad (2)$$

$$V(L) \sim \left[L \cdot \ln\left(\frac{L}{r}\right)^2 \right]^{-1} \quad \text{for } r \gg \kappa^{-1} \quad (3)$$

where r is the radius of the rod and κ^{-1} is the Debye length.

The force is strictly non additive and basically infinitely long ranged. Instead, two planar conducting surfaces interact with a short ranged potential.⁵¹

The problem becomes more intricate, as the temperature dependent contributions decrease with another factor that is related to the reciprocal of the Debye length, i.e. as $\exp(-\kappa L)$.

The concept of recognition, that depends on the physico-chemical features of the materials and of the surrounding medium, was captivating. But the claims for generality went too far. In fact at the end the theory turned out to comprise an integration trick. The mystique of quantum field theory (QFT) was exposed and the entire building collapsed to a semi-classical theory: it was shown to be nothing more than Maxwell's equations for the electromagnetic field with boundary conditions plus the Planck hypothesis for quantisation of light.^{31,51}

The equivalence of QFT with a semi-classical theory brought about a deep extension of the theory. But the theory on molecular interactions is constructed at zero temperature, for example the Casimir-Polder and Casimir interactions for "retarded" van der Waals interactions. "Retardation" refers to a reduction in the interactions because of the finite speed of light. The problem is that all this is quite wrong!^{52,53}

In a similar way the discussion of resonance or retarded Forster interactions involving excited state-quantum state interactions - that are the basis for disputed quantum computing procedures - are even more incorrect and with no physical correspondence.⁵⁴ Nonetheless the visions, as in the case of the DLVO theory, endure and cheer the Boetians.

Furthermore, another overlooked development emerges if we try to relate Casimir-Lifshitz forces at finite temperature in a vacuum and particle physics. Weak interactions (mesons) seem to merge naturally and quantitatively.^{55,56}

We have mentioned these matters because however arcane that may appear, it is reassuring that the same errors underlie both physical chemistry and physics.

6. HOFMEISTER PHENOMENA AND THE INADEQUACY OF DLVO THEORY

Hundred and fifty years have passed, since the pioneering work of Franz Hofmeister in Prague at the end

of the 19th century, and physical chemistry is still unable to comprehend and predict specific ion effects. Unless one introduces arbitrary parameters like postulated ion size. As in the Debye-Hückel theory, the size is adjustable and different for every solvent and temperature.⁵⁷ The issue propagates and affects Born energies, interfacial tensions, activities, pH, pK_as, buffers, ion binding, viscosities and all other bulk or interfacial experimental parameters.⁵⁸

Hofmeister investigated the relative effectiveness of different salts in precipitating albumin in water and established the so-called “Hofmeister series”:⁵⁸

anions at fixed cation:

citrate³⁻ > CH₃COO⁻ > SO₄²⁻ > F⁻ > Cl⁻ > Br⁻ > I⁻

cations at fixed anion:

N(CH₃)₄⁺ > NH₄⁺ > Cs⁺ > Rb⁺ > K⁺ > Na⁺ > Li⁺ > Ca²⁺ > Mg²⁺

Such series occur in chemistry, biology, biochemistry, geochemistry, practically everywhere. It is not universal but depends on substrate and probably dissolved gas.⁵⁸ Hofmeister’s original work is translated and re-published in Ref. 59.

Two examples are illustrative of the problem.

6.1 Measuring the pH

If one measures the pH of 1:1 strong sodium electrolytes in buffered solutions with a glass electrode, the “pH” change in a phosphate buffer follows a Hofmeister sequence. But if sodium is replaced by potassium salts the sequence reverses! And using a cacodylate buffer at the same stated pH as phosphate the sequence reverses from the phosphate case also.^{34,60} This and several other common measurements are inexplicable with classical theory, because it does not have room for specific ion effects.

None of the measurements make any sense in classical theory. According to common knowledge and understanding the two buffers must give the same results, and these must not - according to textbook theory - depend on the nature of background electrolyte (Hofmeister effects). Though the measurements are performed in terms of that erroneous theory. If we ask what a pH measurement in the ocean means, it makes sense only if interpreted as Alice in Wonderland says: *When I use a word, Humpty Dumpty said, in rather a scornful tone, it means just what I choose it to mean—neither more nor less.*⁶¹ The same problem emerges in a plethora of different phenomena and measurements, like ion binding to proteins.

6.2 Indirect Forces and the Activity of Enzymes

Another stark example of the failure and inadequacy of theory is any explanation of the energy that drives enzyme action. The cutting by a restriction enzyme of linear DNA^{44,62} is an essential tool of molecular biology. Like the problem of pH, cutting efficiency makes no sense in terms of DNA-enzyme forces predicted by DLVO. The energy required to cut segments on the DNA chain seems to be indirect and subtle. It seems to be given by hydrophobic cavitation that originates free radicals.

Figure 3 shows the efficiency of enzyme (expressed as percentage of linear DNA) as a function of the electrolyte concentrations for a set of sodium salts. Similar results exist for cation sequences.^{44,62a} As for our pH problem the phenomenon is remarkably ion specific. It depends on the buffer used to set the nominal pH value of 7.5. Strikingly, the trend reverses when the phosphate buffer is replaced by cacodylate.⁴⁴ The standard theories of forces cannot explain the experiments. Nor does it provide any hint at the source of the energy to carry out the enzymatic activity. Specific ions, both cations and anions, and buffer anions compete to set hydration and inter-substrate and enzyme water structure that determine association. The enzyme dimerises, diffuses up and down the linear DNA chain to find the right palandromic sequence (Figure 4).^{62b} There follows hydrophobic cavitation, a cooperative harnessing of all the weak van de Waals forces that creates free radicals. These then cut the DNA at precise palandromic sequence. Whether the cavitation phenomenon depends on dissolved gas is unknown. That this mechanism is likely can be seen if a free radical scavenger is added to the mix. It stops the enzyme dead. The gap between physical theories and real molecular biology is evident. But, importantly this example shows there is a way through what seems to be a bewilderingly inexplicable mess.

6.3 More on Hofmeister Effects: Unpleasant Facts and Pleasant Consequences

As I mentioned, specific ion effects emerge dramatically in a myriad of other phenomena, e.g., in the formation of self-assembled micelles, vesicles and microemulsions from surfactants. Interestingly here we observed that forces with different coions and counterions and forces between interfaces can change very remarkably.^{34,58,63,64}

The DLVO theory unsuccessfully tries to explain such variability by importing extra non predictive parameters like ion size. These are often absurd. The ansatz of

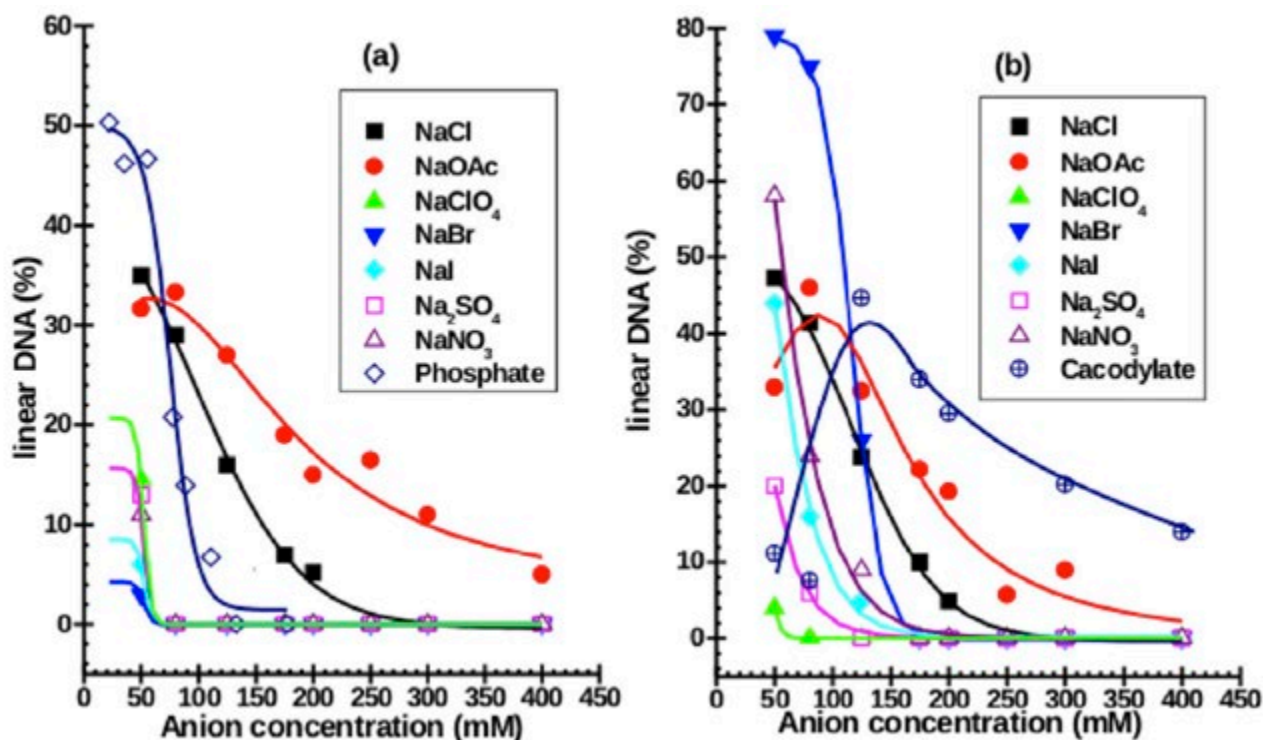


Figure 3. Enzyme cutting efficiency versus the concentration of the electrolyte at pH 7.5, for a set of different 1:1 sodium salts. The buffer used was phosphate (a) or cacodylate (b). Reprinted from Ref. 44, Copyright 2016, with permission from Elsevier.

DLVO theory that supports the entire fabric of the discipline is flawed. In fact physics does not allow to add electrostatic forces, treated in non-linear theory, to van der Waals forces treated in a linear theory. The problem is not simply a matter of approximation, the entire theory has to be rewritten. The bad consequences are that most measurements like pH and ion binding - that are based on the classical theory - are of unsure meaning. On one hand this is unpleasant and disappointing and is therefore almost universally ignored. On the other hand, a great effect is that the few who do not try to hide or

neglect the problems are in a good position to use forces due to specific ion effects. Deryaguin and Overbeek both were well aware of the limitations of their theory of interactions of colloids, of specific ion effects and that it failed above a concentration of 50 mM.

The best advice of the IUPAC Committee on pH is to avoid electrolyte concentrations above at most 100 mM. And anything more complicated: Forget it. For a detailed account of the present state of affairs and opinion on Hofmeister effects see a recent Current Opinion in Colloid & Interface Science special issue⁶³ and a recent paper of Leontidis.⁶⁴ The physical chemistry of electrolytes, and electrochemistry, got stuck in a frustrating swamp, a parameter-rich hiatus for a century.

More recently the recognition that we lack the quantification and inclusion by *ab initio* quantum mechanics of ion size, hydration and dispersion forces was understood and at least partially accepted. Some promising advances on Born self energies, interfacial tensions, ion activities and the vexed problem of the air-water interface potential. Average ionic activities of twenty one monovalent electrolytes can be actually predicted with just three universal parameters. Whether these advances can be extended to asymmetric, and mixed electrolytes and include temperature is still an open question.⁶⁵⁻⁶⁹

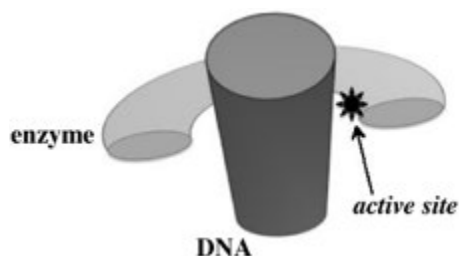


Figure 4. Cartoon of the problem of restriction enzymes. The enzyme cuts a DNA strand at a specific sequence of nucleotides. The star represents the enzyme active site. Adapted from Ref. 62b with permission of Springer.

7. HYDROPHOBIC FORCES AND DISSOLVED GAS

However, the challenge generated by the flaws in the foundations of the theory and the disregard of Hofmeister effects is a minor concern.⁴⁴

Long ranged hydrophobic forces between interfaces have been measured and reported in several papers. But the mystery that surrounds this kind of forces remains: when the dissolved atmospheric gas is removed from the sample these forces disappear. Although tricky, this fact offers a possible hint to clarify the mechanism: Surface-induced water structure can extend only a six molecular diameters or so. The perturbation lowers the density of a thin film compared with bulk water. This causes a density lowering in the gap between the interfaces and generates the force due to the difference between the pressure inside the gap and outside. The range should be about 3 nm, i.e. 6 water molecules. Dissolved gas molecules play the same role that defects do in a solid. They disturb the tensile strength of a thin film of water between the two surfaces. The fluctuations or defects that result in the lowering of the liquid film density are carried from the surfaces from one gas molecule to another and percolate across the gap. Ions can either oppose or promote these complex fluctuations in the interfacial liquid density.

Further discussion on the mechanisms of hydrophobic forces can be found in the literature.⁷⁰⁻⁷³ Yaminski pioneered studies on hydrophobic forces along with — and independently of Pashley and Kitchener. He actually had read and understood Gibbs' work, famous for its obscurity.

“Hydrophobic” forces exist, extend across long distances and depend on interacting surfaces and dissolved gas, no matter which microscopic mechanisms control them. Unfortunately they cannot be easily simulated. They are not explained or predicted by classical theory, but must be part in any picture of self-assembly and interactions in biologically relevant systems.

An outstanding, surprising and graphic demonstration of surface forces arises when a mixture of a hydrocarbon and water is almost completely de-gassed.⁷⁴ Some years ago it was reported that cavitation occurs when two hydrophobic surfaces immersed in water were pulled apart. This means that the removal of dissolved gases may facilitate ‘oil mixing with water’ because dissolved gases promote cavitation. This idea has now been well established. The degassed oil-water dispersion remains stable for several hours, whereas a regular mixture (with dissolved gas in) phase separates very rapidly.

If dissolved gases significantly affect hydrophobic interactions then direct surface force measurements should be able to detect and quantify such effects. These

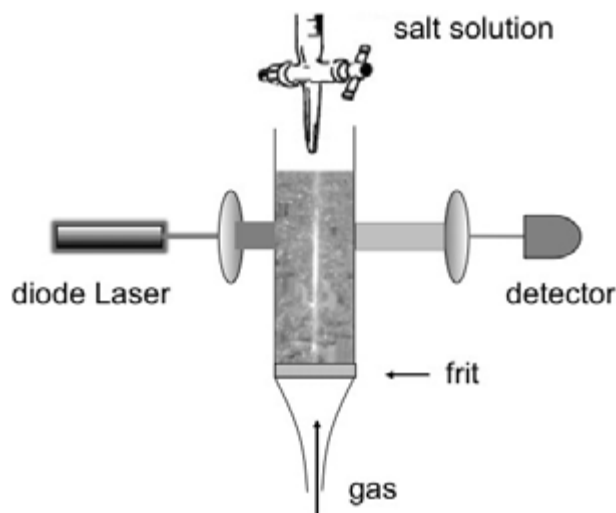


Figure 5. Scheme of the apparatus for producing bubbles and measuring their optical density. The gas is admitted from the bottom, passes through the frit and bubbles through the liquid contained in the chromatographic column. From the top more solvent or a salt solution can be added. Courtesy of Vincent S. J. Craig.

have been reported, although the topic is fraught with contradictory results. In the future it will be interesting to check the effect of dissolved gases on coalescing a single oil droplet, an experiment that has not yet been performed.

Dissolved gas and other poorly soluble solutes must propagate the attractive force between two hydrophobic surfaces to a much longer distance than should be predicted from merely a solvent molecular ordering perturbation, which in water can extend a few nanometers. By comparison, hydrophobic attractions have been reported out to about 90 nm.

The gas problem poses more than just a dilemma.

The solubility of a gas in water depends also on salt nature and concentration. So far this evidence has been simply ignored. As Descartes might have said “I breathe, therefore I am”. Fish philosophers would have a similar view. And they are certainly correct.

8. BUBBLE-BUBBLE INTERACTIONS: A CASE OF NON HOFMEISTER ION SPECIFICITY

An even more perplexing problem is the phenomenon of bubble-bubble coalescence in electrolytes. It is hard to think of a simpler and relaxing experiment – contemplate the ocean. In fresh water bubbles coalesce (look at a water fall). Instead the ocean is foamy, and this is not a consequence of pollution or of the presence of organic matter. The effects of salts on inhibiting bubble-

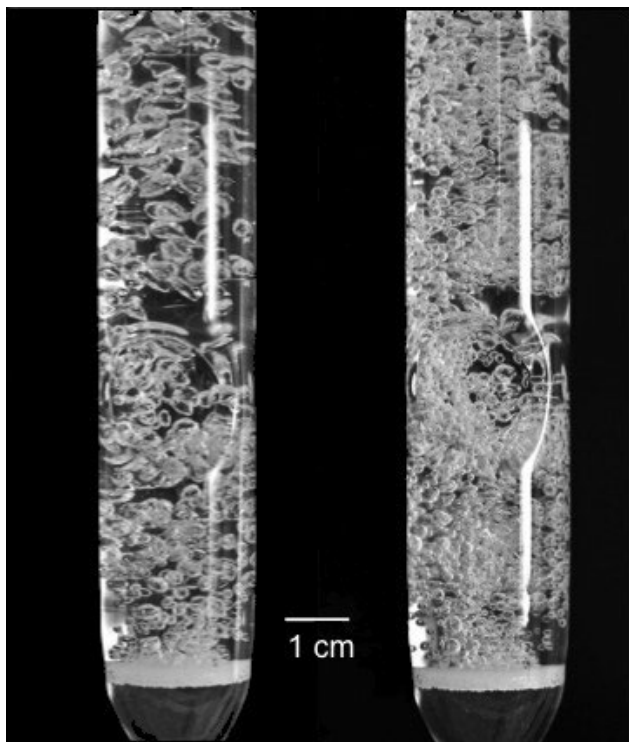


Figure 6. The gas bubbles diffuse through water (left) and through a 0.3 M NaCl solution. In the salt solution the bubbles coalescence is remarkably reduced. Courtesy of Vincent S. J. Craig.

bubble coalescence has been well studied for more than 30 years.⁷⁵⁻⁷⁹ But there is still no explanation at all. The background (and more references) is described in Ref. 44. This is the experiment: air or another gas are passed through a frit to a column filled with salt solutions. Figure 5 illustrates the very simple apparatus. The bubbles collide as they rise in the column and fuse. The column remains clear. As the salt concentration increases, in a sharply defined range the bubbles no longer fuse and the column becomes opaque. It is filled with a mass of fine bubbles. The effect is the same for a whole range of all salts (see Figure 6) and scales with the Debye length of the electrolyte 1:1, 2:1, 1:2, 3:1, etc. The phenomenon occurs for one class of ion pairs. For another class no effect occurs the bubbles continue to fuse at all concentrations!

This is inexplicable within the framework of a classical physical chemistry theory of forces between bubbles (DLVO). In fact DLVO predicts a bubble coalescence enhancement with added salt because (i) it should screen out any electrical double layer repulsion between negatively charged bubbles and (ii) should increase the surface tension — favouring bubble coalescence. The situation is further, and greatly complicated, by the fact that some

salts inhibit coalescence and some do not. And similar effects occur in polar non-aqueous organic solvents too, like methanol, propylene carbonate, formamide and dimethylsulfoxide.

“Explanations” of Hofmeister effects re-appear every decade, but they are specious and wrong.⁴⁴ They reflect the religious fervour in which the DLVO theory is clung to. These results are as profound as they are simple and inexplicable. Temperature, gas type, adsorbed ion hydration and film viscosity and other candidates have all been ruled out of contention and appear not to influence the observations and their ion pair dependence.

The same kind of specific bubble-bubble interaction inhibition occurs for different isomers of sugars or mixtures of sugars.

A related puzzle is that of the *sign* of the air-water interface. Is H_3O^+ or OH^- the more favoured species? Bubbles are negatively charged. It is a simple question. See Ref. 44 for the latest state of play.

8.1. Contingency in Evolution

An interesting speculation is suggested by the bubble bubble salt inhibition phenomenon. In the Ediacaran extinction, 570 million years BP, multicelled animals all died. In the Burgess Shales extinctions, 530 million years BP there were considered to be at least 24 highly successful phyla. That figure may have been reduced by now due to better classification. But only 4 phyla surface to become us. Only 4 survived including us. In the Permian extinction, 230 million years BP 95% of all species disappeared.

These extinctions coincide with known CO_2 cycles and consequent ice ages. There followed precipitation and removal of salt from isolated oceanic regions.

After the ice ages and melting of the ice, there would follow a reduction of salinity below 0.175 M, as for example in the Baltic ocean. The present ocean is about 0.4 M, while all animals including us have Permian ocean salt concentration 0.175 M.

Massive extinction of phytoplankton would follow the end of the ice age. It is possible the extinctions occurred as every species would have died of the bends, due to bubble-bubble fusion!

9. WISHING REASON OF THE OCEAN

Jan Morris in the third of her exquisite volumes on the British empire, *Farewell the Trumpets* began with the fin de siècle celebration of Queen Victoria’s Diamond Jubilee of 1897. She said:⁸⁰

If to the Queen herself all the myriad peoples of the Empire really did seem one, to the outsider their unity seemed less than apparent. Part of the purpose of the Jubilee jamboree was to give the empire a new sense of cohesion. But it was like wishing reason upon the ocean, so enormous was the span of that association, and so unimaginable its contrasts and contradictions.

Physical Chemistry is a bit like that. Like the Empire it made a muddled progress during the same period. And like the Empire it was like wishing reason upon the ocean. Literally!

As Morris said of the Empire that had reached its nadir. Suddenly it was time to go, like the whisking away of an opera set on a revolving stage. And maybe too for our venerable discipline of Physical Chemistry. It ought to be supporting the rambunctious new tribes of the biologists still confident in the first flush of success in a new science, but is not. In our essay, we have seen that what we considered dependable, and the ritual experiments we practiced and their paraphernalia to give us reassurance were false gods.

Think of non Euclidean and random bicontinuous geometries that are taking center stage, of erroneous force laws, of Hofmeister specific effects, of the astonishing pervasive role of dissolved gas and hydrophobic interactions, and of the equally astonishing phenomenon of bubble-bubble interactions. So, is nothing sacred? Probably not. At least now though we can recognise the value of Stephen J. Gould's aphorism on conceptual locks¹⁴ and practice the first steps towards a Damascene insight and conversion. There are difficulties that can be identified. A major one is that the biologists have been seduced into paying lip service to false gods which are now deeply imbedded into their dogmas. Perhaps that can be overcome as the rewards for service have been few.

We began with Morris Kline. In his peroration on the plight of mathematics he said:¹

It behooves us therefore to learn why, despite its uncertain foundations and despite the conflicting theories of mathematics, mathematics has proved to be so incredibly successful.

For the physical sciences in biology and medicine the question is reversed. Why is it that we have been so incredibly unsuccessful? The reasons seem clear enough.

Time to rebuild the temple. Heresy, but necessary.

From that vantage point we return to John W. Draper and his enthusiastic boundless confidence in the Age of Reason.² It parallels the confidence of the Mathematicians at the World Congress in Paris in 1900. Hilbert the acknowledged best of the brightest announced 21 propositions that remained to be proved before the edifice of

mathematics was consistent. The edifice fell to the ground almost immediately after.

Is Draper's confidence justified? Not in the Age of Reason which led us via Kantian certainty to a sterile cul de sac. When the physicists have a theory that allows neutrinos en masse to penetrate 100 light years of solid lead before a few are detected, reason has to go.

10. THE OCEAN FIGHTS BACK

Curiously, we can hope that Draper's confidence will be justified in the new age of unreason. And here is why.

We have identified substantial deficiencies in theory, and in consequence, in measurements that depend on those theories. Suppose those difficulties are resolved — the matter is more complex still. Dissolved gas, cavitation and bubbles, specific ion effects, and temperature, are all components of the ancient Greek view of the elements: earth, air, water and fire. We have been missing air and fire and light, which we have hardly touched on.

We have described some of the astonishing phenomena that attend admitting gas as one of our elements. We have no theory. If we now do include temperature by allowing hot bubbles through a sinter to our electrolyte bubble column marvellous things happen that we never dreamed of. Some are described in Refs. 44 and 81.

Technologies have emerged that allow high temperature aqueous solution reactions to be done at low temperature. The hot bubble surfaces are amazingly reactive. Desalination can be done without membranes very much more cheaply than the best conventional methods. Viruses and drug molecules are killed so that the use of recycled water becomes possible. Removal of heavy metals like arsenic, lead and mercury becomes easy. Carbon dioxide gas bubbles are extraordinarily reactive even at room temperature. And more that experiment reveals, that we can use, and we have not the faintest idea of why they work. These new breakthroughs are pioneered by R.M. Pashley. Watch this space.

Finally in homage to Morris Kline we repeat his translation of some aphorisms of Xenophanes (6th century BC) that seem to be apposite:

The Gods have not revealed all things from the beginning. But men seek and so find out better in time. Let us suppose these things are like the truth. But surely no man knows or will ever know the truth about the gods and all I speak of. For even if he happens to tell the perfect truth, he does not know it, but appearance is fashioned over everything.

There are rapid strides being made to improve and remedy present theories. And what is encouraging is that

when the chemistry is done correctly, when the conceptual locks are removed, more often than not the emerging theories do actually work, predictively.

ACKNOWLEDGMENTS

I have worked on the topics of this paper since 1968 when I began an exciting collaboration with V. Adrian Parsegian. Since then I have had the luxury and privilege of working with very many colleagues and students. I am indebted to them all.

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19. This is how it came about. The late 1950's saw the apogee of attempts to derive quantum statistical mechanical theories of liquids, plasmas, electrons in metals, and nuclear matter, or in ab initio quantum mechanics.
For liquid matter and random media there was and still is no theory in the sense that there is for solids and gases. For solids, an underlying framework on which to build a perturbation theory exists in periodic lattices. For gases it is a completely random distribution function, diagrammatic expansions of partition functions generalised similar expansions in quantum electrodynamics, their resummation was associated with names of Joe Mayer — who predated QED, Montroll and Ward, Bloch and De Dominics. It all became too hard.
Partial resummation gave approximate integral equations that could be solved with certain assumptions connecting direct and indirect distribution functions. These took on names like Hartree-Fock, exchange, hypernetted chain with added bridge diagrams became de rigueur approximations. Random matrices were another trick. The mess was ripe for computers. Monte Carlo and direct simulation of atoms and their interaction became appealing.
Thus a pioneer, John Barker an Australian theoretician working in liquids became frustrated with analytic approaches. He went to IBM in California to access computer power. With colleagues Henderson and Watts they published a landmark paper that computed by simulation the entire phase diagram of argon. When the author pointed out to Watts the fact that their van der Waals interaction was wrong by factor of two, he said, as usual, "no problem we can change the parameters!". This achievement laid the foundations for an entire new industry, computer simulation and the "Vision Thing" in biological simulation. (Overlooked was the fact that even for this simplest possible case, argon, the ground state structure (FCC) and the interfacial tension of the liquid can not be predicted without inclusion of three body forces. These are impossible to include. It is evident that simulation of a liquid like water then is not possible).
IBM seized the opportunity and went on the front foot selling main frame computers and simulation as the way ahead for biology. In this enterprise they were very successful (Clementi - pioneer of Monte Carlo simulation and Heller were two of the scien-

tists who did such marketing very well, citing Barker, Henderson and Watts). The belief of such adepts is unquestioned. The author and V.A. Parsegian were approached at NIH in 1969 to set an example and support the purchase of such a computer, while working in the Division of Computer Research and Technology. Having seen the wreck of Nixon's data driven war on cancer we did not support such silliness).

It was about that time and for ten years later major companies like IBM and Bell Labs moved from an enlightened policy of allowing their scientists to do untrammelled research – the author finished his Ph.D thesis working on white dwarf stars! — to directed market direct profit oriented research.

The same catastrophe took over in models of evolution, economics and other areas.

Here endeth the lesson.

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