

Introduction to Co Bodies

One way to look at co-bodies is that they improve accuracy and dependability of choice by using several different pieces of evidence at the same time instead of only one. Obvious really; we all do it every day; but when it comes down to selecting something on the basis of chemical properties everybody suddenly finds the subject difficult, so this paper goes over things repeatedly from different points of view.

It explains what co-bodies are and what they can do, which is using two or more binding reactions together to identify another molecule, and by way of emphasis gives parallel non-chemical examples, including the remarkable analogy between molecular interactions and ancient Yin-Yang philosophy. The level of scientific knowledge required is quite small.

An earlier paper, "[Semi-synthetic antibody molecules having enhanced affinity and selectivity](#)", was written in 2003 and describes the essential invention in a straightforward way useful to biochemically-aware readers. The theory of selectivity had not been fully developed at that time, nor the theory of the singularity of cancers, so this paper helps to show how the thinking advanced.

Other accounts of various aspects and from varied viewpoints have been published since and will be found at <http://www.trcboyde.net/publications-co-selection-co-bodies-co-affinity.html>. Readers may choose for themselves! Co-bodies bring together themes from many different subjects, which is why it is rather difficult to explain the concepts and why it is worthwhile using several alternative ways of doing so.

Antibodies and the ABO Blood Groups.

Being biochemists, we started off thinking about antibodies.

Natural antibodies select one feature of the target, for example, anti-A binds to the 'A' structure on a Group AB red blood cell, but no other feature on the same target, neither the 'B' and 'O' structures which are also present on this kind of cell.

(Yes, substance O exists. Blood Group O is not merely the absence of A and B, though we don't normally need to test for substance O.)

To identify someone as Group AB you have to conduct two separate reactions with anti-A and anti-B; and you would need to be wide awake to distinguish pure AB cells from an artificial mixture of A and B cells. The antibodies won't do it for you and it isn't a problem in everyday laboratory testing because such a mixture doesn't happen naturally.

In co-body technology different types of antibody (to be exact the binding fragments of each) are linked together so that they can react at the same time with different features of the same target. Anti-A linked with anti-B would give a new molecule, anti-AB, with the new kind of power that it can select for both A and B at once; one experiment not two. More than two antibodies may be combined, such as anti-A + anti-B + anti-O, giving anti-ABO.

Anti-AB and anti-ABO do not exist in nature, and such artificial antibodies would not be used in blood grouping work because it is so easy to determine blood groups the old-fashioned way. But what about ABO groups in organ transplantation? Is it always so easy?

Sheep and goats, mushrooms and toadstools. A broader perspective.

That was an artificial example just to show one kind of thing that might require the use of co-bodies. Let's explore combined selectivity in completely different circumstances.

The job of telling sheep and goats apart may not always be as easy as it sounds (some Middle-Eastern kinds look very much alike to us), but the animals and the herdsmen have no difficulty and they are distinct species which do not interbreed. So it must be possible provided you spread the net wide enough and include all the features that might be useful; shape of head and horns, feel of fleece, smell, behaviour, etc.

Multiple characteristics are needed to make the distinction. Information from different sources must be combined to make the selection reliable, and for mushrooms versus toadstools that is really important.

With any of these examples, we might speak of 'co-selection' or 'conselectivity'. But only the anti-AB/anti-ABO example has the special feature that the selection is the work of a molecule, a single molecule with a selective property all by itself, requiring no helping hand, produced by combining two molecules together. For such things we suggest the new word, co-body, defined next:

Co-body definition. Co-body properties.

“Co-body means a molecule in which two or more distinct and different binding sites complementary to distinct and different epitopes on one and the same target, are linked together in such a way that all can bind at the same time.”

Examples from Nature are known and probably many more will be found. An important point for practical purposes (not essential to the principle of conselectivity in the broadest sense) is that we expect increased affinity compared with the individual binding sites. This increase has been measured.

Expected also are a more refined selectivity, because the co-body uses additional criteria of selection (all the reacting epitopes instead of only one) and an new element of specificity, directed towards the totality of reacting epitopes, which may be viewed as an entity in its own right; a property distinct from the sum of parts.

We should add that an increase in affinity is also expected if the interlinked binding sites are identical to each other (and of course the corresponding epitopes must be identical among themselves. Here too there is altered specificity; to the polyvalent target more than to the monovalent epitope.

There is no reason to be confined to antibodies as the source of binding sites. Almost anything will do, including other proteins, and nucleic acids.

Yin and Yang. Two hands are better than one.

Chinese thinkers of 5,000 years ago came up with the philosophy of Yin and Yang, the matching and balancing of opposites, so that each implies the existence of the other: that is, complementarity; just look at the YinYang symbol. Their purpose was mystical, the search for balance and harmony in the universe, yet the similarity to our modern ideas on how molecules interact is startling.

Association between molecules depends on the exact matching of opposites. DNA strands bind to each other; bases A and T, G and C. Antibody binds to virus or an enzyme to its substrate. Geometrically the fit is excellent, but more than that there is matching of bond-forming capability whether that is hydrogen bonds (which require exact angles and

distances), ionic bonding (less precise but there must be opposite charges), hydrophobic bonds, or the intervention of exactly-placed water molecules. There is detailed complementarity, of overall shape and atomic orbitals.

Recognition of the correct partner molecule depends upon the nature and number of the bonds that can be formed; and in turn that means good matching geometrically, plenty of bond-forming groups - and therefore the total area of contact becomes important. Co-bodies achieve superior affinity by doubling or trebling area of contact, and their novel specificity by additional matches of shapes and bonding.

Two hands are better than one, something Nature knows so well that she has provided her antibodies with two or more binding sites; to act more effectively against things like bacteria or viruses, which have thousands of identical target epitopes on the outer surface.

That is, a natural antibody has two hands, or more, but it is as if they are all right hands or all left since all react with the same YinYang complement. For many purposes, it is better to have both a right and a left hand on the same antibody, to improve the nature and strength of its selectivity. Co-bodies do just that, but without limit on numbers. Two hands are better than one, right and left is better than two of the same kind and three hands is better still.

Applications of immediate commercial value.

These are only from fields closely related to biochemistry, ignoring the whole of industry and most of Medicine. To understand the potential, note first that the specificity and affinity of natural antibodies are not specially impressive, being far exceeded by some other proteins, so that if we can introduce greater affinity, enhanced selectivity, and an entirely new but suitable specificity, our product may have competitive advantage.

Rapid diagnosis of bacterial, fungal and parasite infection.

Rapid, antibody-based techniques exist for many of them. The question is, how good? For a few, the existing method cannot be improved upon (e.g. *Rotavirus*). For others, the tests are hopelessly bad and doctors don't bother because the results are not reliable (e.g. *Clostridium difficile*, *Campylobacter*, *Norovirus*). In such diseases, older, much slower methods must be used, leading to delay in diagnosis and bringing an outbreak under control.

It is pure chance whether a suitable antibody can be derived, a whim of Nature. Co-bodies remove the element of chance.

Cancer diagnosis and treatment.

Importance arises from the nature of the cancer cell, which has surface features differing only slightly from normal, so that the known chemotherapeutics and antibodies cannot select cancer cells well enough to destroy them without damage to their neighbours. Furthermore, cancer cells are unique to each patient, no two cancers are the same, and they change over time as the disease progresses. Only co-bodies can be made with sufficient discriminatory power, and existing technology allows for rapidly creating new ones to match clinical need.

What next?

We think the case is made for immediate application and whatever investment is needed to bring that about.