probabilities (by implication) to depend on patient age or cancer stage, when properly age and stage are part of the feature vector **f** and should have their effect by adding to the dimensionality of $p(\mathbf{f}|C_{RY})$ and $p(\mathbf{f}|C_{LY})$, respectively?

Many of the studies cited by Crile (*1*) and Anglem (*2*) involve different parts of the feature vector **f**. Thus, one study might provide training samples for one part of $p(\mathbf{f} \mid C)$ while another study might provide training samples for another part of $p(\mathbf{f} \mid C)$.

To conclude, any national effort to evaluate future breast cancer data or to reevaluate past breast cancer data should follow guidelines established by a recognized group of experts from the surgical community and the pattern recognition–statistician community. This group of experts should (i) determine a set of features to be included in **f** and the values which these features can have; (ii) agree on various a priori structures to be used in obtaining the estimated probability distributions $p(\mathbf{f} \mid C_{RY})$ and $p(\mathbf{f} \mid C_{LY})$, and agree on a priori relationships among the features in **f**; (iii) establish a computer data bank for patient samples and guidelines for this data to be accessed; and (iv) agree on values for $p(C_{RY})$ and $p(C_{LY})$. (v) Thus, estimates will be obtained for $p(\mathbf{f} \mid C_{RY})$ and $p(\mathbf{f} \mid C_{LY})$ for $Y$ (years) = 5, 10, 15 (for example).

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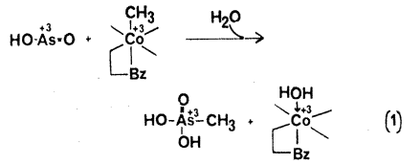
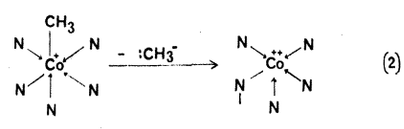
## The Methylation of Arsenic Compounds

In Wood's excellent article on the subject of the biological methylation of metals in the environment (*1*) and in a series of other papers (*2*) he, and his co-workers, have made considerable use of the concept of formal oxidation numbers. However, this concept must be used with considerable caution. In the proposed methylation of arsenite to methylarsonic acid (*3*) by cobalamin, the formal oxidation number of arsenic remains 3+ on either side of the equation. In order that the oxidation number of cobalt remains unchanged (Eq. 2) the methyl group must be transferred as a methyl carbanion. However, in order for the oxidation number of arsenic to remain unchanged, the methyl group must have a formal oxidation number of 1+. This is inconsistent with the methyl carbanion transfer mechanism.

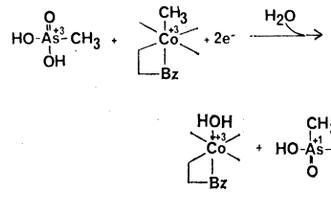


(1)



(2)

In the equation proposed for the methylation of methylarsonic to dimethylarsinic acid (*3*), because the methyl group is assigned a formal oxidation



(3)

number of 1+, the arsenic atom on the right-hand side of the equation ends up with a formal charge of 1+. In order to account for the change in the formal oxidation number of arsenic, two electrons are added to the left-hand side of Eq. 3. What is happening here can be explained by the displacement of $OH^-$ by $CH_3^-$. This is consistent with Wood's methyl carbanion transfer mechanism (Eq. 2). However, neither an oxidation, nor a reduction, is taking place and no electron transfer is involved. The failure to recognize that the change in the oxidation number arises from the formal application of a set of rules, and not to electron transfer, could lead the unwary reader to seek the assistance of a biological electron transport system when none need be invoked.

In Wood's article (*1*), figure 3, which outlines a proposed biological cycle for arsenic, makes liberal use of the concept of formal oxidation numbers. As has been pointed out in the foregoing examples, the failure to recognize that the oxidation numbers are artificial can result in misleading implications.

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I would like to thank Ralph Zingaro and Kurt Irgolic for pointing out some of the problems that can arise from application of the concept of formal oxidation numbers. However, inorganic chemists consistently write about the reduction of mercuric ion to mercurous ion, but when I apply the rule of formal oxidation numbers, I discover that the formal oxidation state of each atom of mercury in mercurous ion is still 2+. I have met distinguished inorganic chemists who are adamant about the application of formal oxidation states, and an equal number who are adamant about valence. Thus it makes it difficult for a biochemist like myself to find consistency. I don't know where Zangaro and Irgolic stand, but perhaps they could urge their colleagues to get themselves sorted out! I thank them for raising the issue, and I give no arguments.

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