This Week's Citation Classic®

CC/NUMBER 49
DECEMBER 8, 1986

Sunda W & Guillard R R L. The relationship between cupric ion activity and the toxicity of copper to phytoplankton. *J. Mar. Res.* 34:511-29, 1976.
[Woods Hole Oceanographic Institution, MA]

We conducted experiments to investigate the relationship between the complexation of copper in solution and its uptake by and toxicity to unicellular algae. Results showed that the biological availability of copper was directly related to the free cupric ion activity, rather than to the total copper concentration or the concentration of copper chelates. [The *SCI*® indicates that this paper has been cited in over 235 publications.]

William Sunda
Beaufort Laboratory
Southeast Fisheries Center
National Marine Fisheries Service
Beaufort, NC 28516-9722

October 8, 1986

It was the winter of 1970, and I was a PhD student in the newly formed Joint Program in Oceanography, offered by the Massachusetts Institute of Technology and the Woods Hole Oceanographic Institution. Nearing the end of my course work, I was in need of a dissertation research topic. Most of my classmates in the Chemical Oceanography Program opted for more traditional pursuits in geochemistry, but I had become fascinated by the interrelationships between the coordination chemistry of metals in solution and the availability of metals to cells.

I was well versed at the time in the physical chemistry of aquatic solutions, but knew very little about biology, a serious deficiency for my planned pursuit. Thus, I set out in search of an adviser who could teach me some biology and how to culture phytoplankton, which I thought would be an ideal model cellular system. The search brought me to the doorstep of Robert Guillard, a well-known phytoplankton physiologist at Woods Hole, in whose laboratory I was to spend the next four-and-a-half years. It took me two years to learn enough physiology to run biologically competent culture experiments and another year and a half to marry the biology to rigorous thermodynamic theory.

In the end, I had run a series of experiments in controlled model chelate seawater solutions that contained different concentrations of copper and trishydroxymethylamino methane (Tris), a synthetic chelator. Increases in the concentration of Tris decreased the cellular uptake and toxicity of copper. Thermodynamic calculations showed that this decrease was directly related to the decrease in free cupric ion activity brought about by increased copper chelation to Tris.

I think that the reason that this paper has been cited so frequently is that it represents the first clear demonstration that the biological availability of trace metals is determined by the free metal-ion activity (or chemical potential) rather than by total metal concentration in solution. This was an idea that had been proposed at various times since at least 1950,[1] but had never been rigorously tested. Subsequent experiments with a number of other metals, organisms, and complexing ligands have shown the importance of free-ion activity in controlling the biological availability of metal ions to be a rather general phenomenon.[2,3] The demonstration of the biological importance of this parameter has led to the development of metal-ion buffer systems to control and quantify the availability of metal ions in biological experiments[3] and to a better understanding of the role of metal complexation in regulating the availability and toxicity of trace metal ions in natural waters.

1. **Hutner S H, Provasoli L, Schatz A & Haskins C P.** Some approaches to the study of the role of metals in the metabolism of microorganisms. *Proc. Amer. Phil. Soc.* 94:152-70, 1950. (Cited 160 times since 1955.)
2. **Morel F M M.** *Principles of aquatic chemistry.* New York: Wiley, 1984. p. 300-6.
3. **Sunda W G & Huntsman S A.** Regulation of cellular manganese and manganese transport rates in the unicellular alga *Chlamydomonas*. *Limnol. Oceanogr.* 30:71-9, 1985.

2A-16