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Standards for modeling

To the editor:

The use of computational methods to understand and predict the behavior of biochemical networks is nothing new. Indeed, computer simulations of such processes predate the advent of digital computers. Recently, the need to efficiently exploit data from high-throughput technologies has led to the development of numerous databases and simulation and analysis packages for understanding biology at the level of the system¹. However, there remains a distinct lack of standards for modeling or simulation.

Researchers have tended to employ different model description languages and different model simulation and analysis environments in their work. In addition, because of the difficulty of translating models manually, published models frequently are neither reused nor explored by others. Worse still, as each analysis package has unique resources, many models are not translatable and can only be studied with a specific software suite.

As computer modeling becomes more established as a way to explore data from high-throughput technologies, the need to reuse models is becoming increasingly acute. Add to this (i) the waste in research effort resulting from software suite developers' attempts to augment their tools with all the features available in other packages, and (ii) the loss of models written in languages and packages no longer supported, and the argument in favor of a standard model description language and a way to integrate software packages from multiple suppliers becomes compelling.

A multinational alliance of ten leading developers of simulation and analysis tools (<http://www.cds.caltech.edu/erato> or <http://www.sbml.org>) has set out to address these issues by developing a shared language for model description and an environment that allows different pieces of software to access and share each other's resources.

This language—XML-based Systems Biology Markup Language (SBML)—is being defined on a series of levels repre-

sented increasingly complex data structures. SBML Level 1, released in March 2001, supports nonspatial biochemical models and all model structures possible in existing analysis and simulation tools. Subsequent releases (termed levels) of SBML will add additional structures and facilities. By freezing SBML definitions at incremental levels, alliance members hope to provide the community with stable standards that software authors can incorporate into their designs. Submodels, arrays and array connectivity, database references, three-dimensional geometry, diagramming, and other features are currently being discussed and developed by the alliance for SBML Level 2.

The Systems Biology Workbench (SBW)² complements SBML by allowing software packages from different manufacturers for simulation and analysis to use each other's resources. As such, SBW provides infrastructure that can be used to interface software components and enable them to communicate among each other. The components in this case may be simulation codes, analysis tools (e.g., bifurcation analysis and metabolic control analysis)³, user interfaces, database interfaces, script language interpreters, or any piece of software that conforms to SBW's simple public Application Programming Interface (API).

To ensure its widespread use, SBW offers interface libraries in a wide range of programming languages and is being released freely under the GNU LGPL Open Source License. All applications using SBW are equal from a user perspective, and retain their authors' licensing terms. SBW-enabled packages are also entirely unaltered by being connected through SBW, except for menu changes needed to make additional resources available.

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Wheat, rye, and barley on the cob?

To the editor:

Modern domesticated maize (*Zea mays*) provides about 21% of global human nutrition¹. The plant is robust and productive. The major product of maize (except for forage) is the seeds formed on thick, long cobs. These typical cobs appeared several millennia ago when maize became domesticated, probably in southern Mexico^{2,3}. Given the similarity of the wild female maize spike to the spike structure of wheat, rye, and barley, we propose that these major crops could be engineered with cobs resembling those of modern maize.

The wild progenitors of domesticated maize, the annual teosintes (*Zea mays* ssp. *mexicana* and ssp. *parviglumis*), have a thin female inflorescence comprising several nodes that carry female flowers resembling the hermaphroditic spikes of wheat, rye, and barley. The male inflorescence has not been changed drastically during domestication. In contrast, the modest female inflorescence of teosinte has evolved into a totally different structure, the large, thick maize cob⁴. The domesticated plant also has become much less branched and more robust. These dramatic developmental alterations required a change in the action of several major genes and several modifier genes^{5,6}.

Three of the major genetic factors (*teosinte branched*, *teosinte glume architecture*, and the *two ranked* gene) have been characterized. The *teosinte branched* gene acts to change the architecture of the plant from branched and grasslike to the single-stalk form of cultivated maize⁶. The *teosinte glume architecture* gene acts to eliminate the large, hard casing on teosinte kernels⁷. The *two ranked* locus contributes to the production of kernels around the entire circumference of the ear^{8,9}. All these changes were accomplished by selection of intermediate forms, some of which were found in prehistoric excavations¹⁰.

These intermediate forms can be demonstrated by crossing wild teosinte with modern (domesticated) maize and examining the segregation of characters in the progeny^{4,5,11}. Cloning of the array of genes involved in the transformation of wild maize into the current crop is likely to be completed soon.

Several wild diploid wheats of the section Sitopsis (such as *Aegilops speltoides*) that were the progenitors of the wild tetraploid emmer wheat (a progenitor of bread wheat) have an ear morphology like that of wild maize ears, even more than do current domesticated wheats, barley, or rye. Thus, current wheats, barley, and rye

1. Kitano, H., *Science*, **295**, 1662–1664 (2002).
2. Hucka, M. et al. The ERATO Systems Biology Workbench: An Integrated Environment for Multiscale and Multitheoretic Simulations in Systems Biology, pp. 125–143 in *Foundations of Systems Biology*, Kitano, H., (ed.) (The MIT Press, Cambridge, 2001).
3. Cascante, M., Boros, L., Comin-Anduix, B., de Atauri, P., Centelles, J., Lee, P.W.N., *Nat. Biotechnol.*, **20**, 243–249, (2002).