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Inflammation Research

Amine System Project

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Introduction

Histamine, polyamines and other biogenic amines have pleiotropic physiological effects and the impairment of their metabolism is associated with highly prevalent pathological situations [1]. In spite of the evidence for the involvement of both polyamines and histamine in cancer and other angiogenesis- and/or inflammation-dependent diseases, questions concerning the molecular processes behind these effects remain to be answered. This may be due to the dispersion of available data in specialized literature. Therefore, new systemic approaches are needed to advance our knowledge of the role of biogenic amine metabolism in pathophysiological conditions [2]. Here, we describe our approach to achieve this goal: to build an interconnected database to obtain emergent information on the molecular basis of biogenic amine metabolism and functions.

Materials and methods

We are currently building a bilingual (English-Spanish) online platform containing three working areas: an ontology-based *integration* area for the available information on the components of the system, a *predictive* and a *training* area. Our basic ontology will be based on the Gene Ontology, GO (www.geneontology.org), the molecular biology ontology TAMBIS (www.daml.org/ontologies/99) and BioPAX standard (www.biopax.org), proposed to model metabolic networks. The Amine Metabolism Ontology (AMO) is the Domain Ontology that we will develop from GO and BioPAX and will be used as the pivot that will integrate the whole system. The predictive area will be supported on our previous experience on protein modeling, metabolic modeling and biological network analysis and will use methods described by us elsewhere [3–5]. More details on this project can be obtained at www.asp.uma.es.

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Results and discussion

The age of systems biology has arrived [6]. Systems biology is the analysis of the relationships among the elements in a biological system in response to genetic or environmental perturbations, with the goal of understanding the system as a whole. A "system" can be anything from a gene regulatory network or a metabolic network to a cell, a tissue, an organism or an ecosystem. Hence, our project focuses on histamine and polyamine biology as the "system". To achieve the goal of a more efficient advance in knowledge in order to control this system and its involvement in pathophysiological conditions, an online platform with three working areas is under construction. The architecture of the whole project is depicted in Figure 1.

The *integration* working area will integrate the available information of the system components from relevant public databases at the different levels of its study: for example, concentrations, structures, assigned functions.

The *predictive* working area will include tools to make possible the predictive simulation at three biological levels: metabolic regulation, protein structure modeling and gene regulation, as previously suggested by us [2]. For each of these three levels we have already got valuable results: the first 3D structural model for mammalian histidine decarboxylase [3, 7], the first mathematical model of mammalian polyamine metabolism [4] and a first network of human transcription factor interactions [5].

To make possible the automatic relationship between these two working areas, we aim to design an ontology allowing us to represent mathematical models, taking as a starting reference the Systems Biology Markup Language (www.sbml.org).

Finally, in the *training* working area a tutorial on the use of the other areas of our platform will be provided, as well as other relevant information to help in the training of students and researchers interested in systems biology.

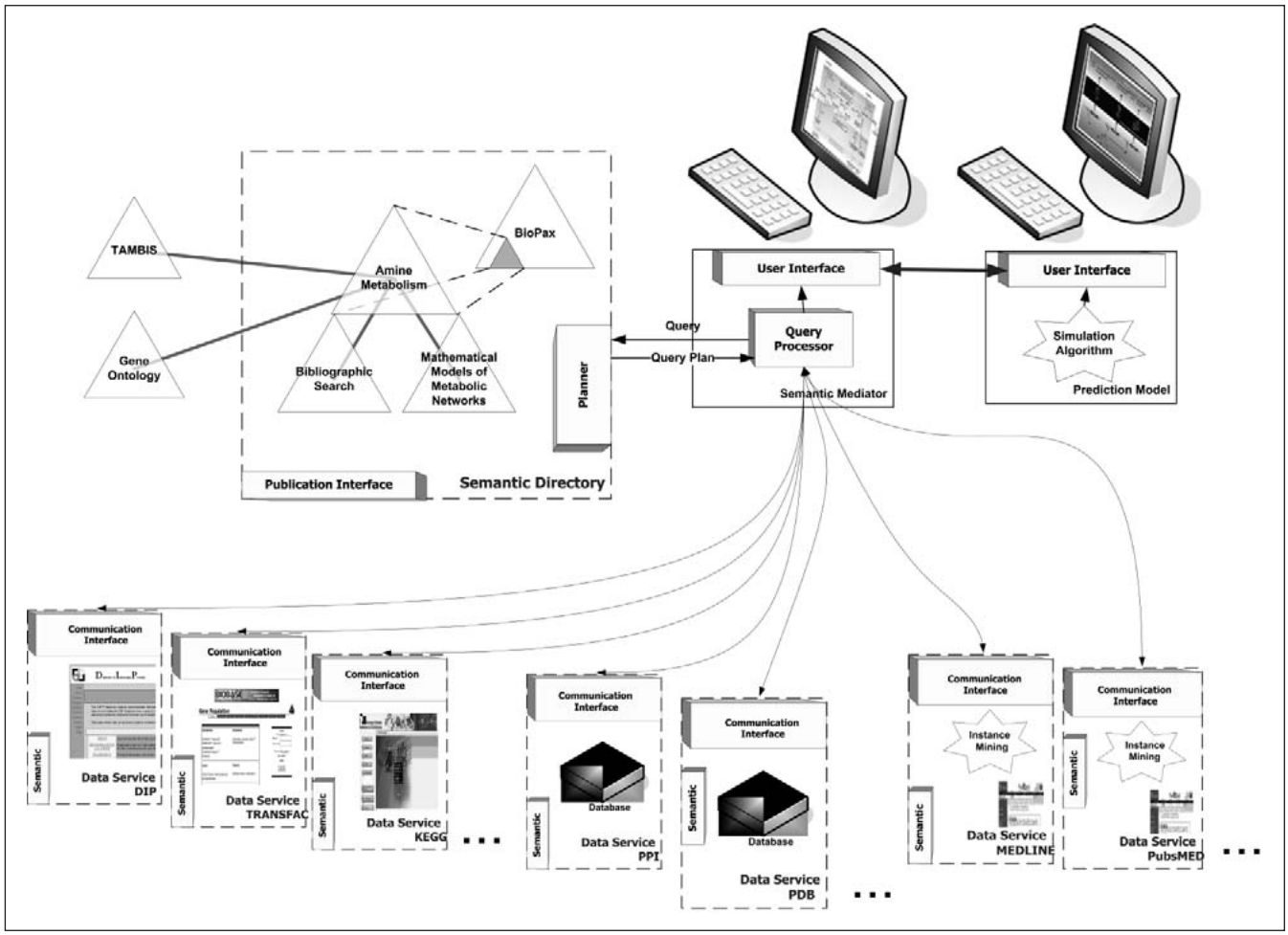

Fig. 1. Conceptual architecture of the Amine Systems Project. The kernel of the system is composed of three inter-related ontologies. The Amine Metabolism Ontology (AMO) is the pivot Domain Ontology. AMO is related with two, more specific ontologies oriented towards the bibliographic search (BSO) and Mathematical Modeling (MMO) of metabolic networks. The AMO is defined in terms of a standard vocabulary (the Gene Ontology, GO) and it is also related to several other standard ontologies. Relevant databases and information services are integrated with the AMO in a semantic mediation system.

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