ABSTRACT

Summary: The Thermodynamics of Enzyme-catalyzed Reactions Database (TECRDB) is a comprehensive collection of thermodynamic data on enzyme-catalyzed reactions. The data, which consist of apparent equilibrium constants and calorimetrically determined molar enthalpies of reaction, are the primary experimental results obtained from thermodynamic studies of biochemical reactions. The results from ∼1000 published papers containing data on ∼400 different enzyme-catalyzed reactions constitute the essential information in the database. The information is managed using Oracle and is available on the Web.

Availability: http://xpdb.nist.gov/enzyme_thermodynamics/

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Thermodynamic data on enzyme-catalyzed reactions play an essential role in the prediction of the extent of reaction and the position of equilibrium for any process in which these reactions occur. The importance of understanding the thermodynamics of these biochemical reactions was emphasized by Krebs and Kornberg 47 years ago in their monograph A Survey of the Energy Transformations in Living Matter (Krebs and Kornberg, 1957). Their monograph contains a useful appendix on Gibbs free energy data of biological interest and some data on the thermodynamics of enzyme-catalyzed reactions. However, the amount of data available at that time was extremely limited. While several reviews on this subject have subsequently appeared, the absence of a comprehensive collection of this information led two of us (R.N.G. and Y.B.T.) to begin the systematic collection of this data ∼15 years ago. Our evaluated data were published as a series of reviews in the Journal of Physical and Chemical Reference Data (Goldberg et al., 1993; Goldberg and Tewari, 1994a,b, 1995a,b; Goldberg, 1999). The results from ∼1000 published papers containing data on ∼400 different enzyme-catalyzed reactions constitute the essential information in the database. The website database contains all this information and is managed using Oracle. Having this information available in a true database form on the Web serves to complement several existing and related bioinformatics sources on the Web: UMBBD (Ellis et al., 2003, http://umbbd.ahc.umn.edu/), ENZYME (Enzyme Nomenclature, 1992, http://www.chem.qmw.ac.uk/iubmb/enzyme/), BRENDA (Schomburg et al., 2002, http://www.brenda.uni-koeln.de/), KEGG (Kanehisa et al., 2002, http://www.genome.ad.jp/kegg/kegg.html), and the SwissProt Enzyme Nomenclature Database (Bairoch, 2000, http://us.expasy.org/enzyme/).

The importance of this information lies in its applications both in biochemistry and in industrial enzymology. The data are also essential for metabolic control analysis (MCA) (see Fell, 1997, http://bms-mudshark.brookes.ac.uk/), an important part of systems biology. Specifically, the full application of MCA requires both thermodynamic and kinetic data as well as a knowledge of metabolite concentrations. The result is a quantitative description of metabolic processes, a detailed understanding of which may yield an understanding of the differences between the normal and the diseased states of the living system as well as the ability to successfully engineer organisms to accomplish specific aims. This approach requires a very significant amount of data (and effort) and has thus far seen limited application. However, the application of the thermodynamic data to industrial processes involves straightforward calculations, which permit engineers to optimize product yields and to calculate the energy requirements of a reaction or process.

The TECRDDB contains several pages of discussion of the essential background on the thermodynamics of enzyme-catalyzed reactions (see: Thermodynamic Background, the
**Table 1.** Layers used for the expression of data.

<table>
<thead>
<tr>
<th>Layer 1</th>
<th>Layer 2</th>
<th>Layer 3</th>
<th>Layer 4</th>
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<tbody>
<tr>
<td>phosphoenolpyruvate&lt;sub&gt;3-&lt;/sub&gt;(aq), + H&lt;sub&gt;2&lt;/sub&gt;O(l) = pyruvate-(aq) + HPO&lt;sub&gt;4&lt;/sub&gt;&lt;sup&gt;2-&lt;/sup&gt;(aq)</td>
<td>phosphoenolpyruvate&lt;sub&gt;3-&lt;/sub&gt;-&lt;sup&gt;3-&lt;/sup&gt;(aq), + H&lt;sub&gt;2&lt;/sub&gt;O(l) = pyruvate-(aq) + HPO&lt;sub&gt;4&lt;/sub&gt;&lt;sup&gt;2-&lt;/sup&gt;(aq)</td>
<td>phosphoenolpyruvate&lt;sub&gt;3-&lt;/sub&gt;-&lt;sup&gt;3-&lt;/sup&gt;(aq), + H&lt;sub&gt;2&lt;/sub&gt;O(l) = pyruvate-(aq) + HPO&lt;sub&gt;4&lt;/sub&gt;&lt;sup&gt;2-&lt;/sup&gt;(aq)</td>
<td></td>
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<tr>
<td>5alpha-pregnane-3beta,17alpha,21-triol-20-one(aq) + NAD(aq) = 5alpha-pregnane-17alpha,21-diol-3,20-dione(aq) + NADH(aq)</td>
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The existing collection of thermodynamic data has seen use for the calculation of standard molar Gibbs free energies of formation for a substantial number of biochemical species (Albertby et al., 1994). These programs that permit one to calculate values of apparent equilibrium constants $K'$ of biochemical reactions as a function of pH and ionic strength. Computer codes (Akers and Goldberg, 2001, http://www.mathematica-journal.com) that permit one to conveniently calculate values of apparent equilibrium constants $K'$ from values of (standard) equilibrium constants $K$ and also to perform the inverse calculation significantly enhance the usefulness of the information in the database.

The website is constructed using PERL and an ORACLE database. IUPAC recommendations for enzyme thermodynamic data are rich in the use of special characters (e.g. greek letters), superscripts and subscripts. The use of these special characters presents special difficulties for database software. For this reason, many databases [e.g. the Protein Data Bank (http://www.rcsb.org/pdb/) and the SwissProt Enzyme Nomenclature Database (http://us.expasy.org/enzyme/)] use a flat naming convention, which is devoid of greek letters, superscripts and subscripts. We developed new techniques and tools for the implementation of IUPAC recommendations in a database environment. In our implementation, the data are expressed in four layers (Table 1). Layer 1 has the data in the flat form and Layer 2 has the data in the IUPAC form stored as HTML code. Layer 3 has the data in the flat form together with synonyms (if any). Layer 4 has the data in the IUPAC form. This form is generated from Layer 2 as text during the display of results. Each of these layers is generated for every data item (e.g. reaction, enzyme, and so on).

The Web interface provides several different search options for querying the database. The query results are generated dynamically, sorted and displayed in tabular form. The options from the first Web page are: Thermodynamic Background; How to Use This Database (Help); Enzyme-Catalyzed Reactions: Search using predefined values; Enzyme-Catalyzed Reactions: Search with user defined values; Enzyme-Catalyzed Reactions: Show distinct values; Enzyme-Catalyzed Reactions: Show all values;
Fig. 1. Representative thermodynamic data found in a search.

References: Search references; Abbreviations; and Prior Version: Search prior version.

Search option No. 1 (Predefined Values) provides drop-down lists (scroll bars) that give values for each of the data items, such as reaction, enzyme and EC number by using the components of data in Layer 1. The user can make a selection of multiple values using different data items. The user can control the sorting and display of data by the use of check boxes. Search option No. 2 (User Defined Values) allows the user to enter his own selection and is designed to support several constraints for different data items in a query. Search option No. 3 (Distinct Values) allows the user to view all the unique data values of a particular data item, such as enzyme or reactant. Each of these search options allows the user to view the thermodynamic data (Fig. 1) found in the search. The user can also establish a direct link to the database by using one or more of the following key words: Reactant, EC, Method, Enzyme, Buffer, pH and Cofactor. For example, http://xpdb.nist.gov/enzyme_thermodynamics/enzyme_compose_query.pl?EC=1.1.1.47 displays the data for EC number 1.1.1.47.

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REFERENCES


Thermodynamics of enzyme-catalyzed reactions