IS THE EVOLUTION OF BIOCHEMISTRY TEXTS DECREASING FITNESS? A CASE STUDY OF PEDAGOGICAL ERROR IN BIOENERGETICS

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ABSTRACT

The initial impetus for this research was the discovery by the authors of a variety of common and consistent errors and misconceptions in pedagogical literature on the topic of thermodynamics in biochemistry. A systematic survey was undertaken of material on thermodynamics in biochemistry textbooks commonly used in Australian Universities over the period from the 1920s up to 2010. Four common areas of error and misconception were identified, and several factors associated with the initiation and propagation of troublesome pedagogical material through successive editions of biochemistry textbooks were recognised. These factors included the introduction of multiple authors and also often the departure of the original author of a particular textbook. The very nature of biochemistry as a rapidly expanding discipline leads to the constant introduction of new material in textbooks and the contraction of older material such as thermodynamics. Material is also often fragmented into a number of smaller sections in modern textbooks. Moreover, less development is likely to be applied to this older material, with considerable reuse of material from previous editions. The lessons learned from charting these particular errors in thermodynamics in biochemistry textbooks may provide insight into how troublesome pedagogical material evolves in other disciplines.

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INTRODUCTION

Teaching thermodynamics to biochemistry students has always been regarded as challenging and, in recent years, this challenge has increased considerably. As the ‘traditional’ biochemistry curriculum has been compressed to allow more detailed coverage of topics such as biochemical genetics and cell signalling, the time allocated to thermodynamics has been reduced. At the same time, students undertaking biochemistry studies are increasingly less likely to have undertaken foundation studies in physical chemistry. Should we be surprised that these students are intimidated by the complexity of thermodynamics?

Given the fundamental importance of a good understanding of thermodynamic principles to key aspects of biochemistry and physiology, a variety of materials aiming to familiarise students with basic concepts of bioenergetics has been developed. However, inaccuracies may be introduced when one attempts to illustrate and simplify complex concepts.

The present study was triggered when one of us (BC) was asked to review an interactive CD-ROM designed to assist medical students with introductory biochemistry. While the overall package was judged to be useful, it was found that the section dealing with ‘bioenergetics’ contained several inaccuracies. This prompted a quick search of some widely-used biochemistry textbooks, revealing the following consistently occurring errors:

- confusion between entropy *creation* (deriving exclusively from free energy dissipation) and entropy *exchange*; and
- confusion between *sequential* reactions and *coupled* reactions.

Further research showed that thermodynamic error is common in contemporary mainstream textbooks of biochemistry. We therefore undertook an historical survey of textbooks in biochemistry to discover where pedagogical errors first arose in the treatment of bioenergetics and to investigate how such errors evolved over time.

LITERATURE SEARCH

The initial search was designed to explore the evolution of the presentation of material on thermodynamics in biochemistry textbooks. It was decided to restrict the initial search to the Monash University library catalogue system. Our early discussions identified the timeline for the development of biochemistry as a separate discipline and the earliest writers in this field. The first two names raised by this discussion (who subsequently went on to publish respected and widely used biochemistry textbooks) were Albert H. Lehninger and Lubert Stryer. Initially, the earliest publications by these authors were found: Lehninger (1965; 1970) and Stryer (1970). After examination of the material in these books to give a baseline of the early presentation of thermodynamics in the context of biochemistry, a broad search of the Monash University Library database using the key search term *'biochemistry'* gave 1647 titles (or 83 pages of results). The search was then restricted to books only.

A selection of textbooks published through the last four decades was briefly examined to gain an appreciation of the variety of presentation of thermodynamics during this period. We decided that textbooks written with a medical and physiological slant were of limited value for the project, either because the coverage was only very cursory or because the development of the material was limited. Therefore, the focus was placed on those textbooks that were intended to be used in a more generalist biochemistry course such as might be found within a science degree.

We wanted to narrow the focus further to a short list of commonly recommended and used textbooks. It was decided to look at eight textbook series, all of which have multiple editions and are, or have been, in common usage in biochemistry courses in Australia (See Table 1). The authors of those texts are mainly American, but at least one series is relatively recent and has Australian authors. In the initial analysis, an early edition, a mid-range edition and a later edition were looked at to get an idea of changes, development and rigour of presentation of thermodynamics material in each book. Where interesting patterns were noted, we examined closely all editions of the book from the first edition to the most recent. Particular note was taken of changes in publisher and authors, especially in cases where an initial author was no longer involved.

Table 1: List of the eight textbook series surveyed in this study

Authors	Title of Book Series, Dates of publication
Lehninger (Albert L. Lehninger up to 1983) then Lehninger, Nelson and Cox (Albert L. Lehninger, David L. Nelson, Michael M. Cox, 1993), then Nelson and Cox (David L. Nelson, Michael M. Cox)	*Biochemistry: the molecular basis of cell structure and function* (1970, 1975 (2nd ed.)) *Principles of Biochemistry* (1982, (only Lehninger) 1993 (2nd ed)) *Lehninger Principles of Biochemistry* (2000 (3rd ed.), 2005 (4th ed.), 2008 (5th ed.))
Garrett and Grisham (Reginald H. Garrett, Charles M. Grisham)	*Biochemistry* (1995, 1999 (2nd ed.), 2007 (updated 3rd ed.))
Boyer (Rodney F. Boyer)	*Modern Experimental Biochemistry* (1986) *Concepts in Biochemistry* (2002 (2nd ed.), 2006 (3rd ed.))
Moran and Scrimgeour Horton (formerly Moran and Scrimgeour) (H. Robert Horton ... [et al.].)	*Biochemistry* (1994 (2nd ed.)) (Rev. ed. of: Biochemistry / J. David Rawn. c1989) *Principles of Biochemistry* (1993, 1996 (2nd ed.), 2002, (3rd ed.), 2006 (4th ed.))
Stryer (Stryer, Lubert) followed by (Jeremy M. Berg, John L. Tymoczko, Lubert Stryer in 2002) – Now called *Berg*	*Biochemistry* (1975, 1981, (2nd ed.), 1988 (3rd ed.), 1995 (4th ed.), 2002 (5th ed.), 2007 (6th ed.))
Voet and Voet (Donald Voet, Judith G. Voet) then new title and Voet, Voet and Pratt (Donald Voet, Judith G. Voet, Charlotte W. Pratt from 1999)	*Biochemistry* (1990, 1995 (2nd ed.), 2004 (3rd ed.)) *Fundamentals of biochemistry* (1999, 2006 (2nd ed), 2008 (3rd ed.))
Elliot and Elliot (William H. Elliott & Daphne C. Elliott)	*Biochemistry and Molecular Biology* (1997, 2001 (2nd ed.), 2005 (3rd ed.), 2009 (4th ed.))
Zubay (Geoffrey L. Zubay – coordinating author)	*Biochemistry* (1983, 1993 (3rd ed.), 1998 (4th ed.))

Biochemistry emerged as a distinct discipline in the 1930s (Boyer, 2000), and was developed rapidly over the next two decades. The first biochemistry textbook used at Monash University, *Principles of Biochemistry* by White, Handler, Smith and Stetten (1959), was identified by a search of early Monash University handbooks. Subject descriptions for Biochemistry were found for the faculties of Medicine and Science for 1961 (Monash University was established in 1958). An examination of the material on thermodynamics in all available editions of the set text (White et al., 1959; White, Smith and Handler 1964; 1973) as well as other biochemistry textbooks going back to 1920, led us to the conviction that the writings of Lehninger and Stryer (Lehninger, 1965; 1970; Stryer, 1970) were the first attempts to truly apply thermodynamics to the biochemistry of cellular processes.

TYPES OF PEDAGOGICAL ERRORS

The errors found in our search can be classified into four areas.

1. **There is frequent confusion of the terms *free energy* and *total energy*, with *free energy* often used when it is actually the *total energy* of system being referred to.**
   Such a use of the term *free energy* when conceptually it is the *total energy* of the system being discussed occurs in Section 1.4 of *Biochemistry* (Moran, Scrimgeour, Horton, Ochs, & Rawn, 1994). There is also a lack of identification of *free energy* as the specific biochemically important concept. As an example, in their textbook *Biochemistry: The Molecular Basis of Life*, McKee and McKee state ‘energy is more commonly defined, however, as the capacity to do work’ (McKee and McKee, 2009; p.105). This is problematic as, in the context of biochemistry (i.e. with no heat engine possibilities), only *free* energy has the capacity to do work.
2. **A failure to clarify the distinction between sequential reactions (sharing common intermediates) and coupled reactions.**
   A subsection heading in the textbook *Biochemistry* states ‘a thermodynamically unfavourable reaction can be driven by a favourable one’ (Stryer, 1981; p. 239; 1988; 1995; Berg, Tymoczko, & Stryer, 2002; 2007). This kind of example regarding coupled reactions is extremely widespread in the pedagogical literature and is fundamentally flawed on two grounds:
   - It fails to identify the need for stoichiometric coupling of such reactions into a new coupled reaction in which the independent operations of the original endergonic process and exergonic process are *forbidden processes* (i.e. forbidden by the coupling enzyme).
   - It can lead students to form the misconception that all it takes is sufficient energy for an exergonic step to drive an endergonic step in a reaction sequence (metabolic pathway) when the two steps share a common intermediate
3. **There is a failure to identify entropy creation as a consequence of free energy dissipation**
   This is usually coupled with a failure to distinguish between entropy creation and entropy exchange. These types of errors are found, for example, in biochemistry textbooks by Lehninger (1993) and McKee and McKee (2009).
4. **The misleading classification of biochemical reactions as either reversible or irreversible** (Lehninger, 1970; Moran et al., 1994).
   This is an unhelpful classification system which fails to deepen students’ understanding of the dependence of ‘reversibility’ on the subcellular locus of the respective enzymatic coupling operation. To take an obvious example of the ATP/ADP-P_i system, chemiosmotic coupling by the mitochondrial H^+-ATPase favours ATP synthesis while chemiosmotic coupling by the plasmalemmal Na^+,K^+-ATPase favours ATP breakdown; in each ATPase instance, the respective process operates exergonically, as do all spontaneous processes everywhere and at all times. In that sense, both ATPases are operating exergonically, or ‘irreversibly’; however, with regard to the ATP/ADP-P_i system, one exergonic process produces the ‘reverse’ effect of the other exergonic process.
   Similarly, within a sequential metabolic pathway, some steps may be rate-limiting while others are not. If the pathway has a net direction of forward reaction then *all* steps will be operating exergonically (irreversibly), despite the fact that rate-limiting steps will be more displaced from local equilibrium than will non-rate-limiting steps. In short, the proximity to equilibrium of living processes is not something that can be categorised in any pedagogically useful way.

WHY DO ERRORS EVOLVE? EVOLUTIONARY PATTERNS

It is the rare modern biochemistry text that is authored by a single person. Figure 1 follows the evolution of the biochemistry textbooks initially authored by Albert L. Lehninger, then with co-authors

David L. Nelson and Michael M. Cox and finally as a book still bearing Lehninger's name when he is no longer a contributing author (Lehninger, 1965; 1970; 1971; 1973; 1975; 1982; Lehninger, Nelson, & Cox, 1993; Nelson & Cox, 2000; 2005; 2008).

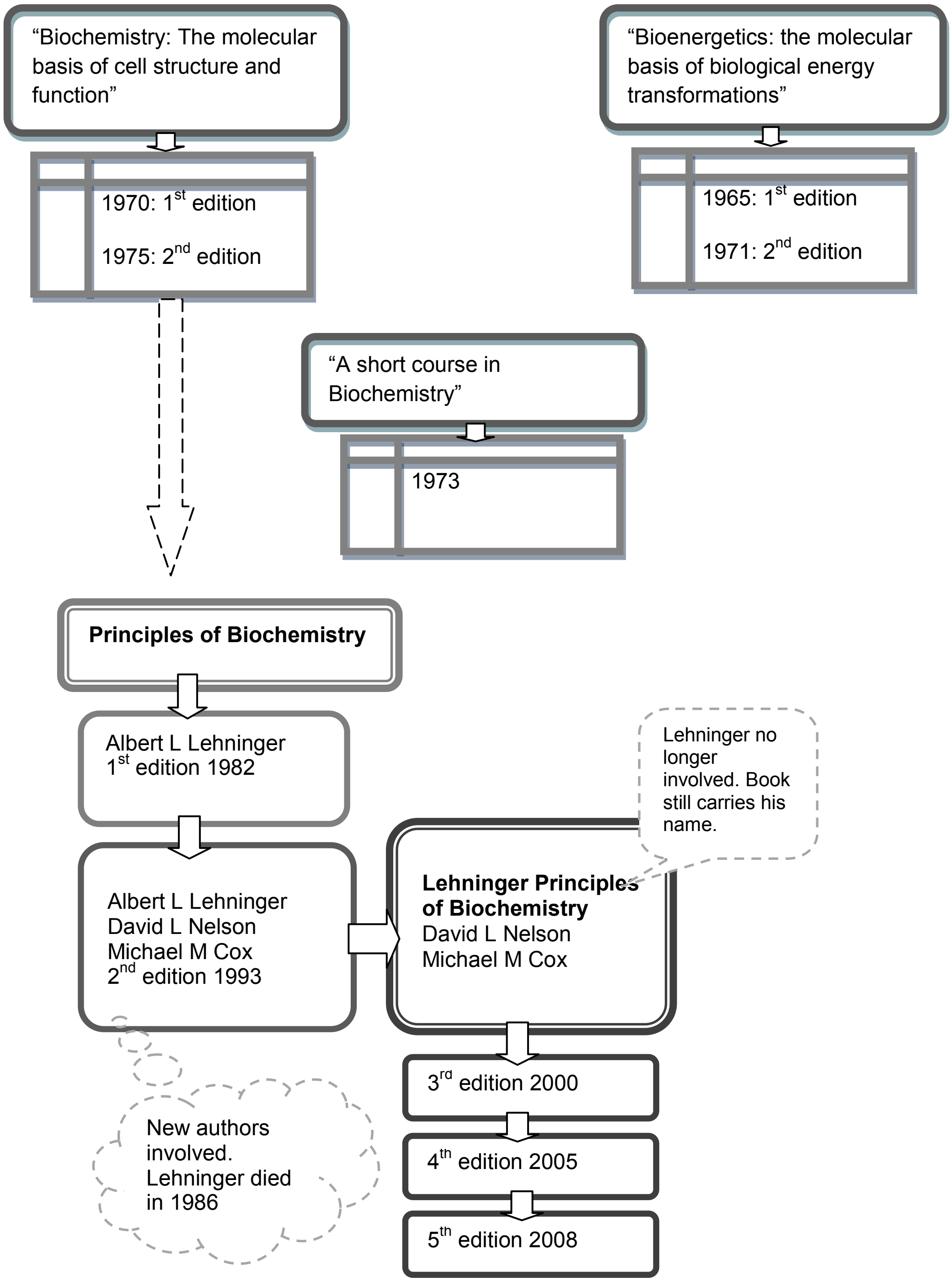

Figure 1: The evolution of biochemistry texts authored by Albert L. Lehninger (1965 – 2008)

Such a change of authors during the progression of a series of books is not unusual. Further examples can be seen in Table 1 (e.g. Moran & Scrimgeour et al. becomes Horton et al.; Stryer becomes Berg, Tymoczko, & Stryer; Voet & Voet becomes Voet, Voet, & Pratt).

New authors are often brought into an existing writing team because of their knowledge of a particular area, often an area of recent importance. This tends to create pools of authors with differing areas of expertise which may lead to a lack of critical review of material in established areas of the text. We found, for example, considerable reuse of material on thermodynamics from the original editions in both of the long running biochemistry textbook series we followed, Lehninger and Stryer. To compound this problem further, some credited authors may have contributed no actual material to the current edition of the textbook. The page giving the authors' credentials in *Biochemistry* (Moran et al., 1994) shows that, of the five authors, only two actively contributed to the new edition. J. David Rawn 'did not write chapters for the new edition' (Moran et al., 1994; p. v), though admittedly the book is based on a previous edition for which he was sole author. Raymond S. Ochs 'did not actively contribute to *Biochemistry*' (Moran et al., 1994; p. v) and H. Robert Horton 'did not write chapters for *Biochemistry*, but his textbook *Principles of Biochemistry* … was a substantial source of information, ideas and narrative' (Moran et al., 1994; p. v). This leads to considerable reuse of legacy material from previous editions rather than critical analysis and rewriting in light of the currently accepted paradigm.

'The rapid development and expansion of every phase of biochemical knowledge' (White, Handler, & Smith, 1964; p. vii) has been noted almost since the emergence of the discipline. Since the 1950s, biochemical knowledge has grown to incorporate such major discoveries as the structure of DNA, genetic information flow, recombinant DNA, gene therapy, bioinformatics and, more recently, the cell cycle and stem cells. This is by no means an exhaustive list.

> The burgeoning biochemical literature gives serious pause to authors contemplating a new edition of a textbook of biochemistry (White, Handler, & Smith, 1964; p. vii).

The explosion of the discipline and the sheer size and scope of current biochemistry textbooks means that material has to be discarded in order to include new material to keep the book to a workable size. Detailed discussions of the underlying principles of thermodynamics, which had pages or chapters devoted to them in the earliest textbooks, are reduced essentially to formulas in later work. For example, the second edition of Lehninger's *Principles of Biochemistry* (1993) contains 29 pages of material on thermodynamics; in the current fifth edition (Nelson & Cox, 2008), there are only seven pages. It is interesting to note that, at least in the case of this text, there is relatively less problematic material in the latest edition. We suspect that space constraints, which have led to thermodynamics being presented essentially as annotated formulas with minimal explanation, are the probable reason for the reduction in error.

In later editions of biochemistry textbooks, material on thermodynamics is often dispersed throughout the book (in enzyme sections for example) rather than in a self-contained section on thermodynamics. Whilst this can be valuable in providing understanding of the application of thermodynamics to a particular topic, the broader application of thermodynamic concepts in biochemistry is not being made clear to the student; the whole picture has become fragmented.

The propagation of error-filled material from historical sources to current textbooks is by no means confined to thermodynamics or bioenergetics or even to biochemistry as a discipline. Similar work, for example, has been undertaken in tracking the source of a misconception regarding the nature of a proof of prime numbers by Euclid in the mathematical literature (Hardy & Woodgold, 2009). Other similar published investigations include a catalogue of the treatment of the photoelectric effect in physics textbooks (Klassen, 2008) and an investigation of high school biology textbooks as sources of misconceptions about genetics (Cho, Kahle, & Nordland, 1985). Our tracking of particular errors in thermodynamics pedagogy within biochemistry textbooks has provided insight into the nature of their evolution. This approach could be applicable to other disciplines.

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