Signal Transduction

(Second Edition)

信号转导

（原著第二版）

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导　读

细胞的生老病死离不开与其环境的相互作用，而这种相互作用正是由信号转导来完成。了解细胞内信号转导过程和机理是生命科学的基础问题；由于其复杂性和重要性，细胞信号转导的研究也一直是生命科学的前沿领域。

那么，什么是信号转导？信号转导是指信号分子由细胞外传到细胞内部引起细胞行为改变的过程。信号分子包括物理性质的（光、电、机械能等），化学性质的（味觉、嗅觉等）和生物性质的（激素、生长因子等）。细胞在感受到这些信号后，产生一定的响应，如：发出信号影响其他细胞，或本身发生增殖、分化、运动或死亡。细胞行为的改变最终导致胚胎发育和成体内各器官、组织的内平衡稳定和各种生理活动的顺利进行。因此，信号转导的异常会导致包括出生缺陷、肿瘤、心血管疾病、代谢疾病等多种疾病的发生。

本书较全面地概括了目前我们对信号转导理解的方方面面，主要分为两大部分：前九章介绍所谓“经典”信号转导的基本内容，主要集中在激素及其受体，第二信使（环核苷酸和钙离子）的产生和作用。对跨膜 7 次的 G 蛋白偶联受体，特别是肾上腺素受体，有详细的论述。第一章主要介绍了信号转导的基本概念和研究历史；第二章着重介绍了作为第一信使的激素、生长因子等；第三章介绍了受体，包括肾上腺受体和离子通道受体，和配体一受体相互作用；第四章着重介绍了 GTP 结合蛋白，包括三聚体 G 蛋白和小 G 蛋白（Ras 等）；第五章介绍 G 蛋白的效应酶：腺苷酸环化酶和磷酸酯酶 C；第六章介绍了与 G 蛋白偶联的视觉、嗅觉信号转导；第七章描述了细胞内钙信号；第八章介绍重要的钙效应分子；第九章以蛋白激酶 A 和蛋白激酶 C 为例子，介绍磷酸化和去磷酸化对蛋白活性的调控。第十章介绍在核内影响转录的细胞内受体一核受体。然后，在第十一章到二十三章中，主要介绍生长因子和黏附分子介导的信号转导过程。第十一章着重介绍生长因子，包括神经生长因子、转化生长因子等的发现，及与癌症发生的关系；第十二章主要细化了受体蛋白酪氨酸激酶的信号转导，包括 MAP 激酶；第十三章介绍包括整合素在内的黏联分子、相关信号转导以及生理功能；第十四章主要介绍 Wnt 信号；第十五章至第十七章描述了与免疫、炎症有关的信号转导通路，包括 Toll 类受体、T 细胞受体和 NF-κB 信号通路以及 STAT 信号通路；在第十五章还描述了泛素化和 SUMO 化对蛋白的活性和稳定性的调控；第十八章介绍了胰岛素激活的信号，特别是肌醇脂类和蛋白激酶 B 相关信号通路；第十九章再一次讨论了蛋白激酶 C 在细胞转化中的作用及非经典蛋白激酶 C 对细胞极性的调控；第二十章以 TGF-β 家族为例，详尽介绍了相关信号通路和调控机制，以及它们在发育和肿瘤形成中的作用；第二十一章介绍了蛋白磷酸酶，包括酪氨酸、丝氨酸/缩氨酸、双特异磷酸酶以及脂类磷酸酶；第二十二章描述了 Notch 信号通路，以及在发育和小肠干细胞中的作用；第二十三章介绍了肿瘤治疗相关的干预手段和药物开发策略。最后，第二十四章描述了蛋白结构域的概念和它们在信号转导中的重要性。

在本书2003年的第一版中，作者主要概述了经典的信号转导通路，特别是G蛋白偶联受体及其相关的第二信使通路，并介绍了生长因子和黏附分子介导的信号转导，包括蛋白质的磷酸化和肌醇脂类在信号转导中的作用。而在本版（第二版）中，内容和篇幅都有较大的扩展。原有的章节也有进一步的充实和细化，总结了我们对信号转导的最新了解，如在第二十章对TGF-β信号通路的最新知识有较详尽的描述，并增加了许多的新内容，如核受体信号通路、与免疫有关的NF-κB信号通路、与发育有关的Notch信号通路，以及与癌症治疗有关的信号通路的干预等。这些内容的充实大大提高了本书的参考价值。

在本版中，作者特别强调了分子结构如何决定蛋白功能。还继承了第一版的一个特点，即强调了信号转导的历史发现，有机地结合了历史上的重要文献和新近的研究发现，并为核心文献和历史性文献提供了详尽的参考资料。书中有大量漂亮的概念性彩图，可谓文图并茂，有助于对关键内容的理解。对高年级本科生、研究生和相关的科研教学人员而言，本书是一本非常有用的信号转导入门书和参考书。

陈晔光

北京　清华园

2010年2月2日

前　言

在介绍《信号转导》第一版时，我们问过一个问题："这本书是为谁而著?"最诚恳的回答是为我们自己而写。我们虔诚地希望这本书将为各个层次的学生和专业人员提供指导性和趣味性阅读。为什么要出第二版呢? 主要理由应该是，我们不仅受本领域的巨大进步而鼓舞，也受到多个非常好的评论和感谢函的鼓励。这些评论和信函为本书的撰写提供了建设性的意见和建议。

在此期间（约 7 年），"信号转导"涵盖的大领域无情地蔓延扩大，但随着时间的推移，现在不只是一个而是两个作者（BDG 和 PERT）已超过了英国大学里规定的年龄，至少关闭了自己的实验室，并离开自己的办公桌。因此，首先，我们两位老者很感激 IJsbrand Kramer 的重大贡献，他撰写了此新版本下半部的大部分。没有他就没有第二版的问世。然而，像以前一样，我们的目标始终是创作一个单一的文本，就像是一人构想、一人写作一样。这样，我们希望避免由多个专家撰写的但没有经过仔细编辑的内容。

虽然我们涉及了本学科的前沿，但是我们也试着纳入一些基本知识，并介绍一些历史背景。当然，我们知道有些重要内容应该放到"信号转导"内，没有把它们纳入会有争议，但是我们认为不可能面面俱到。但是，在这新版中忽略的内容与第一版不同。被去除的部分主要是与细胞周期和凋亡有关，而新增加的内容有核受体、发育和肿瘤治疗。像从前一样，通过此书的写作，我们受益颇丰，当我们知道的越多，我们越有勇气去挑战，至少可以去重新检验一些被公认的教条。我们也学会了尊重前人的智慧，正是他们在 19 世纪和 20 世纪初期的无所束缚的思想和一些偶然的发现，导致了现代学科的建立，如生理学、药理学、细胞生物学，以及一些相关的临床学科，特别是内分泌学和免疫学。

本书分为两部分：前九章介绍所谓"经典"信号转导的基本内容，主要集中在激素及其受体，第二信使的产生及其作用，特别是环核苷酸和钙离子。正是由于此领域的发展，特别是 G 蛋白的发现，导致了"信号转导"（signal transduction）这一词的使用，虽然"transduction"是从其他地方借用过来的（见后面的定义）。第十章扩展了这种模式，介绍在核内影响转录的细胞内受体。然后，在第十一至第二十三章，主要介绍生长因子和黏附分子介导的信号转导过程，特别是通过蛋白质的共价修饰和含肌醇的脂类，如磷酸化、去磷酸化、切割或泛素化。此领域研究的一个重要目的是试图了解导致癌症的细胞转化机制，希望能寻找到有效的治疗方法。最后，第二十四章反射一个贯穿本书的主题，即蛋白结构域的概念和它们在信号转导中的重要性。

在本书的写作过程中，许多朋友和同事给我们提供了很多有益的建议和想法，他们包括：John Blenis（Boston），Alex Bridges（Ann Arbor），Zhijan Chen（Dallas），Jean Dessolin（Bordeaux），Elisabeth Genot（Bordeaux），John Kuriyan（Dallas），Michel Laguerre（Bordeaux），Patrick Lemaire（Marseille），David Litchfield（London，Ontario），Alfonso Martinas Arias（Cambridge，UK），Joan Massagué（New York），Juan Modolell（Madrid），Alexandra Newton（La Jolla），François Schweisguth（Paris），Pat Simpson（Cambridge，UK），Nick Tonks（Cold Spring Harbor），Colin Ward

(Parkville)，Xuewu Zhang (Dallas)。Geoffrey Strachan 建议把法文和德文译成同时期(19 世纪) 的英文。

还有其他许多人，无法在此一一列出他们的名字，他们的知识使我们受益匪浅。为了感谢他们的贡献，我们在这里引用了信号转导的先驱之一所写的文章[1]：

《关于皮特尤里》作者 Sydney Ringer，M. D. 和 William Murrell，M. R. C. P. 威斯敏斯特医学院应用生理学讲师，皇家胸科医院助理内科医生

不久以前，伦敦大学的一个学生（很遗憾，我们忘记了他的名字）给了我们一小袋皮特尤里（Pituri）的枝叶，这是一种有趣的药物。我们把它给了 Gerrard 先生，而他从中提取到了微量的生物碱，并以 1∶20 的比例配成了一些水溶液。在研究了皮特尤里的叶子后，Baron Mueller 认为它是来源于一种名叫 Duboisia Hopwoodii 的灌木。皮特尤里生长在 Darling 河和 Barcoote 至西澳大利亚的沙漠灌丛中。据说当地人在长途跋涉中靠咀嚼它的叶子来增强体质，正像玻利维亚人用可可叶子一样。Bennett 博士在 1873 年 5 月新南威尔士医学报上撰文说皮特尤里是一种刺激性麻醉剂，新南威尔士人服用它正像东方人吃槟榔一样，它似乎是烟草的代替品。它一般以干叶子出售，通常被磨成粉，所以人们看不出它原来是什么样的。

皮特尤里只限于 Mallutha 族的男人们服用。在真正服用之前，他们只咀嚼一匙左右的干叶子，跟一些枝叶烧成的灰混在一起，稍稍咀嚼后就放在耳后（据说这样做可增强它的药效），然后不时地嚼一嚼，直到最后被吞服。在服用后，当地人在谈生意或决斗时就会勇气十足。当服用过量时，它会使人狂怒。对于不习惯服用它的人，皮特尤里会引起严重的头痛。

当然，这篇文章的作者当时根本没听过“信号转导”这个词，它是一百年后才在生物学文献中出现的。Ringer 和 Murrell 所描述的生物碱皮特尤里与阿托品的药理特征有一些共性（如增加勇气，引起狂怒、失意、头痛），这些感觉在我们编写此书时并不陌生。本领域和其他领域的学生和研究人员也将会熟悉这些感觉。让我们话归主题。当 Ringer 检测皮特尤里对 4 名男性的作用时，他注意到皮特尤里也引起困倦、虚弱无力、脸色苍白、眩晕、呼吸加快、瞳孔放大、细弱和惊厥抽搐，并且高剂量会增加大量的唾液分泌[2]。皮特尤里也拮抗 Muscarine 对心脏的作用。这并不是我们的经验，这也使人们怀疑在他们的学生、同事、雇工中，谁会心甘情愿或不怎么情愿地把自己当成实验用的豚鼠，从而推进科学进步。Ringer 和他的朋友们有意回避进行自我实验的会员资格，这些进行自我实验的名人包括呼吸过一氧化氮和其他毒气的 Humphry Davey 爵士；呼吸过致死气体的 John Scott Haldane；还有最近的 Barry Marshall，他吞过幽门杆菌来证明它能引起胃溃疡，与 Robin Warren 一起获得 2005 年的诺贝尔生理医学奖。这群体的另一成员 Charles Edouard Brown-Séquard 在第一章中有重点描述。

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1. Ringer S, Murrell W. On pituri. *J Physiol*. 1878：377-383.
2. Ringer S. On the action of pituri on man. *Lancet*. 1879：290-291.

来自《简明牛津英语词典》（1994 年第三版，1977 年修订，牛津大学出版社）：

Transduction (trɒnsˌdʌ·kʃən). *rare.* 1656. [ad. L. *tra(ns)ductionem*, *tra(ns)ducere*; see TRADUCE.] The action of leading or bringing across.

Traduce (trădiū·s), *v.* 1533. [ad. L. *traducere* to lead across, etc.; also, to lead along as a spectacle, to bring into disgrace; f. *trans* across + *ducere* to lead.] †1. *trans.* To convey from one place to another; to transport -1678. †b. To translate, render; to alter, modify, reduce -1850. †c. To transfer from one use, sense, ownership, or employment to another -1640. †2. To transmit, esp. by generation -1733. †b. *transf.* To propagate -1711. †c. To derive, deduce, obtain *from* a source -1709. 3. To speak evil of, esp. (now always) falsely or maliciously; to defame, malign, slander, calumniate, misrepresent 1586. †b. To expose (to contempt); to dishonour, disgrace (*rare*) -1661. †4. To falsify, misrepresent, pervert -1674.

1. b. Milton has been traduced into French and overturned into Dutch SOUTHEY. a. Vertue is not traduced in propagation, nor learning bequeathed by our will, to our heires 1606. 3. The man that dares t., because he can With safety to himself, is not a man COWPER. b. By their own ignoble actions they t., that is, disgrace their ancestors 1661. 4. Who taking Texts .. traduced the Sense thereof 1648. Hence **Tradu·cement**, the, or an, action of traducing; defamation, calumny, slander. **Tradu·cingly** *adv.*

来自《牛津英语词典》（第二版，2008 年，牛津大学出版社）网络版：

Transduction 的定义：

1. 下传或跨过的作用；
2. 转导信号的作用或过程；
3. （微生物学）使用病毒或病毒型颗粒把遗传物质从一个细胞转移到另一个细胞。

注　释

我们使用如下的蛋白结构数据：

• 蛋白数据库（Protein Data Bank）（http：//www. pdbr. org）：H. M. Berman，J. Westbrook，Z. Feng et al.，The protein data bank. Nucleic Acid Res 28，235-242（2000）.

• 化学结构：我们使用 EPSRC 的 Chemical Database Service at Daresbury：D. A. Fletcher，R. F. McMeeking，and D. Parkin，The United Kingdom Chemical Database Service，J Chem Inf Comput Sci 36，746-749（1996）.

大部分的蛋白结构用如下的软件生成：

• PyMOL（Warren Delano，Delano Scientific LLC，Palo Alto，USA；http：//www. delanoscientific. com/）.

其他结构用如下的软件生成：

• RasMol（Roger Sayle and E. James Milner-White，RasMol：Biomolecular graphics for all，Trends Biochem Sci 20，374（1995））

• CHIME（Eric Martz，Universisty of Massachusetts，Amherst，MA，USA and MDL Information Systems，Inc.，San Leandro，CA，USA.）

如何观看分子结构的立体图

立体图比常见的平面图有多得多的信息。互联网上有看立体图的便宜方法。但是，只要做点努力，大多数人都能学会用肉眼看立体图，除非某人正好不幸有眼疾，如弱视。实践是关键。

从立体对图中，有两种方法能看到三维图。你可让视觉交叉，即左眼看右边的图而右眼看左边的图，或者让眼岔开，即每只眼看它前面的图。电脑产生的图往往是分岔的图。为了看本书中的图（和大部分的印刷图），你应该用左眼看左边的图，右眼看右边的图。如果两眼没法合成一张三维图，试试如下的方法：首先，把你的鼻子挨到立体对图之间和下面。两个图像会重叠，但是图像会模糊不清（虽然这时你可能注意到一些三维性）。然后，把纸慢慢地拿开，但小心别转动纸，把注意力集中在三维图上，等到眼睛聚焦。注意，如果你试着用聚合方法去看分岔的一对图，图会是三维，但是会倒位。

参考资料

我们试图为几乎所有的叙述、所讨论的实验和发现提供原始的文献来源，主要原因是本书所涉及的领域众多，已远远超过我们已有的经验或专长。因此，翔实的文献引用可以确保我们下笔有据，我们所写的并不是简单的凭空想象。另外，因为我们把引用原始的历史材料作为本书的一大特点，所以把现代文献引入也符合逻辑。我们希望这本书能起到有价值的资源作用，任何人想进一步了解的话都能找到基本文献综述。

缩写

过去，许多有生物活性的分子和蛋白质（主要是酶）的名字与它们的作用或功能有

关，缩写也被很好地建立并一目了然。最近，由于大量新基因产物的出现，命名和缩写变得完全随机了。为了不被一连串的笨拙定义和翻译而打乱正文，每章（第 12 章后）后附有专用的表，列出名字和它们的缩写以及它们在 SwissProt 和 OMIM 数据库中的获取号。

基因和基因产物

按惯例，首字母是小写时指基因（如 ras），而首字母是大写时指蛋白产物（Ras）。酵母基因是大写（RAS）。前缀 v-和 c-特指病毒或细胞来源（v-Ras，c-Ras）。

氨基酸

通常使用的是标准的三连字母缩写。当不方便或不适合用三连字母缩写时，就使用单字母符号。下表列出两种缩写：

Amino acid	Three-letter code	Single-letter code
Alanine	Ala	A
Arginine	Arg	R
Asparagine	Asp	N
Aspartate	Asp	D
Cysteine	Cys	C
Glutamate	Glu	E
Glutamine	Gln	Q
Glycine	Gly	G
Histidine	His	H
Isoleucine	Ile	I
Leucine	Leu	L
Lysine	Lys	K
Methionine	Met	M
Phenylalanine	Phe	F
Proline	Pro	P
Serine	Ser	S
Threonine	Thr	T
Tryptophan	Trp	W
Tyrosine	Tyr	Y
Valine	Val	V

（陈晔光　译）

Preface

Introducing the first edition of *Signal Transduction*, we asked the question, for whom had this book been written, and the simplest response was that it had been written for ourselves. We added the pious hope that it might also be instructive and entertaining for students and professionals at many levels. So why a second edition? The main reasons must be that we have not only been spurred on by the enormous progress in the field but also encouraged by a number of very favourable reviews and letters of appreciation that have offered constructive criticism and new ideas for the development of the text.

In the intervening period (around seven years), the general territory covered by the expression 'signal transduction' has spread inexorably wider, but with the passing of time, not just one, but now two of the authors (BDG and PERT) have gone beyond the age at which it is normal, in British universities at least, to close up their labs and depart their desks. So at the outset, it is beholden on these two greybeards to acknowledge the major contribution of IJsbrand Kramer who undertook the drafting of most of the second half of this new edition. Without him, there would be no second edition. Yet, as before, the aim throughout has been to create a single text as if conceived by one mind, written by one hand. In this way, we hope that it avoids the worst excesses of the skimpily edited texts compiled from articles by multiple specialist authors.

Although we have touched the leading edges of the subject, we have also endeavoured to provide an elementary basis with some historical background to all the topics covered. There has been no attempt to be comprehensive and we are aware that many important topics that well qualify for inclusion are conspicuous only by their absence. However, the omissions in the new edition are not the same as those of the first. Gone now are the major sections on the cell cycle and apoptosis; instead we have new chapters covering nuclear receptors, development, and cancer therapy. As previously, we have been the main beneficiaries as students of our own subject. As we learned more, we were encouraged to challenge, or at least to re-examine, some of the well-established dogmas. We have also learned to respect the wisdom of our forebears, whose freedom of thought and sometimes serendipitous discoveries in the 19th and early 20th centuries led to the creation of the modern sciences of physiology, pharmacology, biochemistry, and cell biology, and related clinical fields, especially endocrinology and immunology.

The book conveniently divides in two parts. The first nine chapters provide the nuts and bolts of what might be termed 'classical' signal transduction.

They concentrate mainly on hormones, their receptors, and the generation and actions of second messengers, particularly cyclic nucleotides and calcium. It was the advances in this area, particularly the discovery of the G proteins, that originally gave rise to the expression 'signal transduction', although the word 'transduction' was stolen from elsewhere (see definitions, below). Chapter 10 extends the paradigm, dealing with the intracellular receptors that, in the nucleus, influence transcription. Then, in Chapters 11–23, attention is concentrated on processes set in action by growth factors and adhesion molecules, particularly through the covalent modification of proteins and inositol-containing lipids, for example by phosphorylation, dephosphorylation, cleavage or ubiquitylation. An important, though not exclusive, impetus to research in this area has been the quest to understand the cellular transformations underlying cancer, with the hope of devising effective therapeutic procedures. Finally, Chapter 24 reflects back on a theme that runs throughout the book. It deals with the concept of protein structural domains and illustrates their central importance in signalling mechanisms.

In preparing the book, we have had the benefit of advice and opinions from many friends and colleagues. These include John Blenis (Boston), Alex Bridges (Ann Arbor), Zhijan Chen (Dallas), Jean Dessolin (Bordeaux), Elisabeth Genot (Bordeaux), John Kuriyan (Dallas), Michel Laguerre (Bordeaux), Patrick Lemaire (Marseille), David Litchfield (London, Ontario), Alfonso Martinas-Arias (Cambridge, UK), Joan Massagué (New York), Juan Modolell (Madrid), Alexandra Newton (La Jolla), François Schweisguth (Paris), Pat Simpson (Cambridge, UK), Nick Tonks (Cold Spring Harbor), Colin Ward (Parkville), Xuewu Zhang (Dallas). Geoffrey Strachan advised on the translation of French and German texts into contemporary (19th century) English.

Many others, too numerous to name individually, have given us the benefit of their knowledge and understanding. In acknowledgement of their contribution we offer the following quotation by one of the pioneers of signal transduction:[1]

Of course, the authors of this paper would themselves never have recognized the expression 'signal transduction' and it would be a further 100 years before it made its appearance in the biological literature. The sensations brought about by pituri, an alkaloid that according to Ringer and Murrell induces some of the pharmacological effects of atropine (courage, infuriation, frustration, and headaches), are not dissimilar to those experienced by us in the writing of this book. Indeed, they will be familiar to any students and investigators in this and other fields of research. However, we should not take this too far. When Ringer tested the effects of the application of pituri on four men,[2] he noted that it also caused drowsiness, faintness, pallor, giddiness, hurried and superficial breathing, dilatation of the pupils, general weakness with convulsive twitchings and in large doses copiously increased salivary secretion.

ON PITURI. By SYDNEY RINGER, M.D., and WILLIAM MURRELL, M.R.C.P., *Lecturer on Practical Physiology at the Westminster School of Medicine, and Assistant Physician to the Royal Hospital for Diseases of the Chest.*

QUITE recently a student of University College, London, whose name we have unfortunately forgotten, gave us a small packet containing a few twigs and broken leaves of the powerful and interesting drug Pituri. These we placed in Mr Gerrard's hands, and he kindly made first an extract from which he obtained a minute quantity of an alkaloid, and with this he made a solution containing one part of the alkaloid to twenty of water.

Baron Mueller, from an examination of the leaves of pituri, is of opinion that it is derived from Duboisia Hopwoodii. Pituri is found growing in desert scrubs from the Darling River and Barcoote to West Australia. The natives, it is said to fortify themselves during their long foot marches, chew the leaves for the same purpose as Cocoa leaves are used in Bolivia. Dr G. Bennett in the New South Wales Medical Gazette, May, 1873, says Pituri is a stimulating narcotic and is used by the natives of New South Wales in like manner as the Betel of the East. It seems to be a substitute for tobacco.

It is generally met with in the form of dry leaves, usually so pulverized that their character cannot be made out.

The use of pituri is confined to the men of a tribe called Mallutha. Before any serious undertaking, they chew these dried leaves, using about a tea-spoonful. A few twigs are burnt and the ashes mixed with the leaves. After a slight mastication the bolus is placed behind the ear (to increase it is supposed its strength), to be again chewed from time to time, the whole being at last swallowed. The native after this process is in a sufficiently courageous state either to transact business or to fight. When indulged in to excess, it is said to induce a condition of infuriation. In persons not accustomed to its use pituri causes severe headache.

It also antagonized the action of muscarine on the heart. This has not been our experience, which leads one to wonder who, among their students, colleagues, and servants may have offered themselves up as willing – or perhaps less than willing – guinea pigs in the furtherance of scientific research. Ringer and his friends apparently eschewed membership of the very honourable brotherhood of self-experimenters of which the more famous members include Sir Humphry Davey, who breathed nitrous oxide as well as other more noxious gases; John Scott Haldane, who too inhaled lethal gases; and more recently Barry Marshall, who swallowed a culture of *Helicobacter pylori* to show that it caused stomach ulcers and who with Robin Warren was awarded the Nobel Prize in Physiology or Medicine in 2005. Another member of this

fraternity, Charles Edouard Brown-Séquard, figures prominently in the first chapter.

References

1. Ringer S, Murrell W. On pituri. *J Physiol.* 1878:377–383.
2. Ringer S. On the action of pituri on man. *Lancet.* 1879:290–291.

From the Shorter Oxford English Dictionary (3rd edition, 1994, with corrections 1977, © Oxford University Press:

Transduction (trɑnsˌdʌ·kʃən). *rare.* 1656. [ad. L. *tra(ns)ductionem, tra(ns)ducere*; see TRADUCE.] The action of leading or bringing across.

Traduce (trădiū·s), *v.* 1533. [ad. L. *traducere* to lead across, etc.; also, to lead along as a spectacle, to bring into disgrace; f. *trans* across + *ducere* to lead.] †1. *trans.* To convey from one place to another; to transport –1678. †b. To translate, render; to alter, modify, reduce –1850. †c. To transfer from one use, sense, ownership, or employment to another –1640. †2. To transmit, esp. by generation –1733. †b. *transf.* To propagate –1711. †c. To derive, deduce, obtain *from* a source –1709. 3. To speak evil of, esp. (now always) falsely or maliciously; to defame, malign, slander, calumniate, misrepresent 1586. †b. To expose (to contempt); to dishonour, disgrace (*rare*) –1661. †4. To falsify, misrepresent, pervert –1674.

1. b. Milton has been traduced into French and overturned into Dutch SOUTHEY. 2. Vertue is not traduced in propagation, nor learning bequeathed by our will, to our heires 1606. 3. The man that dares t., because he can With safety to himself, is not a man COWPER. b. By their own ignoble actions they t., that is, disgrace their ancestors 1661. 4. Who taking Texts .. traduced the Sense thereof 1648. Hence **Tradu·cement**, the, or an, action of traducing; defamation, calumny, slander. **Tradu·cingly** *adv.*

From the Oxford English Dictionary (2nd edition, 2008 © Oxford University Press) online:

transduction

(trɑːnsˈdʌkʃən, træns-) [ad. L. *transductiōn-em* (usually *trāductiōnem*), n. of action f. *tra(ns)dūcĕre*: see TRADUCE.]

1. The action of leading or bringing across. *rare.*

1656 BLOUNT *Glossogr.*, *Transduction*, a leading over, a removing from one place to another. **a1816** BENTHAM *Offic. Apt. Maximized, Introd. View* (1830) 19 In lieu of *adduction*, as the purpose requires, will be subjoined *abduction, transduction*,..and so forth.

2. The action or process of transducing a signal.

1947 *Jrnl. Acoustical Soc. Amer.* XIX. 307/1 It is rather interesting..that the direct method of electronic transduction, instead of the indirect method of employing a conventional transducer and then amplifying the output with a vacuum tube, has not been developed. **1970** J. EARL *Tuners & Amplifiers* iv. 87 Low impedance pickup cartridges..using the moving-coil principle of transduction. **1975** *Nature* 17 Apr. 625/1 The transduction of light energy into neural signals is mediated in all known visual systems by a common type of visual pigment.

3. *Microbiology*. The transfer of genetic material from one cell to another by a virus or virus-like particle.

1952 ZINDER & LEDERBERG in *Jrnl. Bacteriol.* LXIV. 681 To help the further exposition of our experiments, we shall use the term transduction for genetically unilateral transfer in contrast to the union of equivalent elements in fertilization. **1960** [see F III. 1l]. **1971** *Nature* 18 June 466/1 It has been suggested that transduction of genes by viruses was an important mechanism in evolution for spreading useful mutations between organisms not formally related. **1977** *Lancet* 9 July 94/2 These were derived by selection of sensitive variants from gentamicin-resistant strains or by transduction of this resistance to sensitive strains.

Hence **transˈductional** *a.*, of or pertaining to (genetic) transduction.

1956 *Genetics* XLI. 845 (*heading*) Linear inheritance in transductional clones. **1980** *Jrnl. Gen. Microbiol.* CXIX. 51 Transductional analysis revealed that one of the four mutations carried by strain T-693 was responsible for constitutive synthesis of both isoleucine and threonine biosynthetic enzymes.

Notes

For protein structural data we have made use of:

- The Protein Data Bank (http://www.pdbr.org): H. M. Berman, J. Westbrook, Z. Feng et al., The protein data bank. Nucleic Acid Res 28, 235–242 (2000).
- For chemical structures we wish to acknowledge the use of the EPSRC's Chemical Database Service at Daresbury: D. A. Fletcher, R. F. McMeeking, and D. Parkin,The United Kingdom Chemical Database Service, J Chem Inf Comput Sci 36, 746–749 (1996).

Most of the protein structures were generated using the following software:

- PyMOL (Warren Delano, Delano Scientific LLC, Palo Alto, CA, USA; http://www.delanoscientific.com/).

Other structures were obtained using

- RasMol (Roger Sayle and E. James Milner-White, RasMol: Biomolecular graphics for all, Trends Biochem Sci 20, 374 (1995))
- CHIME (Eric Martz, University of Massachusetts, Amherst, MA, USA and MDL Information Systems, Inc., San Leandro, CA, USA.)

How to view stereo images of molecular structures

There is much more information in a stereoscopic image than in a conventional flat projection. Inexpensive viewers for looking at stereo pairs are available via the Internet, but with a little effort most people can learn how to view stereo images with unaided eyes, unless you are unfortunate enough to have an ophthalmological condition such as one very weak eye. Practice is the key.

There are two ways of seeing a 3D image by observing a stereo pair. You may either cross your eyes, so that the left eye views the right-hand image and vice versa, or you may allow your eyes to diverge, so that each eye looks at the image in front of it. Computer-generated images are usually for divergent viewing. To view the images in this book (and most printed images), you should view the left image with the left eye and the right image with the right eye. If the two do not readily fuse into a single 3D image, try the following.

First touch your nose to the page between and below the stereo pair. The two images will now be superimposed, but the picture will be very

blurred (although you may notice some three-dimensionality at this stage). Now move the page slowly away from you, but take care not to rotate it. Concentrate on the 3D aspect and wait for your eyes to bring it into focus.

Note that if you attempt to view a divergent pair using the convergent strategy (crossed eyes) the image will be 3D but inverted in a confusing way.

References

We have tried to provide original text sources to nearly all the statements, experiments, and discoveries discussed. The main reason for this is that we ourselves have necessarily had to extend the treatment of nearly all the topics presented far beyond the areas of our own experience or expertise. Thus, the comprehensive lists are there to provide us with some sort of reassurance that what we have written has not simply been conjured out of the air. Also, because we have made a particular feature of presenting original historical source material by quotation, which necessarily required referencing, it seemed logical also to include literature references to modern sources as well. Thus we hope that this book may serve as a valuable resource, in the manner of a basic literature review, for anyone wanting to explore further.

Abbreviations

Historically, the names of many biologically active compounds and proteins (mainly enzymes) were related to effect or function and the abbreviations are well established and fairly obvious. More recently, as waves of new gene products have landed upon the literature, the matter of naming and abbreviation has become completely random. In order not to disrupt the text with a succession of clumsy definitions and translations, dedicated tables have been appended at the end of each chapter (from Chapter 12 onwards), linking the names to their abbreviations and their accession numbers in the SwissProt and OMIM databases.

Genes and gene products

According to convention, acronyms and abbreviations printed in lower case indicate genes (e.g. ras). When capitalized, they indicate their protein products (Ras). The genes of yeast are printed in upper case (RAS). The prefixes v- and c- indicate viral or cellular origin (v-Ras, C-Ras).

Amino acids

Generally the standard three-letter abbreviations are used. Where this is inconvenient or otherwise unsuitable, the single-letter codes have been used. Both sets of abbreviations are listed in the following table.