

ENCYCLOPEDIA OF

MOLECULAR BIOLOGY

VOLUME 1

Thomas E. Creighton

European Molecular Biology Laboratory
London, England



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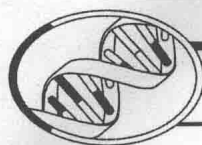
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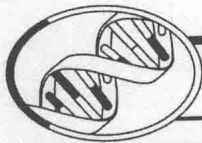
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PREFACE

The Wiley Biotechnology Encyclopedias, composed of the *Encyclopedia of Molecular Biology*, the *Encyclopedia of Bioprocess Technology: Fermentation, Biocatalysis, and Bioseparation*, the *Encyclopedia of Cell Technology*, and the *Encyclopedia of Ethical, Legal, and Policy Issues in Biotechnology*, cover very broadly four major contemporary themes in biotechnology. The series comes at a fascinating time in that as we move into the twenty-first century, the discipline of biotechnology is undergoing striking paradigm changes.

Biotechnology is now beginning to be viewed as an informational science. In a simplistic sense, there are three types of biological information. First, there is the digital or linear information of our chromosomes and genes, with the four-letter alphabet composed of G, C, A, and T (the bases Guanine, Cytosine, Adenine, and Thymine). Variation in the order of these letters in the digital strings of our chromosomes or our expressed genes (or mRNAs) generates information of several distinct types: genes, regulatory machinery, and information that enables chromosomes to carry out their tasks as informational organelles (eg, centromeric and telomeric sequences).

Second, there is the three-dimensional information of proteins, the molecular machines of life. Proteins are strings of amino acids employing a 20-letter alphabet. Proteins pose four technical challenges: (i) Proteins are synthesized as linear strings and fold into precise three-dimensional structures as dictated by the order of amino acid residues in the string. Can we formulate the rules for protein folding to predict three-dimensional structure from primary amino acid sequence? The identification and comparative analysis of all human and model organism (bacteria, yeast, nematode, fly, mouse, etc.) genes and proteins will eventually lead to a lexicon of motifs that are the building block components of genes and proteins. These motifs will greatly constrain the shape space computational algorithms must search to successfully correlate primary amino acid sequence with the correct three-dimensional shapes. The protein-folding problem will probably be solved within the next 10 to 15 years. (ii) Can we predict protein function from knowledge of the three-dimensional structure? Once again the lexicon of motifs with their functional as well as structural correlations will play a critical role in solving this problem. (iii) How do the myriad of chemical modifications of proteins (eg, phosphorylation, acetylation) alter their structures and modify their functions? The mass spectrometer will play a key role in identifying secondary modifications. (iv) How do proteins interact with one another and/or with other macromolecules to form complex molecular machines (eg, the ribosomal subunits)? If these functional complexes can be isolated, the mass

spectrometer, coupled with a knowledge of all protein sequences that can be derived from the complete genomic sequence of the organism, will serve as a powerful tool for identifying all the components of complex molecular machines.

The third type of biological information arises from complex biological systems and networks. Systems information is four-dimensional because it varies with time. For example, the human brain has 1012 neurons making approximately 1015 connections. From this network arises systems properties such as a memory, consciousness, and the ability to learn. The important point is that systems properties cannot be understood from studying the network elements (eg, neurons) one at a time; rather, the collective behavior of the elements needs to be studied together. To study most biological systems, three issues need to be stressed. First, most biological systems are too complex to study directly; therefore they must be divided into tractable subsystems whose properties in part reflect those of the system. These subsystems must be sufficiently small to analyze all their elements and connections. Second, high-throughput analytic or global tools are required for studying many systems elements at one time (see below). Finally, the systems information needs to be modeled mathematically before systems properties can be predicted and ultimately understood. This will require recruiting computer scientists and applied mathematics into biology—just as the attempts to decipher the information of complete genomes and the protein folding and structure/function problems have required the recruitment of computational scientists.

I would be remiss not to point out that there are many other molecules that generate biological information—amino acids, carbohydrates, lipids, etc. These too must be studied in the context of their specific structures and specific functions.

The deciphering and manipulation of these various types of biological information represent an enormous technical challenge for biotechnology. Yet major new and powerful tools for doing so are emerging.

One class of tools for deciphering biological information is termed high-throughput analytic or global tools. These tools can study many genes or chromosome features (genomics), many proteins (proteomics), or many cells rapidly: large-scale DNA sequencing; genome-wide genetic mapping; cDNA or oligonucleotide arrays; two-dimensional gel electrophoresis and other global protein separation technologies; mass spectrometric analysis of proteins and protein fragments; multiparameter, high-throughput cell and chromosome sorting; and high-throughput phenotypic assays.

A second approach to the deciphering and manipulation of biological information centers around combinatorial strate-

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COMMONLY USED ACRONYMS AND ABBREVIATIONS

Å	angstrom (10^{-10} m)	G	Gibbs free energy of a system
Ab	antibody	G	guanine base
Ac	acetyl group	G-protein	guanine-nucleotide binding regulatory protein
ADP	adenosine diphosphate	GABA	g-aminobutyric acid
Ala	alanine residue (also A)	GalNAc	N-acetylgalactosamine residue
AMP	adenosine monophosphate	GdmCl	guanidinium chloride (guanidine hydrochloride)
Arg	arginine residue (also R)	GDP	guanosine diphosphate
Asn	asparagine residue (also N)	Glc	glucose residue
Asp	aspartic acid residue (also D)	GlcNAc	N-acetylglucosamine residue
ATP	adenosine triphosphate	Gln	glutamine residue (also Q)
ATPase	adenosine triphosphatase	Glu	glutamic acid residue (also E)
Bq	becquerel	Gly	glycine residue (also G)
bp	base-pair	GMP	guanoine monophosphate
BSA	bovine serum albumin	GSH	glutathione, thiol form
C	cytosine base	GSSG	glutathione, disulfide form
cal	calorie (4.18 J)	GTP	guanosine triphosphate
cAMP	3',5'-cyclic AMP	GTPase	guanosine triphosphatase
CD	circular dichroism	H	enthalpy of a system
CoA	coenzyme A	h	hour
cDNA	complementary DNA	His	histidine residue (also H)
cGMP	3',5'-cyclic GMP	HLA	histocompatibility locus antigen
Cmc	critical micelle concentration	HPLC	high pressure liquid chromatography
Cys	cysteine residue (also C)	Hz	hertz, frequency
Da	dalton	IEF	isoelectric focusing IgG, IgA, IgM, etc.
DMSO	dimethyl sulfoxide		immunoglobulin G, A, M. etc.
DNA	deoxyribonucleic acid	Ile	isoleucine residue (also I)
DNase	deoxyribonuclease	Ins	inositol residue
DTT	dithiothreitol	IR	infrared
EDTA	ethylenediamine tetraacetic acid	J	joule
EG	[ethylenbis(oxonitrilo)] tetraacetic acid	K	degrees Kelvin, absolute temperature
EGF	epidermal growth factor	k	rate constant for a specified reaction
ELISA	enzyme-linked immunosorbent assay	K_a	association constant
EM	electron microscopy	K_d	dissociation constant
EPR, ESR	electron paramagnetic (or sign) resonance	K_{eq}	equilibrium constant for a specified reaction
ER	endoplasmic reticulum	K_m	Michaelis constant
EXAFS	extended X-ray absorption fine structure	kb	kilobases
FAD	flavin-adenine dinucleotide	kcal	kilocalorie (4.18 kJ)
fMet	N-formyl methionine	kDa	kilodalton
FMN	flavin mononucleotide	LDL	low density lipoprotein
FPLC	fast protein liquid chromatography	Leu	leucine residue (also L)
		Lys	lysine residue (also K)

m	meter	RNase	ribonuclease
mAb	monoclonal antibody	RNP	ribonucleoprotein
Met	methionine residue (also M)	rRNA	ribosomal RNA
MHC	major histocompatibility locus		
min	minute	S	entropy of a system
mol	mole	S	Svedberg sedimentation unit (10^{-13} s)
M_r	relative molecular mass	s	second
mRNA	messenger RNA	s	sedimentation coefficient
MS	mass spectroscopy	SDS	sodium dodecyl sulfate
mtDNA	mitochondrial DNA	snRNA	small nuclear RNA
Mur	muramic acid residue	SRP	signal recognition particle
MurNAc	N-acetylmuramic acid residue		
		T	temperature
NAD ⁺	nicotinamide adenine dinucleotide (oxidized)	T	thymine residue
NADH	nicotinamide adenine dinucleotide (reduced)	TF	transcription factor
NADP ⁺	nicotinamide adenine dinucleotide phosphate (oxidized)	Thr	threonine residue (also T)
NADPH	nicotinamide adenine dinucleotide phosphate (reduced)	T_m	midpoint of temperature induced transition
NMR	nuclear magnetic resonance	Tri	tris(hydroxymethyl) aminomethane
		tRNA	transfer RNA
PAGE	polyacrylamide gel electrophoresis	Trp	tryptophan residue (also W)
PBS	phosphate-buffered saline	TTP	thymidine triphosphate
PCR	polymerase chain reaction	Tyr	tyrosine residue (also Y)
PEG	polyethylene glycol		
pH	negative logarithm of hydrogen ion concentration	U	uracil residue
		UDP	uridine diphosphate
Phe	phenylalanine residue (also F)	UMP	uridine monophosphate
P_i	inorganic phosphate	UTP	uridine triphosphate
PP_i	inorganic pyrophosphate	UV	ultraviolet
p.p.m.	parts per million		
Pro	proline residue (also P)	V	volume
		V_{max}	maximum enzyme catalyzed velocity
R	gas constant ($8.21451 \text{ J/(K}^1 \text{ mol}^{-1})$)	Val	valine residue (also V)
RIA	radioimmunoassay		
WT	wild-type		
RNA	ribonucleic acid	Xyl	xylose residue

CONVERSION FACTORS

SI Units (Adopted 1960)

The International System of Units (abbreviated SI), is being implemented throughout the world. This measurement system is a modernized version of the MKSA (meter, kilogram, second, ampere) system, and its details are published and controlled by an international treaty organization (The International Bureau of Weights and Measures) (1).

SI units are divided into three classes:

BASE UNITS

length	meter [†] (m)
mass	kilogram (kg)
time	second (s)
electric current	ampere (A)
thermodynamic temperature [‡]	kelvin (K)
amount of substance	mole (mol)
luminous intensity	candela (cd)

SUPPLEMENTARY UNITS

plane angle	radian (rad)
solid angle	steradian (sr)

DERIVED UNITS AND OTHER ACCEPTABLE UNITS

These units are formed by combining base units, supplementary units, and other derived units (2-4). Those derived units having special names and symbols are marked with an asterisk in the list below.

Quantity	Unit	Symbol	Acceptable equivalent
*absorbed dose	gray	Gy	J/kg
acceleration	meter per second squared	m/s ²	
*activity (of a radionuclide)	becquerel	Bq	1/s
area	square kilometer	km ²	
	square hectometer	hm ²	ha (hectare)
	square meter	m ²	
concentration (of amount of substance)	mole per cubic meter	mol/m ³	
current density	ampere per square meter	A/m ²	
density, mass density	kilogram per cubic meter	kg/m ³	g/L; mg/cm ³
dipole moment (quantity)	coulomb meter	C·m	

[†]The spellings "metre" and "litre" are preferred by ASTM; however, "-er" is used in the *Encyclopedia*.

[‡]Wide use is made of Celsius temperature (*t*) defined by

$$t = T - T_0$$

where *T* is the thermodynamic temperature, expressed in kelvin, and *T*₀ = 273.15 K by definition. A temperature interval may be expressed in degrees Celsius as well as in kelvin.

Quantity	Unit	Symbol	Acceptable equivalent
*dose equivalent	sievert	Sv	J/kg
*electric capacitance	farad	F	C/V
*electric charge, quantity of electricity	coulomb	C	A·s
electric charge density	coulomb per cubic meter	C/m ³	
*electric conductance	siemens	S	A/V
electric field strength	volt per meter	V/m	
electric flux density	coulomb per square meter	C/m ²	
*electric potential, potential difference, electromotive force	volt	V	W/A
*electric resistance	ohm	Ω	V/A
*energy, work, quantity of heat	megajoule	MJ	
	kilojoule	kJ	
	joule	J	N·m
	electronvolt [†]	eV [†]	
	kilowatt-hour [†]	kW·h [†]	
energy density	joule per cubic meter	J/m ³	
*force	kilonewton	kN	
	newton	N	kg·m/s ²
*frequency	megahertz	MHz	
	hertz	Hz	1/s
heat capacity, entropy	joule per kelvin	J/K	
heat capacity (specific), specific entropy	joule per kilogram kelvin	J/(kg·K)	
heat-transfer coefficient	watt per square meter kelvin	W/(m ² ·K)	
*illuminance	lux	lx	lm/m ²
*inductance	henry	H	Wb/A
linear density	kilogram per meter	kg/m	
luminance	candela per square meter	cd/m ²	
*luminous flux	lumen	lm	cd·sr
magnetic field strength	ampere per meter	A/m	
*magnetic flux	weber	Wb	V·s
*magnetic flux density	tesla	T	Wb/m ²
molar energy	joule per mole	J/mol	
molar entropy, molar heat capacity	joule per mole kelvin	J/(mol·K)	
moment of force, torque	newton meter	N·m	
momentum	kilogram meter per second	kg·m/s	
permeability	henry per meter	H/m	
permittivity	farad per meter	F/m	
*power, heat flow rate, radiant flux	kilowatt	kW	
	watt	W	J/s
power density, heat flux density, irradiance	watt per square meter	W/m ²	
*pressure, stress	megapascal	MPa	
	kilopascal	kPa	
	pascal	Pa	N/m ²
sound level	decibel	dB	
specific energy	joule per kilogram	J/kg	
specific volume	cubic meter per kilogram	m ³ /kg	
surface tension	newton per meter	N/m	
thermal conductivity	watt per meter kelvin	W/(m·K)	
velocity	meter per second	m/s	
	kilometer per hour	km/h	
viscosity, dynamic	pascal second	Pa·s	
	millipascal second	mPa·s	
viscosity, kinematic	square meter per second	m ² /s	
	square millimeter per second	mm ² /s	
volume	cubic meter	m ³	
	cubic decimeter	dm ³	L (liter) (5)
	cubic centimeter	cm ³	mL
wave number	1 per meter	m ⁻¹	
	1 per centimeter	cm ⁻¹	

[†]This non-SI unit is recognized by the CIPM as having to be retained because of practical importance or use in specialized fields (1).