

Index

24-well Linbro plates 79

A

AAS see polarization anisotropy of
anomalous scattering

ab-initio structure determination 494–500
hybrid method 526
versus substructure solution 495
see also direct methods

absence of prior knowledge 335

absences

data 454–7
integral 416
random 454
strong reflections 454–5
systematic 305–6, 374, 416, 561

absolute configuration 302

Bijvoet pairs 301–3
Flack parameter 635

absolute error 320–1

absorption 250, 284–97, 309

air 285

characteristic emissions 287

edges 284, 285–7

atomic number 293
chemical shifts 287
energies 294
selenomethionine labelling 173

fluorescence 287

heavy atoms 285

heavy elements 297

mass absorption coefficient 285

photon energy 284–5

spectroscopic terms 286

wavelength selection 289–91

absorption edge fine structure (XAS)
286–7

absorption edge scans 288–9

absorption near edge structure (XANES) 286–8

abstract writing 728

accuracy

central limit theorem 324
normal distributions 322
weighted averages 332–3

ACE see angiotensin-1 converting enzyme

acentric reflections

distributions 351, 361, 362–3
Patterson maps 486
Rice distribution 362–3
twinning 392–3

acentric structure factors 361, 364

acentric Wilson distributions 350

acetylcholine binding protein

(AChBP) 62

acetylcholinesterase (AChE) binding
pocket 716

N-acetylglucosaminyltransferase I
(GntI) 165–6

AChBP see acetylcholine binding protein

AChE see acetylcholinesterase

acid dissociation constants 48–9

acidic residues 43–4

activation 91–2

active sites

cholinesterases 716

crystallization 123–5

dissociation constants 123

kinases 715

ligands 670–1, 707–8

occupancy, *B*-factors 262–3, 277, 448–50

structure prediction 714–15

additives 87, 97–9

adenine 66

ADIT (computer program) 725

adjacent atom scattering 263–4

advanced cloning techniques 158–60

Advanced Light Source (ALS) 383

Advanced Photon Source (APS) 377

affinity tagging 84, 85, 167

histidine 85, 167

protein production 142

AFM see atomic force microscopy

air, X-ray absorption 285

alanine 28, 42, 220

alcohol 62

algebra

basic linear 740–3

probability 316–19

algorithms

crystallization optimization 121

evolutionary search 575–80

genetic 575

non-stochastic optimization 649–52

optimization 621

stochastic searches 652–4

allosteric binding 7

α/β -barrels 200–1

alpha carbons

protein data bank files 739

structure validation 717–19

trace identification 676–8

see also carbon backbone

α -helices 32–4, 677–8

α -turns 37–8

α -zingers 381

ALS see Advanced Light Source

Alzheimer's disease 716

amide bonds 29–32, 629–30

amide residues 45–6

amino acids 39–49

acidic residues 43–4

alanine 28, 42, 220

arginine 44

asparagine 45–6, 671–2, 701

aspartate 44

basic residues 44–5

charged residues 43–5

chirality/planarity 630–1

classification 40

cysteine 46–7, 162

glutamate 44

glutamine 45–6, 671–2, 701

glycine 43

histidine 44–5, 85, 167, 671–2, 701

hydrogen bonding 33–5, 39, 45–6, 50–2, 668

hydrophobic residues 42

isoleucine 42

left handed 40, 631

letter code 41

leucine 42

lysine 44

methionine 43

modified residues 48

phenylalanine 42

pK_a values 48–9

polar residues 45–7

proline 42–3

real space fitting 610–11

restraints 629–31

selenomethionine 16, 43, 125, 171–3,
536–9

serine 45

side chain interactions 49–54

surface entropy reduction 150–3

threonine 45

tryptophan 45–6

tyrosine 45

valine 42

see also residues; side chains

γ -aminobutyric acid (GABA), neuroreceptor
structure model 62–3

AMoRe (computer program) 579, 590

amphiphiles 128–30, 175

amplitude 15–16

electromagnetic waves 252

structure factors 275–7

X-ray diffraction 251

see also intensity

angiotensin-1 converting enzyme (ACE) 178

angles, scattering diagrams 256

anisotropy 263, 401–2

B-factors 636, 641, 659

birefringence 120

corrections, model building 610

displacement factors 636

ellipsoid 263, 483, 641

likelihood functions 596–7

manifestations in data 457

model building 640–5

scaling 17, 401–2, 483, 620, 641–2

tensors 291, 356, 636, 641

tests 427

translation-libration-screw

parameterization 642–4

truncation of data 642

annealing 387, 653

anodes (X-ray) 374, 375

anomalous correction coefficients 537–8

anomalous diffraction 16, 250, 288

absorption 284, 297

atomic scattering factors 260, 293

data collection 408–10

dispersive atom selection 292–3

electron density 447

Friedel's law 291–2

handedness ambiguity 507–8

heavy atom soaking 125–7

Patterson maps 465, 486

phasing 292–3, 477, 503, 508–9

polarization anisotropy 291

proteins 296

ratios 294

resonance 287–8

signal estimation 293–5

structure factors 283–4, 295–7

substructure phasing 477

transition metals 293

see also multi-wavelength anomalous
diffraction

anomalous dispersion see anomalous
diffraction

anomalous merging *R*-values 413, 530

anomalous scattering, see also

anomalous diffraction

anomalous scattering factor 288

antibody scaffolding 130–1, 174

apo-proteins 98

approximation see estimation

APS see Advanced Photon Source

area detectors 379–81

Argand diagrams 275–6, 280

arginine 44

arithmetic mean 325

ARP/*w*ARP (computer program)

automated ligand building 708–9

dummy atom refinement 657

model building 535, 675, 678

molecular replacement 590

artifacts, crystallization 83–4

asparagine 45–7, 671–2, 701

aspartate 44

assembly 81–2

associativity 226

assumptions

heavy atom refinement 514–16

model parameterization 623

asymmetric units 206–7

coordinate files 19–20

definition 208

Laue groups 298

molecular replacement 589–90

non-crystallographic symmetry 548–9

search algorithms 576–7

space groups 228–9

structure factors 279

asymmetry 208–11

atomic force microscopy (AFM) 92, 94, 388

atomic mass unit 754

atomic numbers, absorption edges 293

atomic positions

from distance vectors 489

heavy atom refinement 513–23

Patterson functions 468–9

atomic resolution 451–3
 atomic scattering factors 257, 259–61, 287–8
 B-factors 448
 Cromer–Mann coefficients 260
 definition 259
 electron density 261
 ions 260–1
 normalized structure factors 352
 ATOM records 725, 738–40
 autocorrelation 182, 466–7
 AutoDep (computer program) 725
Autographa californica 165
 autoinduction, *Escherichia coli* 163
 automar (computer program) 405
 automated ligand building 708–9
 automated model building 673–9
 ARP/wARP 675
 electron density maps 676–9
 multi-wavelength anomalous diffraction data 679–82
 automated search methods 492–4
 automated water building 656
 autoSHARP (computer program) 481, 526
 auxotroph labelling 171
 Avogadro number 754

B

Babinet's principle of complementarity 593
 β - α -motifs 56
Bacillus thuringiensis (Bt) 82, 161
 bacteria
 induction 162–3
 posttranslational modifications 160–1
 transformation 162–3
 bacterial membrane proteins 175
 baculovirus (BV) 165
 BALBES (computer program) 591
 BAP see biotin acceptor peptide
 β -barrels 61
 α/β -barrels 200–1
 bases see nucleotides
 basic local alignment search tool (BLAST) 146–7
 basic residues, properties 44–5
 basis vectors 215
 batch crystallization 105–6
 batch variation 85
 Bayes' factors 662, 695
 Bayesian inference 333–47, 367, 694
 definition 334
 negative intensities 343–5
 Bayes' theorem 318–19, 334–6
 prior knowledge, absence 335
 expression 336
 restraints 646
 BChE see butyrylcholinesterase
 B-DNA 65
 bending magnets 377
 benzodiazepines 62
 Bessel functions 358–9
 fast rotation 583
 heavy atom refinement 517
 X-ray term 647
 best estimates, weighted averages 333
 best map coefficients 461
 best phase 511–12
 β -bulges 36–7
 β -lactam rings 335
 β -sheets 36, 37, 455, 677–8
 β -strands 35–6, 61
 β -turns 37–8
B-factors 6, 259, 261–3, 447–50
 anisotropic displacement 641
 atomic scattering attenuation 263
 definition 262, 263
 electron density 447–50
 model building 620, 642, 644, 706–7, 709
 normalized structure factors 351–2
 overall 457, 620, 642
 partial occupancy 262–3, 277, 448–50
 positional uncertainties 659
 protein data bank files 739–40
 restraints 635–6
 scaling 355–7
 structure validation 706–7, 709
 tests (wilson plots) 427
 bias 317
 mental 695
 model 459, 462, 608
 phase 459, 462
 reduction 626–7
 solvent flipping 526

bias minimized maps 618, 656–7
 bidentate ligands 84
 Bijvoet pairs
 absolute configuration 301–3
 anomalous diffraction 288
 data collection strategies 396, 408
 peak data sets 289–90
 phasing equations 502–3
 structure factors 280
 substructure phasing 477
 wavelengths 293
 binding constants 123–5, 712–13, 715–16
 binding sites
 analysis 712–17
 crystallization 123–5
 kinases 715
 ligand density 671
 ligand validation 707–8
 prediction 714–15
 binning 356
 bioinformatics 145–53
 buried surface area 63–4
 sequence retrieval 146–7
 site prediction 148–9
 surface entropy reduction 150–3
 biotin acceptor peptide (BAP) 169
 birefringence 120
 bitopic membrane proteins 60–1
 BKP see Bragg–Kendrew–Perutz nomenclature
 BLAST see basic local alignment search tool
 BLASTN see nucleotide-level search
 BLASTP see protein sequence alignment searches
 BME see β -mercapto ethanol
 body centering 217–19
 Boltzmann constant 754
 bond angles 26–7
 restraints 629–30
 via metric tensor 744–5
 bond lengths, distances
 metal coordination 754
 restraints 629–30
 see also interatomic distances
 bond energies 50
 Bragg conditions 389
 Bragg equation 264–6
 from Laue equations 265
 in reciprocal lattice representation 270–1
 Bragg–Kendrew–Perutz (BKP) nomenclature 34
 Bravais centering 210
 space group determination 416
 Bravais lattices 216–19
 brilliance 267, 378
 Bt see *Bacillus thuringiensis*
 Buccaneer (computer program) 678
 buffers 80, 87, 99–101, 166
 bulk solvent correction 17, 591–3
 exponential model 592–3
 flat model 593
 model building 610, 620
 buried surface area 63–4
 Buster (computer program) 649
 butyrylcholinesterase (BChE) 716
 BV see baculovirus
 Byron's Bender 609

C

cadmium 99
 Cahn–Ingold–Prelog rules 302
 calcium-binding EF hand motif 56–7
 calcium ion coordination 57
 calmodulin 560–1
 capillary diffusion 107–8
 capillary mounting 126, 384
 capsid structure 26
 capturing the audience 728
 carbon backbone
 electron density tracing 676–7
 real space fitting 610–11
 structure validation 701–4
 torsion angles, validation 631–2
 see also α carbons; protein backbone
 carbon α -carbon α bonds 356
 carbon scattering factors 260
 carbonyl reductase 714
 Cartesian space
 conventions 553
 non-crystallographic symmetry 548, 552–6, 558–9
 rotations 552–5
 transformations 557, 558–9
 vectors 552
 Cartesian world coordinates 19–20, 232–4, 744
 case studies, structure validation 720–4
 CATH see Classes, Architecture, topology, Homologous superfamily database
 cathode ray tubes 374–5
 cations 99, 670, 681
 CC see correlation coefficients
 CCD see charge-coupled devices
 CD see circular dichroism spectroscopy
 cell-free (CF) expression 166–7
 cell membrane structure 6
 cell parameters 19–20
 cell refinement 421–2
 cellular retinoic acid binding protein (CRABP) 717–18
 centered lattices 217–19
 central limit theorem (CLT) 323–5, 366
 maximum likelihood 341–2
 random walks 348
 central moment, definition 315
 centric distributions 351
 centric reflections
 intensity distribution 305
 Patterson maps 485–6
 phase 276, 304
 reciprocal space 303
 centric structure factors, random atom models 348
 centric Wilson distributions, random atom models 349–50
 centric zones 303
 centroid phases
 computation 511–12
 cross-Fourier maps 491
 Sim weights 359
 single isomorphous replacement phasing 501–2
 centrosymmetry 217–19
 molecular scattering 266
 Patterson maps 467
 reciprocal lattices 242–3
 structure factors 279
 substructure solution 506
 CF see cell-free expression
 CFOM see combined figure of merit
 CHAINSAW (computer program) 577, 591
 chaperones 166–7
 characteristic emissions 287
 characteristic fluorescence 374
 characteristic radiation 372, 373–4
 charge, isoelectric point 83
 charge-coupled devices (CCD) 380–1, 455
 charged residues 43–5, 83
 charge flipping 500
 chemical modification 65–7
 chemical plausibility 6, 69–70, 712–13
 chemical shifts 287, 288
 Cheshire groups 489–90, 585–6
 Chinese hamster ovary (CHO) cells 165–6
 chirality
 α -helix 32–4
 amino acids 630–1
 asymmetry 208–9
 centres 27–8
 circular dichroism 183–5
 mirror planes 220
 PP-II helix 35
 restraints 630–1
 symmetry operations 203
 chiral point groups 225
 chiral space groups 214, 219–23, 227, 244, 300–6
 absolute configuration 302–3
 systematic absences 306
 Chi-squared 326
 chloride ion coordination 681
 CHO see Chinese hamster ovary cells
 cholinesterase inhibitors 716
 cholinesterases 716
 chromatin 70–1
 chromatography 85
 chromium anodes 374
 circular dichroism (CD) spectroscopy 183–5
 cis-peptides
 bonds 29–30
 protein data bank files 737
 Classes, Architecture, topology, Homologous (CATH) superfamily database 57–8
 classification
 amino acids 40
 helices 34

- membrane proteins 59–61
- turns 37–8
- clathrates 90
- cleavage planes 83
- cleavage sequences 168
- cloning 142–3, 154–5, 158–60
 - advanced techniques 158–60
 - directional 154–5
 - protein production 142–3
- closed groups 225–6
- closed packed lattices 549
- Clostridium botulinum* neurotoxin 55
- closure 203, 225, 509–10, 513–14
- CLT see central limit theorem
- ClustalW2* (computer program) 146–7
- CMC see critical micelle concentration
- CMOS see sensitive complementary metal oxide semiconductors
- CNS (computer program)
 - macromolecular refinement 629, 632, 634, 642, 645, 648–9
 - molecular replacement 579, 590
 - optimization 651
 - restrained maximum likelihood refinement 649
 - rotations 553
 - slow cooling protocol 654
 - substructure solution 481
 - translation searches 494
- co-crystallization 122–7
- codons 162
- co-expression 169–70
- cofactors 87, 97–9
- coherence 250, 251, 267
- collimators 376
- colony PCR 155
- color symmetry 211
- combinatorial design 144, 155–7, 158
 - directed evolution 156–7
 - DNA shuffling 157
 - random DNA truncation/fragmentation 155–6
- see also stochastic design
- combinatorial libraries 189
- combined figure of merit (CFOM) 423
- combined map averaging 569–71
- commensurately modulated structures 406
- commensurately modulated
 - superstructures 560–1
- COMO (computer program) 579, 590
- competent cell transformation 162–3
- competitive replacement 123–5
- complementarity, Babinet's principle 593
- complementary strands 65
- completeness, of diffraction data 414–15, 455–6
- complex conjugates 254
- complexes 25
- complex numbers 253–5
- Compton scattering 256
- Compton sources (CS) 372, 379
- concanavalin A 37, 161
- concentration 85
- conditional distributions 357–65
 - error reduction 359–61
 - expression 316, 357
 - model errors 364
 - non-crystallographic symmetry 549
 - structure factors 357–65
- conditional structure factor probabilities 361
- conditioning information 337–8
- confidence intervals 317, 322
- conformation 7
 - analysis 179–88, 190–1
 - nuclear magnetic resonance spectroscopy 185–6
 - side chains 47–8, 672–3
- conjugate gradient minimization 652
- conjugate phase 280
- connectivity 523
- consensus sequences 132–3
- constrained-restrained least squares refinement (CORELS) 629
- constraints 32, 620, 627–9
- contamination 85
- contour levels 449–51
- contrast, of map 261, 523, 534
- convergence 620, 640, 664
- convergence radius 614
- conversions
 - between ZXZ and XYZ conventions 553
 - energy 754
- convolution 182, 445
 - electron density autocorrelation 466–7
 - Fourier's theorem 442–5
 - Gaussian functions 445
 - Patterson functions 466–7, 468
 - real space 444
 - reciprocal space 444
 - residue identification 679
 - Sayre's equation 496
- convolution integrals 444–5, 567–8
- convolution theorem 442, 567–8
- CONVROT (computer program) 553, 558
- cooling 5
 - charge-coupled devices 381
 - X-ray generators 374–5
 - see also cryo...
- coordinate files 19–20
- deposition 725
- formats 737–40
- coordinates
 - crystallographic 744–8
 - deposition pre-check 726
 - fractional 215–6
 - notation 215
 - precision 658–62
 - Protein Data Bank files 738–40
 - unit cells 202
- coordination
 - calcium ions 57
 - chloride ions 681, 754
 - magnesium 449
 - metal ions 449, 754
 - solvent 82–4, 449
 - water 53–4, 82–4
- Coot (computer program) 665
- copper anode 374
- CORN rule 28
- correlated probabilities 316–17
- correlation 625–6
- correlation coefficients (CC) 330–1
- cosine rule 618, 749
- cosmic radiation 381
- Coulomb charge 754
- counter-diffusion capillary crystallization 107–8
- counting statistics 319–21
- covalent bonding 46–7, 50
- covariance 328–33
 - correlation coefficients 330–1
 - linear merging *R*-factor 332–3
 - R*-values 330–1
- CRABP see cellular retinoic acid binding protein
- crambin 506
- critical energy 378
- critical micelle concentration (CMC) 128–30, 175
- critical radius of nucleation 93
- Cromer-Mann coefficients 259–60
- cross-correlation 565
- cross-crystal map averaging 566
- cross-Fourier maps 490–2
- cross-rotation 565
 - locked function 584
 - searches 581–2
- cross-validation 17, 359, 454, 623–7
 - backbone torsion angles 632
 - data requirements 625
 - flat bulk solvent model 593
 - free *R*-value 624–5
 - parameterization 623–7
 - real space 626–7
 - sigma-A 617, 625
 - structure validation 704
- cross-vector peaks 487
- cryobuffers 80
- cryocrystallography 5, 79–80, 384–8, 432
 - annealing 387
 - cooling 13–14, 372, 382–3
 - crystal harvesting 126–7, 385–6
 - equipment 382–3
 - hyperquenching 387–8
 - ice rings 400
 - loops 384
 - mounting 126–7, 384–6
 - protein structure 387
- cryogenic, definition 369
- cryoloops 384
- cryomounting 126–7, 384–6
- cryoprotectants 385–6, 387
- CRYST1 records 738
- crystal classes see crystallographic point groups
- crystal geometry 197–246
 - basic concepts 198–214
 - lattices 215–19
 - reciprocal lattices 237–43
 - screw axes 219–23
 - space groups 223–36
 - unit cells 200–8
- crystallizability 189
- crystallization 77–140
 - affinity tags 85
 - analysis 118–22
 - batches 105–6
 - buffers 80, 99–101
 - cocktails 83, 95–101
 - co-crystallization 122–7
 - contamination 85
 - cost 80
 - detergent exchange 128–30
 - diagrams 93–4
 - dialysis 106–7
 - entropy 90–1
 - estimation of success 149–54
 - feasibility scores 150
 - free energy 90
 - free-interface diffusion 107–9
 - growth 94–5
 - membrane proteins 62, 128–30
 - multivariate sampling 114–15
 - optimization 121–2
 - pH 99–101
 - plates 79
 - polymorphisms 84, 122
 - protein engineering 143–55
 - protein properties 84–7
 - protein stocks 87
 - reagents 116–17
 - robotics 112–13
 - screening 115–18
 - seeding 111
 - self assembly 91–5
 - sequence 144–5
 - soaking 122–7
 - solvents 82
 - strategies 113–22
 - surface entropy reduction 150–3
 - techniques 101–13
 - two-tiered approaches 117–18
 - workflow 80
 - see also protein crystallization
- crystallization cocktails 83, 95–101
 - additives 97–9
 - buffers 99–101
 - precipitants 97
 - salts 96–7
- crystallographic axes 562–3
- crystallographic coordinates 215–16, 744–8
- crystallographic fragment screening 711
- Crystallographic Information Format (mmCIF) 19
- crystallographic restriction theorem 203, 751
- crystallography
 - history 2–3, 248, 379–80
 - instrumentation 372–83
 - Nobel prizes 496
 - versus solution studies 8
- crystal monochromators 375–6, 378
- crystals
 - conformational change 7–8
 - contacts 83, 201
 - diffraction 267–8
 - diffraction image inspection 399–403
 - faces 84
 - growth 13, 112
 - habits 84
 - harvesting 13–14, 126–7, 384–95
 - lattices 78, 81, 216–19
 - modulated structures 404–6, 407
 - morphologies 80–1
 - mosaicity 388–90
 - mounting 13–14, 126–7, 384–95
 - packing 7, 83–4
 - stability 82–3, 186, 190–1
 - see also protein crystals
- crystal structure
 - Laue groups 297–9
 - morphologies 80–1
 - protein crystals 84
 - space groups 223–36
- CS see Compton sources
- cubic lattices 217–19
- cubic phases 130
- cubic space groups 120, 227
- cumulative distribution functions (CDF) 322–3, 354, 366, 392–4, 427–8

cumulative normalized intensity distributions 354

cutoffs

- signal-to-noise ratio 414
- sulfur single-wavelength anomalous diffraction 530–1, 532

cyclic groups 226

cyclic operations 203

cyclotrons 377

cysteine 46–7, 162

cytochromes 577

cytosine 66

D

*d*TREK* (computer program) 405

Dali see Distance matrix alignment database

dAMP see deoxyadenosine monophosphate

dark current 381

data

- absences 454–7
- completeness 455–6
- correlation 625–6
- error models 410–11
- file deposition 725–7
- indexing 403–4, 405, 409
- integration 410
- intensities versus phase 462
- likelihood functions 594, 615
 - Bayes' theorem 318
 - structure validation 695
- observations 627
- parameterization 6, 22–45
- phase versus intensities 462
- publication 727–32
- raw 410
- reduction 411–17
- resolution 400–1, 450
- restraints 639
- scaling 410
- signal-to-noise ratio 407
- statistical presentation 429–30
- strategy generation 406–11, 419–21
- unmerged 411
- wedges 455–6

data analysis 410–31, 433

- primary 426–31
- quality 411–17

data collection 14–15, 384–437

- anisotropy 401–2
- decision making 399–411
- detector parameters 404
- exposure time 401
- inspection/decision making schema 400
- large unit cells 402
- modulated structures 404–6, 407
- mosaicity 402–3
- practical example 419–21
- satellite reflections 406, 407
- split reflections 402
- strategies
 - anomalous diffraction 408–10
 - highly redundant sets 424–6
 - high-resolution structures 408
 - molecular replacement phasing 407–8
 - multi-wavelength anomalous diffraction 409–10
 - single-wavelength anomalous diffraction phasing 409
 - sulfur single-wavelength anomalous diffraction 409
- strategy overview 396
- Table 1 430

Data Processing Suite (DPS) 405, 419

data quality 433

- descriptors 416
- merging *R*-value 412–15

data-to-parameter ratio 17, 622–45

- improvement 638–9
- macromolecular refinement 640
- optimization 343
- protein structures 627
- restraints 636, 637–40

DCM see direction cosine matrix

de Broglie wavelength 249, 261

Debye effects 356

decision making 399–411

deductive logic versus inductive

- inference 333–4

deglycosylation 177–8

degrees of freedom (DoF) 235–6

delta function 449

denatured protein 111

de novo model building 678–9

density averaging 528–9, 565–71, 600–1

density histograms 523, 527–8

density modification 16, 418, 441, 474, 528, 541–2

anomalous diffraction 293

definition 523

electron density map improvement 523–7

enantiomorph problem 505–6

figure of merit 612

phase 474, 480, 503–5

deorthogonalization matrix 233–4

non-crystallographic symmetry 558–9

protein data bank files 738

structure factor calculation 279

deoxyadenosine monophosphate (dAMP) 66

deoxynucleotides (dNTP) 158–9

deoxyribonucleic acid (DNA)

- B type 65
- chromatin 70–1
- combinatorial design 155–7
- crystallization 65
- damage 65–7
- discovery 65
- DNA topoisomerase I 159
- manipulation 154–5
- protein complexes 66–9, 132–3
- recognition motifs 6 7–9
- shuffling 157
- structure 64–7
- targeted design 145–55
- truncation 155–6
- see also nucleic acids

deoxyribonucleosides 64

β -D-2-deoxyribose 66

dependent probabilities 316–17

deposition 725–7

derivative crystals 293–5

derivative-difference Fourier maps 491–2

derivative Patterson maps 491–2

derivative proteins 476, 513

descriptive statistics 325–7

design of oligonucleotides 132

see also protein engineering

detector parameters 404

detectors 379–81

detergent exchange 128–30

detergents 87, 97–9, 174–5

determinacy limit 622, 654

determinants 741–2

direction cosine matrix 555

deuterium exchange mass spectroscopy (DXMS) 187–8

diacylglycerols 129

DIALIGN-TX (computer program) 147

dialysis 96, 106–7

diazepam (Valium®) 62

dielectric polarizability 250

difference data

- anisotropic scaling 483
- high intensity differences 483
- local scaling 482
- noise removal 484–5
- outlier detection 483
- preparation 482–5
- sigma-cutoff 484
- substructure solution 474–5

difference maps

- density 463–5
- model building 611
- Patterson 482, 485–94
 - manual solution 487–92
 - substructure phasing 485–6
- structure validation 18

diffraction 2, 247–311

- anisotropy 457, 641, 643, 706
- anomalous atom selection 292–3
- attenuation 263
- Bragg equation 264–6
- crystals 267–8
- definition 251
- Ewald sphere 270–2
- excluded regions 272–4
- extinctions 305–6
- Fourier transformations 269
- Friedel pairs 291
- geometry 270–5
- history 2
- intensity 281–4
- interpretation 264

lattice disorder 456–7

Laue equations 264

limits 272–4

molecular motion 262

neutron scattering 261

non-linearity 275

optical transforms 273–4

reciprocal space 274, 297–307

structure factors 268–70

see also scattering

diffraction-component precision index (DPI) 659–60

diffraction images 396–7

- exposure time 401
- frames 395
- ice rings 400
- indexing 420
- initial inspection 399–403
- modulated structures 404–6
- satellite reflections 406, 407
- spot finding 420

diffraction limits 272–4, 397

diffractometers 272, 372, 373, 376, 380

diffuse scattering 256, 399

diffusion 122–3

dihedral angles, restraints 629–30

dimers 577, 579–80

dimethyl sulfoxide (DMSO) 123

diphtheria toxin repressor (DtxR) 132–3

dipolar interactions 52, 100–1, 250

direction cosine matrix (DCM) 552–6, 742–4

- conventions 553
- Eigenvalues/vector 555–6
- mathematical properties 555
- spherical coordinates 750
- trace 553, 555

directed evolution 142, 144, 156–7, 158

directional cloning 154–5

direct methods 482, 494–500

- occupancy refinement 498–500
- phase 474, 475, 480
- Sayre's equation 496
- tangent formula 495–7
- triplet relations 495–6
- see also *ab-initio* structure determination

direct rotation function 583

discrete distribution 315

discretization 356

dispersion 250

dispersive differences 288

- data collection 408
- Patterson maps 465
- protein structure factors 295–7
- substructure phasing 477

displacement

- anisotropy 263

dissociation constants 123–4

distance

- minima 498
- vectors 486–7, 489

Distance matrix alignment (Dali) database 57–8

distributions see probability distribution functions

disulfide bonds 46–7

- buffers 166

chaperones 166–7

Escherichia coli 162

yeasts 164–5

disulfide isomerase (DsbC) 166

disulfide oxidoreductase (DsbA) 166

divergence, sequence to structure 578

DLS see dynamic light scattering

DM (computer program) 522, 527, 569

DMMULTI (computer program) 566

DMSO see dimethyl sulfoxide

DNA see deoxyribonucleic acid

DNA topoisomerase I 159

dNTP see deoxynucleotides

docking algorithms 715–16

DoF see degrees of freedom

domain expression 55–6, 148

domain rotation functions 565

domains 25, 55–6

- alignment analysis 147–8
- architecture 58–9
- crystal growth 80
- crystallization 94–5
- non-merohedral twinning 390
- truncation 55–6, 82, 148

domain structure databases 57–8

domain swapped dimers 148

dose mode 401

double crystal monochromators 378
 double diffraction 120
 DPI see diffraction-component precision index
 DPS see Data Processing Suite
 β -D-ribose, structure 66
 DsbA see disulfide oxidoreductase
 DsbC see disulfide isomerase
 DtxR see diphtheria toxin repressor
 dual-space direct methods 497–500
 dummy atom refinement 528–9, 573, 655–7
 DXMS see deuterium exchange mass spectroscopy
 dyad product 239–40, 643
 dyad symbol 203
 dynamic light scattering (DLS) 92, 180–3

E

EBI see European Bioinformatics Institute
E. coli see *Escherichia coli*
 EDS see Electron Density Server
 effective resolution 414, 453
 EGF-R see epidermal growth factor receptor
 Eigenvalues 441–2, 555–6
 Eigenvectors 555–6
 elastic scattering 180, 256
 electric field vector 249
 electrodynamics 372–3
 electromagnetic radiation 6, 249–55
 dipolar interactions 250
 particle-wave relationship 251–2
 scattering 180
 spectrum 249
 waves
 Bragg equation 265
 components 251
 superposition 252–5
 electromagnet 377
 electron beam 374–5
 electron density
 arithmetic proof of real value 749–50
 atomic scattering factors 261
 back transformation 443
 calculation 445–51
 estimation 593
 Fourier transformations 446–8
 limit of resolution 453
 probability distributions 257
 electron density maps 16, 47, 439–72, 512–13
 α -helices 677–8
 alpha carbon traces 676–8
 anomalous data 447
 autocorrelation 466–7
 automated model building 676–9
 B-factors 447, 448–9
 β -sheets 677–8
 bulk solvent correction 591–3
 coefficients 465
 construction 439–72
 density averaging 528–9, 565–71, 600–1
 density modification 523–7
 derivative-difference Fourier maps 491–2
 difference maps 463–5, 491–2
 dummy atom placing 528–9
 Fourier transformations 440–5
 histogram matching 504, 523, 527–8
 improvement 523–9
 incomplete data 453–7
 information content 451–3
 intensity errors, effect of 458–9
 ligands 670–1, 707–8
 maximum likelihood 461
 non-crystallographic symmetry 565–71, 600–1
 Patterson function 468
 phase 457–65, 611–14
 quality 523, 534, 614–20
 real space averaging 566–7, 569
 real space fitting 610–11
 reciprocal space averaging 567–9
 reconstruction 439–72
 residue identification 678–9
 resolution 451–3
 secondary structure 7, 676–8
 site occupancy 262–3, 277, 448–9
 solvent coordination 688–70
 solvent flattening 523–5, 567–8
 solvent flipping 525–6
 structure validation 18, 701, 704–7
 three-dimensional 449–51
 Electron Density Server (EDS) 705–6
 electrons
 free 256–7
 polarization 180, 250

relativistic speed effects 377
 scattering 251
 synchrotrons 376–9
 X-ray generation 375
 emission
 characteristic 287
 principles 376–8
 spectra 373
 empirical potentials 652–3
 empty density 682
 enantiomers 222, 302–3
 density modification 505–6
 multi-wavelength anomalous
 diffraction phasing 538–9
 Patterson maps 487
 single-wavelength anomalous
 diffraction 505–6, 533
 enantiomorphic point groups 225
 enantiomorphic space groups 416
 enantioselective reduction, ketones 714
 endoglycosides, protein engineering 177–8
 endoplasmic reticulum (ER) 164
 energy
 atomic number 293
 conversions 754
 mass/wavelength relationship 249
 X-ray absorption edges 294
 see also wavelength
 energy minimization 652–5, 701–4
 backbone torsion angles 632
 structure validation 704
 ensembling 598
 entropy
 charge flipping 500
 crystallization 90–1
 solvent flipping 504, 525–6
 envelope identification 678
 enzyme-free cloning 159
 enzymes
 binding pocket analysis 712–17
 restriction 154, 156
 solid state 7
 epidermal growth factor receptor (EGF-R) 55
 epitaxy 111, 388–90
 epitopes
 DNA topoisomerase I 159
 thrombin 168
 Tobacco Etch Virus protease 168
 EPMR see Evolutionary Program for Molecular Replacement
 epsilon factors 280, 306–7, 350
 epsilon zones 352
 equilibrium 123–5
 equipment see instrumentation
 equipoint positions 229–30
 equivalent points 216
 ER see endoplasmic reticulum
 ERRAT (computer program) 717
 error
 absolute 320–1
 best map coefficients 461
 cumulative distribution 323
 function 323
 phasing ambiguity 507
 propagation 328–33, 366
 reduction 358, 359–61
 relative 320–1
 error models 338, 364, 410–11
 likelihood based 614–20
 molecular replacement 613–14
Escherichia coli (*E. coli*) 160, 161–4
 estimation
 anomalous diffraction 293–5
 best estimates, weighted averages 333
 log-likelihood 339–40
 restraint count 638
 sigma-A 616–17, 625
 eucentric point 382
 Euclidean normalizers 489–90
 eukaryotic homeodomain protein 68
 Euler angles 583
 Euler axis 552
 direction cosine matrix 555–6
 fractional coordinates 558
 Euler's formula 255, 749
 Euler's number 255
 European Bioinformatics Institute (EBI) 146–7
 evaluation
 anisotropy 401–2
 exposure time 401
 model accuracy 657–62

resolution 400–1
 stereochemistry 698–704
 Evolutionary Program for Molecular Replacement (EPMR) 575–80
 evolutionary search algorithms
 molecular replacement 573, 575–80
 multi-trial solution landscapes 578–9
 workflow 576
 Ewald sphere 270, 397
 Bragg equation 265
 reciprocal lattices 270, 271–2
 EXAFS see extended X-ray
 absorption fine structure
 excitation scans 287, 288
 excitation spectra 372
 excluded regions 272–4
 excluded volume effect 97
 exclusive or statements (xor) 317
 exhaustive sampling 115
 exonuclease III (exoIII) 156
 expectation values 282, 315, 317, 327, 660–2
 correction 306–7
 distribution integration 327–8
 random atom models 349
 target functions 621
 see also mean
 experimental phasing 16, 473–545
 electron density improvement 523–9
 handedness ambiguity 507–8
 heavy atom refinement 513–23
 isomorphous signal estimation 477–8
 multi-wavelength anomalous diffraction
 536–9
 phasing equations 500–13
 quality evaluation 611–14
 reagent selection 114–22
 restraints 634–5, 648–9
 substructure methods 475–500
 sulfur single-wavelength anomalous
 diffraction 529–35
 twinning 394
 see also phasing
 exponential bulk solvent model 592–3
 exposure times 401–2
 expression 12, 157–75, 189–90
 alternative systems 166
 bacterial systems 161–4
 cell-free 166
 chaperones 166–7
 domains 55–6
 endoplasmic reticulum 164
 Escherichia coli 160, 161–4
 fusion tags 167–71
 host strains 142–3
 induction 162–3
 insect cell systems 165
 isoforms 161
 mammalian cells 165–6
 membrane proteins 173–5
 natural sources 161
 project planning 12
 resolubilization 163–4
 temperature 163
 yeast systems 164–5
 extended X-ray absorption fine structure (EXAFS)
 287, 288
 extensive parameters 114
 extinction
 rules 230–1
 systematic 280

F

F_{ab} , fragment crystallization 130–1
 face centering 217–19
 factorial designs 115–16
 Fast Fourier Transform (FFT) algorithms 405, 443
 fast rotation function 583
 FedEx crystallography 3
 FEL see Free Electron Lasers; free electron
 X-ray laser
 FFT see Fast Fourier Transform
 algorithms
 FID see free-interface diffusion
 figure caption creation 730
 figure of merit (fom) 359
 cross-Fourier maps 491
 initial phases 612
 map averaging 569–70
 molecular replacement 613
 file deposition 725–7
 film, X-ray detection 379

filters, X-rays 375
FINDNCs (computer program) 565
 fine slicing 398, 402–3
 first analysis, of data 426–31
 Fishers information 660
 Flack parameter 635
 flash-cooling 5, 79, 126–7, 384–6
 flat bulk solvent model 593
 flexibility 7, 24, 707, 717
 flipping
 charge 500
 NQH residues 671–2, 701
 solvent 504, 525–6
 fluorescence 287, 372
 focusing 250
 folding 25
 fold recognition 589
 fom see figure of merit
FORTRAN (computer language) 19, 555
 four-fold screw axis 220–1
 four-fold symmetry 204–7
 Fourier Cat 462
 Fourier coefficients 6, 441
 difference density maps 463–5
 Sim weights 359
 Fourier convolution theorem 442–5
 Fourier Duck 462
 Fourier indexing 403, 405
 Fourier integrals 259, 441–2
 Fourier maps 491–2
 Fourier summations 441–2, 512–13
 Fourier transformations 6, 444, 449, 469–70
 atomic scattering factors 259
 diffraction 269
 electron density autocorrelation 466–7
 electron density calculation 446–8
 electron density reconstruction 440–5
 phase bias 462
 structure factor interpolation 574
 truncation ripples 448
 fractional coordinates 215–16, 244, 558–9, 744–8
 fragility, of protein crystals 82–3
 fragmentation, of DNA 155–6
 fragment screening 124
 frames, of diffraction data 395
 Free Electron Lasers (FEL) 267, 379
 free electrons 256–7
 free-interface diffusion (FID) 107–9
Free Lunch (computer program) 528–9, 534–5
 free radicals 250
 freshness, of protein 85–6
 Friedel pairs 288, 291, 299–301
 Argand diagram 280
 data collection 408
 merging 411, 424
 rotation range 395–6
 Friedel's law 280, 291–2
 Friedel wedges 299–301
FRODO (computer program) 609
 full matrix minimization 651
 function, quaternary structure 62–4
 function, dimers 213
 functional variety, quaternary structure 62–4
 fusion proteins 142
 fusion tagging 167–71
 co-expression 169–70
 Halo Tag 169
 site-specific viral proteases 168
 Strep tag 168–9

G

GABA see γ -aminobutyric acid
 γ -turns 37
 garbage in, garbage out (GIGO) principle 347, 662
 gas constant 754
 gas cushions 387–8
 gateway cloning 159–60
 Gaussian distributions 321–5, 365–6
 closure error 510
 cumulative 322–3
 expression 321
 integration 327–8
 log-likelihood 340
 see also normal distribution
 Gaussian functions
 convolutions 445
 Fourier transformations 449
 gel shift assays 127
 gene fragmentation libraries 156

general positions
 multiplicity 306–7, 548
 reciprocal space 299
 space groups 230
 unit cells 228, 548
 general variance equation 320, 325
 generators
 space groups 2 25–6, 229–30
 X-rays 374–5
 genetic algorithms 575
 geometry 26–8
 constraints 628–9
 diffraction 270–5
 ligand restraint files 7 09–13
 polypeptide chains 28–32
 principles 26–8
 restraints 629–40
 root mean squared deviation 640
 structure validation 700, 709–13
 geometry outliers, model building 683
 GFP see green fluorescent protein
 G-function see reciprocal space interference function
 Gibbs free energy
 crystallization 90
 nucleation 92
 solubility diagrams 88–9
 GIGO see garbage in, garbage out
 glide planes 209
 global reciprocal space restrained refinement 620
 global structure validation 697–8
 glucosidase inhibition 178
 glutamate 44
 glutamine 45–6, 47, 671–2, 701
 glutaraldehyde 123
 glutathione reductase (gor) 162
 glutathione-S-transferase (GST) 169
 glycine 43
 glycoproteins 1, 65, 177–8
 glycosylation
 homodimers 178
 insect cell systems 165
 mammalian cells 165–6
 protein engineering 177
 yeasts 164–5
 GntI see N-acetylglucosaminyl-transferase I
 goniostats 272, 372, 382, 425, 882
 gor see glutathione reductase
 G-protein coupled receptors (GPCRs) 165, 174
 gradient descent algorithms 650–2
 gradient methods 621
 graphical display 20, 609
 green fluorescent protein (GFP) 169, 170
 grid expansion 121
 grids
 electron density calculation 446–8
 Nyquist theorem 448
 three-dimensional 449–51
 grid screening 115
 GROMOS87 force field 711
 groups
 mathematical 203
 see also point groups; space groups
 growth domains, of crystals 80
 GST see glutathione-S-transferase
 guanine 66
 guanosine triphosphate (GTP) 66

H

habit 84
 Hall symbol 228
 Halo tag 169
 handedness, see also chirality
 handedness ambiguity 418
 absolute configuration 302–3
 multi-wavelength anomalous diffraction phasing 538–9
 phasing techniques 507–8
 hanging-drop vapour diffusion 78–9, 102–4
 Harker diagrams 478
 Harker sections 486–92
 definition 492
 deriving location 487–9
 heavy atoms 486–7
 non-crystallographic symmetry 562
 harmonic functions 583
 harvest file deposition 725
 harvesting 13–14, 126–7, 384–95
 flash-cooling process 385
 project planning 13–14
 heat shock proteins 166–7
 Heaviside function 448, 449
 heavy alkali metals 126
 heavy atom derivatives 475
 heavy atom refinement 482, 513–23, 541
 classical 513–14
 improvements 515
 independence of probabilities 519–20
 maximum likelihood 514–22
 non-isomorphism 520
 phase combination 522–3
 phase extension 522
 heavy atoms
 anomalous diffraction 292–5
 cross-Fourier maps 490–2
 gel shift assays 127
 Harker sections 486–7
 isomorphous differences 16
 non-crystallographic symmetry 565
 Patterson maps 465, 466–7, 486–7, 493
 phasing 292–5, 358, 387, 477, 481, 541
 radiation damage 285
 radiation-damage-induced phasing 387
 SHELXD 531–2
 substructure phasing 477
 truncation, of difference data 532
 X-ray absorption 285, 297
 see also ions
 heavy atom soaking 125–7
 heavy atom substructure solution 358, 481–500, 540
 heavy halides, quick soaking 126
 HEK see human embryonic kidney cells
 α -helices 32–4, 677–8
 PP-II helices 35
 π -helices 34
 3_{10} -helix 34–5
 helix nomenclature 34
 helix-turn-helix motifs 68
 hemihedral twinning 390–5
 chiral space group operators 391
 cumulative probability distributions 392–4
 definition 395
 raw moments 390–1
 Hendrickson–Lattman (HL) coefficients 522–3, 634–5
 Hermann–Mauguin space group symbols 226–8
 Hermitian complex functions 282
 Hessian matrix 650
 HETATM records 738
 heterogeneous nucleation 92–4
 heterologous overexpression 142, 160
 heteronuclear single-quantum coherence (HSQC)
 experiments 186
 hetero-oligomeric receptors 62–3
 hexad symbol 203
 hexagonal crystal birefringence 120
 hexagonal space groups 207–8, 227
 Hidden Markov Model algorithms 147
 high energy remote data 290, 536–7
 highly redundant data 424–6
 high performance liquid chromatography (HPLC) 187
 high resolution, definition 408
 high-resolution structures 395, 408, 418–19, 451–3
 histidine 44–5, 47
 flipping 671–2, 701
 tagging 85, 167
 histogram matching 504, 523, 527–8
HKL2000/3000 (computer program) 405
 HL see Hendrickson–Lattman coefficients
 holohedry 391
 homodimers 178, 211–12
 homogeneous nucleation 92–4
 homologs 150
 homology modeling 589, 715–16
 HPLC see high performance liquid chromatography
 HSQC see heteronuclear single-quantum coherence experiments
 human embryonic kidney (HEK) cells 165–6
 hydration shells 53–4
 hydrodynamic radius estimation 182
 hydrogen atoms 27, 260, 633
 hydrogen bonding
 binding pockets 712–13, 715
 helix structure 33–5
 networks 668
 secondary structure 33–5, 39
 side chains 45–6, 50–2
 hydrogen exchange 186–7
 hydrophobic core 41–2

hydrophobicity 53, 68
 hydrophobic membrane proteins 128
 hydrophobic residues 40–3
 hydroxyethyloxytri(ethyloxy)octane (C8E) 129
 hydroxyl groups 45
 hyperquenching 387–8
 hypothesis testing
 Bayes' theorem 334–6, 345–7
 maximum likelihood 336–43
 model building 662
 structure validation 694–6
HySS (computer program) 497

I

ice rings 400
 identification, in density
 alpha carbons 676–8
 residues 678–9
 identity
 definition 226
 matrix 741
 operations 199
 IEF *see* isoelectric focusing
 ignorance, Bayesian method 337
 illustrating articles 728–30
 IMAC *see* immobilized metal affinity chromatography
 imaging plates (IPs) 379
 immobilized metal affinity chromatography (IMAC) 167
iMOSFLM (computer program) 419–22
 see also *MOSFLM*
 improper non-crystallographic symmetry 551–2, 560
 see also non-crystallographic symmetry
 improvement
 data/parameter ratio 638–9
 electron density maps 523–9
 phase data 565–71
 inclusion bodies 98–9
 incommensurately modulated structures 404–6, 407
 incomplete factorial designs 116
 incompleteness
 conditional distributions 358
 electron density data 53–7
 heavy atom refinement 516–17
 likelihood functions 616–18
 maximum likelihood 338
 molecular replacement 590
 Sim distribution 358–9
 independent measurements, best estimates 333
 independent probabilities 316, 519–20
 indexing 403–4, 416–21, 753
 algorithms 405
 definition 403
 non-equivalent operators 418
 practical example 419–21
 re-indexing 416–18, 745–6
 space groups 753
 strategy generation 409
 indoyl ring planar restraints 630–1
 induced dipole moment, polarization 249
 inductive inference versus deductive logic 333–4
 inelastic scattering 256
 inference
 Bayes' theorem 318–19
 evaluation 333–47
 versus deductive logic 333–4
 inflating the variance 520
 translation functions 595–6
 X-ray term 647
 inflection point data 290, 536
 information content of electron density maps 451–3
 Infra-red (IR) frequencies 250
 initial phases, quality evaluation 611–13
 insect cell systems 165
in silico preparation 142–3
 instrumentation 371–83, 431
 charge-coupled devices 380–1
 collimators 376
 cryocooling 382–3
 detectors 379–81
 diffractometers 376
 goniostats 272, 372, 382, 425
 imaging plates 379
 monochromators 374
 mounting robotics 383
 multiwire array detectors 379–80
 optics 375–6
 peak broadening 399

synchrotrons 376–9
 X-ray generators 374–5
 integral absences 416
 integral extinctions 305
 integral membrane proteins 128–30
 integrating out 317–18
 integration
 data collection 410
 practical example 421–2
 probability distributions 327–8
 intein fusion systems 169
 intensities 275–84
 conversion to structure factor amplitudes 329–30
 errors 329–30, 458–9
 overflows 454–5
 structure factor amplitude 281–4
 twinning 392–4
 variance 350
 versus phase 462
 see also amplitude
 intensity distributions
 acentric reflections 350, 363
 centric reflections 349, 363
 crystallization 95
 epsilon factors 306–7
 merohedral twinning 388
 intensive parameters 114
 interactions
 protein crystals 81–2
 side chains 49–54
 interatomic distances
 Harker sections 486–7
 Patterson maps 485–94
 see also bond distances
 intermolecular contacts
 additives 99
 crystal stability 82–3, 181
 internal symmetry 199
 interplanar spacing 238
 interpolation of structure factors 574
 inversion 203, 209, 226
 exceptions 505–6
 matrices 741–2
in vitro directed evolution 156–7
in vivo conversion of nucleotide analogs 70
 ion exchange 128
 ionic bonding 50
 ionic solvents 96
 ionizing radiation 5, 250
 ions 670
 coordination 754
 scattering factors 260–1
 soaking 125–7
 see also heavy atoms
 IPs *see* imaging plates
 IR *see* Infra-red
 iron, scattering factors 260
 irrational number 255
 irregular sheets 36–7
 isoelectric focusing (IEF) 85
 isoelectric point 83, 89, 99–101
 isoforms, protein expression 161
 isoleucine 42
 isomorphous derivatives, Patterson maps 465
 isomorphous difference Patterson maps 485
 isomorphous replacement 16, 81, 125–7, 475–7
 heavy atom soaking 125–7
 history 477
 phase probabilities 510
 selenomethionine 172
 signal change estimation 477–8
 Sim distributions 358–9
 substructure phasing 475–7
 isoniazid, NAD binding 70
 isotropic, definition 201
 isotropic displacement parameters *see* *B*-factors

J
 joint probabilities 316

K
 KcsA channel 131, 173
 ketones 714
 kinase active sites 715
 Kramers–Kronig transform 289

L
 labelling 167–73, 190
 co-expression 169–70
 green fluorescent protein 169, 170

histidine tagging 85, 167
 selenomethionine 16, 43, 125, 171–3, 536–9
 Strep tags 168–9
 laboratory X-ray generators 374–5
lac operon 163
 β -lactam rings 335
Lactococcus, protein expression 161
 L-amino acids 40, 631
 large unit cells 402
 lattice disorder 456–7
 lattice planes 260
 reciprocal lattices 237–9
 X-ray diffraction interpretation 264
 lattice points 215–16
 lattices 78, 81, 199–219, 244
 Laue groups 297–9
 translations 216
 unit cell determination 404
 lattice vectors 199–200, 215–16, 747–8
 Laue diffraction 369
 Laue equations 264, 268
 to Bragg equations 265
 Laue groups 297–9, 395–6, 416
 Laue symmetry 297–9, 404, 416, 422–4
 lead optimization 123
 least squares (LSQ) 338, 340–1
 heavy atom refinement 515
 macromolecular refinement 645
 model building 610–11
 target functions 621
 left handed PP-II helix 35
 Lennard–Jones potential 632, 652, 715
 LERF *see* likelihood enhanced rotation function
 LETF *see* likelihood enhanced translation function
 leucine 42
 leucine zipper 68–7
LIBCHECK (computer program) 710–12
 library enrichment 716
 LIC *see* ligation independent cloning
 ligand restraint files 709–13, 751–2
 ligands
 binding 700, 707, 712–17
 binding pocket analysis 712–17
 building 708–9
 chemical plausibility 712–13
 crystallization 123–5
 electron density 670–1, 707–9
 omit maps 708
 screening 715–16
 ligase 54
 ligation independent cloning (LIC) 158–9
 light scattering 85, 180–3
 light speed 754
LIGPLOT (computer program) 712–13
 likelihood 333–47, 367
 by intuition 526
 central limit theorem 341–2
 functions 317–18, 333–47, 367
 data 594, 615
 electron density maps 528
 error models 614–20
 experimental phase restraints 648–9
 experimental phasing 522
 flat bulk solvent model 593
 heavy atom refinement 514–22
 incompleteness 616–18
 models 594, 615
 molecular replacement 594–9
 multi-parametric 342–3
 multiple isomorphous replacement 518–19
 multi-wavelength anomalous diffraction 521–2
 negative intensities 343–5
 non-isomorphism 518–19, 520
 phase 517–18
 positional errors 616–18
 random atom models 347–51
 single isomorphous replacement with anomalous signals 521
 single-wavelength anomalous diffraction 520–1
 stereochemical restraints 645–9
 structure factors 365
 translations 595–7
 X-ray term 647–8
 maximum 336–43
 ratio 336, 695
 target functions 645–9
 terminology 336
see also maximum likelihood

likelihood enhanced rotation functions (LERF) 598
 likelihood enhanced translation functions (LETF) 586
 limited proteolysis 175, 176
 limit of resolution (LoR) 453
 linear merging *R*-value 332–3, 412
 linear regression 356–7
 linear residual 325
 LINK statements, *REFMAC* 667
 lipid cubic phases 130
 liquid nitrogen 79, 385–6
 LLG see log-likelihood gain
 local-level structure 7, 8, 83, 214, 697–8
 local minima 650
 local operators 551–2
 local real space refinement 610–11
 local scaling 482
 locked rotation functions 584
 locked translation functions 587
 log file deposition 725
 log-free-likelihood 625, 639–40, 662
LOGGRAPH (computer program) 427–8
 log-likelihood 338–40, 342–3
 heavy atom refinement 518
 stereochemical restraints 648
 log-likelihood gain (LLG) 343, 599
 loops 38–9, 667–8, 680
 LoR see limit of resolution
 Lorentz exclusion regions 389
 Lorentz factor 283
 Lorentz and polarization (LP) corrections 410
 Lorentz–Cauchy distributions 287
 low energy remote data sets 290, 295–7, 536
 low resolution structures, validation 717–19
 LP see Lorentz and polarization corrections
 LSQ see least squares
 lunes, diffraction 396–7, 398
 Luzzati *D*-factor 361, 515, 595, 613
 Luzzati plots 658, 706
 lysine 44, 176–7
 lysozyme 83, 96

M
 macromolecular crystallography see crystallography
 macromolecular model building see model building
 macroscopic twinning 94–5, 388–90
 macroseeding 111
 MAD see multi-wavelength anomalous diffraction
 MAE see mean absolute error
 magic angle 382
 magnesium ions 65, 449
MAID (computer program) 678
 maltose binding protein (MBP) 168, 169
 mammalian cell protein expression 165–6
 manual model rebuilding 665–73
 map averaging 441
 cross-crystal 566
 non-crystallographic symmetry 548, 565, 569–71, 600–1
 map coefficients 462–9, 534, 618–20
 selection 465
 map inversion 441, 442, 565
 map-likelihood 528
 residue identification 678
MAPMAN (computer program) 704
 marginalization 317–18, 595, 616
 heavy atom refinement 518
 phase 362–3
 marker atom substructure phasing 474, 475–81, 539–40
 anomalous/dispersive differences 477
 overview 481
 phase problem 474
 principles 477
 marker atom substructure solution 481–500, 540
 anisotropic scaling 483
 difference data 482–5
 direct methods 494–500
 high intensity differences 483
 local scaling 482
 noise removal 484–5
 outlier detection 483
 Patterson maps 468–9, 485–94
 reciprocal space searches 494
 versus *ab-initio* methods 495
 see also substructure solution
 mask generation 534
 mass, relationship with energy 249

mass absorption coefficient 285
 mass spectroscopy (MS) 85, 186–8
 matrices 416–17, 740–3
 matrix inversion 649
 matrix operators 223–4, 745
 matrix sampling 116
 Matthews coefficients 428–9, 549–50
 Matthews probabilities 204, 427–8, 549–50
MATTPROB (computer program) 549
 maximum entropy methods 496, 500
 maximum likelihood (ML) 336–43, 367
 Bayes' theorem 318
 bias minimized maps 618
 central limit theorem 341–2
 definition 337
 electron density maps 461, 528, 618
 error models 338
 experimental phasing 522
 heavy atom refinement 514–22
 least squares 338, 340–1
 map coefficients 573, 618–20, 704
 model building 610–11
 molecular replacement 573, 594–9
 negative log-likelihood minimization 342
 omit maps 626
 optimization 649–52
 posterior probability 336–7
 principle 340–1
 sequence to structure 578
 stereochemical restraints 646
 target functions 621
 variance effects 598
 see also likelihood
 maximum likelihood phase refinement (*MLPHARE*) 516
 maximum likelihood rotation function (MLRF) 597–8
 maximum likelihood translation function (MLTF) 595–7
 maximum posterior methods 337
 maximum posterior refinement 646
 MBP see maltose binding protein
 MD see molecular dynamics
 MD-SA see molecular dynamics-simulated annealing

mean
 arithmetic 325
 expression 317
 see also expectation values
 mean absolute error (MAE) 327, 414–15
 mean *E*-squared minus one 354–5
 mechanosensitive channel 731
 membrane integrating sequence for translation of integral membrane protein constructs (*Mistic*) 174
 membrane proteins 58–62, 174–5
 chaperones 166–7
 classification 59–61
 crystallization 62, 128–30
 expression 173–4, 175
 purification/solubilization 174–5
 β -mercapto ethanol (BME) 98
 merging 411–16, 423–4, 426
 cryocrystallography 386
 Friedel pairs 424
 mean absolute error 414–15
 statistics 411–16
 weighted averages 332–3
 XPREP (computer program) 423–4
 merging *R*-value 412–13
 difference data preparation 484
 sigma 415
 signal-to-noise ratio 414–15
 merohedral twinning 95, 388, 390–4
 cumulative distributions 323, 393–4
 non-crystallographic symmetry 561
 metabolic inhibition, selenomethionine 171–2
 metal cations 99, 670
 metal coordination 754
 metal ions 99, 125–7, 670, 754
 see also heavy atoms
 metastable solutions 78, 79, 88–9, 91–2
 methionine 43
 auxotrophs 171
 selenomethionine 16, 171
 methylation of lysine 176–7
 2-methyl-2,4-pentanediol (MPD) 97
 metric tensor 233, 744–5
 Metropolis Monte Carlo searches (MMC) 653

microfluidic chips 108–9
 microfocus beam lines 378–9
 microseeding 111
 Mie ratio 180, 261
Mfit (computer program) 665
 Miller indices 237–9, 242, 245
 Laue equations 264
 structure factors 268
 minimum distances 498
 MIR see multiple isomorphous replacement
 MIRAS see multiple isomorphous replacement with anomalous signals
 mirror symmetry 203
 chirality 220
 space groups 416
 missing parts, of model 680–1
Mistic see membrane integrating sequence for translation of integral membrane protein constructs
 ML see maximum likelihood
MLPHARE see maximum likelihood phase refinement
 MLRF₀ see Wilson-like maximum likelihood rotation function
 MLRF see maximum likelihood rotation function
 MLTF see maximum likelihood translation function
 MMC see Metropolis Monte Carlo searches
mmCIF see Crystallographic Information Format
 model bias 10, 459, 462, 608
 molecular replacement 599
 omit maps 626–7
 phase 611–14
 model building 10, 16–20, 607–91
 accuracy 616–18, 657–62
 alpha carbons 717–19
 anisotropy 640–5
 ARP/wARP 535
 automation 673–9
 basics 608–20, 666
 convergence 620
 coordinate precision 616–18, 658–62
 cross-validation 623–7
 cycles 610–11
 de novo 678–9
 dummy atom refinement 655–7
 electron density ambiguities 47
 electron density maps 16, 676–9
 empty density 682
 end points 682–3
 evaluation programs 699
 final steps 681–2
 geometry outliers 683
 gradient descent algorithms 650–2
 heavy atom refinement 516–17
 history 608–9
 hypothesis testing 662
 ligands 708–13
 likelihood functions 318, 614–20, 645–9, 695
 log-(free)-likelihood 662
 low resolution structures 719
 Luzzati plots 658
 manual rebuilding 665–73
 missing parts 680–1
 molecular dynamics 652–5
 molecular replacement 589–91
 parameterization 620, 622–45
 phase data evaluation 611–14
 in practice 665–84
 Protein Data Bank files 19–20
 rebuilding 665–73
 refinement 620–64
 restrained refinement 17, 628, 634–5, 649, 666–7
 restraints 629–40, 645–9, 658–9
 simulated annealing 653–5
 solvent structure 668–70, 681
 stereochemistry 698–704
 translation-libration-screw parameterization 642–4
 unrestrained refinement 627
 validation 693–727
 see also model rebuilding
Modeller (computer program) 589
 model likelihood function 318, 594, 614–20, 695
 model rebuilding 665–73
 ARP/wARP 675
 hydrogen bonds 668
 ligand density 670–1
 real space correlation plot 673
 side chains conformations 672–3
 solvents 668–70

- model
- Bayesian inference 337–8
 - correlation coefficient 330–1
 - errors 364, 613–14, 648
 - trimming 577
- modified residues 48
- modulated structures 404–6, 407
- molecular cryptanalysis 8–10
- molecular dynamics (MD) 652–5
- molecular dynamics-simulated
- annealing (MD-SA) 626–7
- molecular replacement (MR) 15, 548, 571–99, 601–2
- bioinformatics 146
 - conditional distributions 358
 - data collection 407–8
 - development 572
 - dimers 577
 - evolutionary search algorithms 573, 575–80
 - figure of merit 613
 - manual model rebuilding 665–73
 - maximum likelihood functions 594–9
 - model bias 599
 - model errors 613–14
 - multi-solution approaches 589–91
 - packing functions 599
 - Patterson rotation searches 581–4
 - phase 458, 474–5, 480
 - bias 15, 572–3, 613–14
 - data evaluation 612–13
 - probe selection 588–91
 - real space 565
 - restrained refinement 666–7
 - rigid body refinement 587–8
 - rotation-translation searches 573, 580–8, 594–9
 - search strategies 588–91
 - side-chain replacement 665–6
 - stochastic searches 580
 - twinning 394
- molecular structure database (MSD) 19
- molecular weight determination 181
- MolProbity* (computer program) 672, 699–701
- MOLREP* (computer program) 579, 590, 591
- molybdenum anodes 374
- monochromators 256, 374, 375–6
- monoclinic lattices 217
- monoclinic space groups 227
- monoclonal antibody 131
- monomodal distributions 510–11
- monotopic membrane proteins 59–60
- Monte Carlo algorithms 342, 653–4
- morphology 84
- mosaicity 94–5, 388–90
- data collection 402–3
 - fine slicing 398
- MOSFLM* (computer program) 405, 419–22
- see also *iMOSFLM*
- mother liquor 82
- motif 25, 56–7, 200–1
- β - α - β 56
 - animal representations 462
 - asymmetry 208–11
 - calcium-binding EF hand 56–7
- mounting 13–14, 126–7, 384–95
- MPD see 2-methyl-2, 4-pentanediol
- MR see molecular replacement
- MrBUMP* (computer program) 590–1
- mRNA 162
- MS see mass spectroscopy
- mtz* format 535
- multi-angle light scattering (MALS) 180–1
- multi-conformer refinement 655
- multidimensional searches 574–80
- multi-domain proteins 55
- multi-layer soft lithography chips 108–9
- multimeric assembly 62–3
- multimodal distributions, phase probabilities 511
- multi-parametric likelihood functions 342–3
- multi-pass membrane proteins 59–61
- multiple diffraction patterns 402
- multiple isomorphous replacement (MIR) 476–7, 479, 480, 506–8
- handedness ambiguity 507–8
 - likelihood functions 518–19
- multiple isomorphous replacement with anomalous signals (MIRAS) 479, 480
- multiplication of matrices 741
- multiplicity
- general positions 306–7
 - point positions 229–30
- multi-solution landscapes 498–500, 578–91
- multivariate sampling 114–15
- multi-wavelength anomalous diffraction (MAD) 289–93, 409–10, 477, 507–9, 536–9
- automated model building 679–82
 - characteristic radiation 374
 - handedness ambiguity 507–8
 - likelihood functions 521–2
 - Patterson maps 486
 - phase ambiguity 479, 480
 - phasing equations 508–9
 - restrictions 292–3
 - substructure solution 536–9
 - synchrotrons 378
 - see also anomalous diffraction
- multiwire array detectors 379–80
- muons 381
- myoglobin 185
- N**
- N-acetylglucosaminyltransferase I (GntI) 165–6
- nAChR see nicotinic acetylcholine receptor
- NAD binding 70
- National Center for Biotechnology Information (NCBI) 146–7
- native Patterson maps see Patterson maps
- native polyacrylamide gel electrophoresis 179–80
- native protein structure factors 476
- NCBI see National Center for Biotechnology Information
- NCS see non-crystallographic symmetry
- near-perfect non-crystallographic symmetry translations 560
- negative intensities 330, 343–5
- negative log-likelihood minimization 342–3
- NER see nucleotide excision and repair complexes
- neurotensin receptor (NTR) 174
- neutrons 261
- neutron scattering 183, 261
- nicotinic acetylcholine receptor (nAChR) 62
- nitrotriacetic acid (Ni-NTA) resin 167
- nitrogen, liquid 385–6
- NMR see nuclear magnetic resonance spectroscopy
- noise
- charge-coupled devices 381
 - enantiomer selection 533
 - removal 484–5
 - see also signal to noise ratio
- nomenclature of helices and screws 34
- nominal resolution 453
- non-bonded interaction restraints 632–3
- non-commutative, definition 223
- non-crystallographic symmetry (NCS) 211–14, 428–9, 547–71, 600–1
- atomic model 564–5
 - carbon backbone torsion angles 703
 - Cartesian transformations 558–9
 - concept 551
 - cross-correlation 565
 - crystallographic transformations 557–8
 - density averaging 565–71, 600–1
 - direction cosine matrix 552–6
 - improper 551–2, 560
 - Matthews coefficients/probabilities 548–9
 - molecular replacement 571–99
 - near-perfect translations 560
 - operators 564–5
 - parallel crystallographic axes 562–3
 - Patterson functions 469, 548–60
 - perfect rotations 560
 - phases 474, 565–71
 - proper 551–2, 560, 563–4
 - real space averaging 566–7, 569, 601
 - real space translations 560–1
 - reciprocal space 561–4, 567–9, 600–1
 - restraints 634, 635
 - rotations 548–60
 - spherical coordinates 556–7
 - structure validation 703–4
 - superpositions 564–5
 - superstructures 212–14
 - transformations 551–65
 - translations 560–2
 - unit cell determination 428, 548–51, 600
- non-equivalent operators for indexing 418
- non-isomorphism 386, 477–8, 518–19, 520
- non-linearity 275
- non-merohedral twinning 388–90
- non-redundant databases 146
- non-stochastic optimization algorithms 649–52
- normal distribution 321–5, 343, 510
- see also Gaussian distribution
- normalization 317
- Rice distribution 363–5
 - Woolfson distribution 363–5
- normalized distributions 353–4
- normalized residual (Z-score) 326–7
- normalized structure factors 278, 351–5, 468, 483, 497
- epsilon factors 306–7
- normalized sum of residuals squared 343
- normalized Wilson distribution 353
- NQ-Flipper* (computer program) 672, 701
- NQH flipping 671–2, 701
- NTR see neurotensin receptor
- nuclear magnetic resonance (NMR) spectroscopy 1, 185–6, 589
- nucleation 78, 79, 92–4, 111
- critical radius 93
 - energy 92
- nucleic acids 64–71
- see also deoxyribonucleic acid
- nucleoside, definition 64
- nucleosome, core particle structure 71
- nucleotide excision and repair (NER) complexes 67–9
- nucleotide-level search (*BLASTN*) 146
- nucleotides 66
- analogs 69–70
 - modification 65–7
- nuisance variables 317–18
- Nyquist theorem 448
- O**
- oblique systems 558
- oblique tiles 199
- observations
- optimization 620
 - total number 627
- Occam's razor 623
- occupancy 123–5, 262–3, 277, 448–500, 709
- octyl- β -glucoside 99, 129
- n-octyl-tetraoxyethylene (OTE) 129
- offsetting
- eucentric goniostats 382
 - large unit cells 402
- OhrB see organic hydroperoxide-resistance protein
- oligonucleotides 132
- oligosaccharides 177–8
- omega-loops 38–9
- omit maps 573, 626–7, 708
- operators 551–2
- OprP 175
- optical rotatory dispersion (ORD) 184–5
- optical transforms 273–4
- optics 256, 375–6, 378–9
- optimization 620–64, 685–7
- algorithms 621, 651
 - constraints 620
 - crystallization 121–2
 - data-to-parameter ratio 622–45
 - end points 682–3
 - experiments 116
 - full matrix minimization 651
 - fundamentals 662–4
 - gradient descent algorithms 650–1
 - hydrogen atom restraints 633
 - log-likelihood 342–3
 - maximum likelihood functions 649–52
 - molecular dynamics 653–4
 - Monte Carlo minimization 653–4
 - parameter estimation 336
 - radius of convergence 654
 - restraints 620, 627–40
 - sparse matrix method 651
 - stochastic 652–5
 - see also refinement
- ORD see optical rotatory dispersion
- ORF7A structure 221
- organic hydroperoxide-resistance protein (OhrB) 148
- organic precipitants 97
- orientation matrix 405
- origin 200–2, 228–9, 244
- inversion exceptions 505–6
 - Patterson maps 489–90, 491
- orthogonal coordinates 232–4, 741–2
- orthogonalization matrix 233–4, 558–9
- orthologs 13, 84–5, 150
- orthorhombic lattices 217–19, 243

orthorhombic space groups 227
 OTE see n-octyl-tetraoxyethylene
 outliers 9–10, 322, 483
 error models 410–11
 geometry 683
 stereochemistry 700
 overall *B*-factors 457, 620, 642
 overall *B*-factor scaling see Wilson scaling
 overall scaling factors 426
 overexpression 171
 overfitting 17
 OVERLAPMAP (computer program) 704
 oxygen 260

P

p53 protein 67, 69
 packing 7, 83–4, 231–2, 235–6
 PAD see pixel array detectors
 Padilla–Yeates plots 706
 PAGE see polyacrylamide gel electrophoresis
 pair-wise interactions 577, 633
 palindromic sequences 133
 parallel design 12, 144–5
 parameter estimation 336
 parameterization 622–45
 anisotropy 640–5
 cross-validation 623–7
 restraint weight adjustment 624–5
 parameter optimization 336
 paratone-N 388
 Parseval's theorem 461, 513
 partial derivatives 649
 partial occupancy 262–3, 277, 448–9
 partial reflections 397
 partial wave superposition 254
 particle-wave relationship 251–2
 pattern hit initiated basic local alignment search
 tool (*PHI-BLAST*) 146
 pattern recognition 9–10
 Patterson correlation function (PC) 583–4, 588
 Patterson difference maps 483, 485–94
 Patterson functions 428–9, 465–9
 direct rotation 583–4
 electron density maps 471
 fast rotation 583
 generation 466–7
 locked rotation 584
 reciprocal space interference function 568
 sharpening 468
 translations 585–7
 Patterson maps 228, 465–9, 495
 acentric reflections 486
 anomalous differences 486
 automated search methods 492–4
 centric reflections 485–6
 centrosymmetry 467
 Cheshire groups 489–90
 cross-Fourier maps 490–2
 difference 483, 485–94
 electron density maps 471
 enantiomers 487
 Harker sections 486–92
 heavy atoms 490–2
 isomorphous differences 485
 manual solution 487–92
 multiple origins 489–90, 491
 non-crystallographic symmetry 429, 560, 561–4
 PEAKMAX (computer program) 488
 peaks 468
 phase ambiguity 487, 507
 rotation-translation searches 573, 580–8
 self-rotation 429, 563–4
 substructure phasing 485–94, 495
 superposition 493–4
 translational non-crystallographic symmetry 429, 562
 Patterson minimum functions (PMF) 497–8
 Patterson searches 482, 492–4, 581–8
 cross-rotation 581–2
 phase problem 474
 rotation functions 581–4, 587
 translation functions 585–7
 Patterson self-rotation 429, 548–60, 563–4, 582–4
 PC see Patterson correlation function
 PCR see polymerase chain reaction
 PCS see dynamic light scattering
 PCV see pooled coefficient of variation
 PDB see Protein Data Bank
 PDF see probability distribution functions
 PDI see protein disulfide isomerase
 peak broadening 399

peak data sets 289–90, 295–7, 536–7
PEAKMAX (computer program) 488
 peak separation 453
 peer review 730–2
 PEG see polyethylene glycol
 peptide bonds 29–32, 629–30
 peptidyl prolyl *cis/trans* isomerases (PPI's) 166
 percentiles, cumulative distribution functions 323
 perfluoroethers 388
 periodicity 255, 263–4
 periodic lattices 198–200
 periodic patterns 200–1
 pH 89, 99–101
 pharmaceuticals, role of polymorphism 84
 phase 15–16, 457–65, 478–81, 565–71
 accuracy 464
 best 511–12
 centric reflections 304–5
 combination 510–12, 522–3
 diagrams 88–9
 differences 258
 electromagnetic waves 252–5
 electron density 457–65
 experimental determination 16
 Friedel's law 291–2
 Hendrickson–Lattman coefficients 634–5
 implied from position 478
 initial acquisition 478–81
 likelihood functions 517–18
 marginalization 362–3
 non-crystallographic symmetry 565–71
 probability distributions 324, 510–13
 quality evaluation 611–14
 Sim weights 359
 triplet relations 495–6
 versus intensities 462
 phase ambiguity 418, 474, 479, 503–5, 506–8, 533
 density modification 503–5
 Patterson maps 487, 507
 phase angles 6, 252–5
 anomalous diffraction 293
 phase bias 317, 459, 462
 Fourier transformations 462
 molecular replacement 15, 572–3, 613–14
 phased translation functions 548, 565, 587
 phase extension 522, 528–9, 538–9, 565, 568
 SHELXE (computer program) 532–3
 sulfur single-wavelength anomalous diffraction 534
 phase probability 482, 541
 phase problem 6, 15–16, 457–8, 470–1
 density modification 474
 solutions 474–5
 Phaser (computer program)
 likelihood enhanced translation functions 586
 molecular replacement 579, 587, 590–1, 599
 non-isomorphism 478
 normal mode perturbation 598
 packing functions 599
 substructure solution 481
 phase restrained refinement 634–5
 phase restriction 276, 280, 303–4
 phase separation 79, 91–2
 phasing 250, 473–545
 anomalous signals 292–3
 central limit theorem 324–5
 centric reflections 305
 graphical equations 479
 handedness ambiguity 507–8
 heavy atoms 125–7, 541
 isomorphous replacement 81
 map-likelihood 528
 molecular replacement 81, 571–99
 multi-wavelength anomalous diffraction with Se-Met 536–9
 probability 509–13, 516
 radiation damage-induced 387
 salvage strategies 458
 selenomethionine labelling 171–3, 536–9
 SHELXE (computer program) 532–3
 single-wavelength anomalous diffraction 290, 417–26, 529–35
 see also experimental phasing
 phasing ambiguity, experimental errors 507
 phasing equations 541
 Bijvoet pairs 502–3
 closure errors 509–10
 multi-wavelength anomalous diffraction 508–9
 single isomorphous replacement 501–2
 single-wavelength anomalous diffraction 502–3
 solution 500–9

PHENIX (computer program)
 dual-space direct methods 497
 macromolecular refinement 629, 632, 642, 649
 optimization 651
 substructure solution 481
 twinning 394
 phenylalanine 42
 phenyl rings, planar restraints 630–1
PHI-BLAST see pattern hit initiated basic local alignment search tool
 phosphocholine detergents 129
 phosphorescent imaging plates 379
 photon correlation spectroscopy (PCS) see dynamic light scattering
 photon energy 284–5
 photon flux 375
 photons 251
 charge-coupled devices 380–1
 counting statistics 319–21
 multiwire array detectors 379–80
 physical constants 754
Pichia pastoris 164–5, 173
 π -helix 34
 pixel array detectors (PAD) 381
 plain rotation axes, protein crystals 83
 planar restraints 630–1
 Planck constant 754
 plane equations, reciprocal lattice 238–9
 plane filling 199–200
 plane groups 201–11
 asymmetry 208–11
 hexagonal 207–8
 tetragonal 204–7
 trigonal 207–8
 plane lattices 199–211
 asymmetry 208–11
 hexagonal 207–8
 tetragonal 204–7
 trigonal 207–8
 plane wave 253–5
 plasmids 142–3
 PMF see Patterson minimum function
PocketFinder (computer program) 715–16
 pocketome 715
 point atoms 351–2
 point groups 203, 225, 280, 297–9, 551–2
 see also space groups
 point positions 229–30
 Poisson distributions 319–21, 365
 polar interactions 52, 100–1, 250
 polarization 120, 256–61, 283
 anisotropy 291
 electromagnetic radiation 180, 249
 refractive index 250
 Thomson scattering 256–7
 polarization anisotropy of anomalous diffraction (AAS) 291
 polarization factor 256–8, 283
 polarization volume 180
 polar residues 45–7
 polar space groups 229, 489, 586
 polyacrylamide gel electrophoresis (PAGE) 179–80
 polychromatic sources, monochromation 375–6
 polycrystalline samples 80–1
 polyethylene glycol (PEG) 79, 97, 127
 polymerase chain reaction (PCR) 142, 158–9
 polymorphisms 84, 122
 polypeptide chains 28–32, 40
 polyproline-II helix 35
 polytopic membrane proteins 61
 polyvinyl alcohol 97
 pooled coefficient of variation (PCV) 413
 porin 61, 129
 positional errors 517, 616–18
 position specific iterated basic-local alignment search tool (*PSI-BLAST*) 146
 positivity 344–7
 posterior probability 334–7, 694
 Bayes' theorem 318, 335
 maximum likelihood 336–7
 structure factors 345
 posttranslational modifications 85, 175–8, 190
 bacteria 162
 expression system choice 160–1
 yeast 164–5
 potassium channel structure 131
 potential functions 652–3
 powder diffraction 80–1
 PP-II helix 35
 PPI's see peptidyl prolyl *cis/trans* isomerases
 precession camera 405

- precision-indicating merging *R*-value 412–13, 530
 prediction of crystallization success 149–54
 preparation
 difference data 482–5
 proteins 11–14, 418–19
 primary structure 25, 737–8
 primer-based DNA manipulation 154–5
 primers 142–3
 primitive lattices 217
 primitive unit cells 201
 principle Euler angle 552, 555–6, 558
 prior probability 10, 318, 646–7
 probability 313–69
 algebra 316–19
 becoming a crystallographer 345–7
 closure error 509–10
 common distributions 365–6
 covariance 328–33
 independence 519–20
 inference 334
 integration 327–8
 prior 10, 318, 646–7
 relative error 320–1
 scattering 256
 sigma-A 359–60
 standard deviation 320–1
 variance 320–1, 325
 weighted averages 332–3
 probability distribution functions (PDF) 9–10, 313–69
 conditional 357–65, 549, 595
 correlation coefficients 330–1
 cumulative 392–4, 427–8
 Gaussian 321–5
 Luzzati D factor 361
 monomodal 510–12
 multimodal 511
 normal 321–5
 Poisson 319–21
 structure factors 347–57, 360–1
 unconditional 347–57
 univariate/unimodal 315
 Wilson scaling 347–57
 see also distributions
 probes
 real space 573
 selection 588–91
PROCHECK (computer program) 699
PRODRG server 711–12
 production of proteins 142–3
 product rule 316
PROFESS (computer program) 565, 569
 projections
 phase difference 258
 unit cells 228
 project planning 11–14
 proline 35, 42–3
PROLSQ (computer program) 628, 644, 651
 proper non-crystallographic symmetry 551–2, 560
 Patterson self-rotation functions 563–4
 see also non-crystallographic symmetry
 property profiling 717
 proportional counters 379–80
PROSA-II (computer program) 717
 protein, flexibility 7, 24, 707, 717
 protein backbone
 torsion angles 631–2
 see also carbon backbone
 protein complexes 64–71, 122–5, 132–3, 707–17
 protein constructs 84, 85
 protein crystallization 77–140
 see also crystallization
 protein crystals
 assembly 81–2
 chirality 222
 domain truncation 82
 evaluating diffraction 400–1
 fragility 82–3
 fundamentals 80–4
 local structure 8, 83
 morphology 84
 plain rotation axes 83
 polymorphism 84
 properties 81–2, 84
 size 13
 stability 82–3
 surface entropy 83
 symmetry 222
 see also crystals
 Protein Data Bank (PDB) 1, 19–20
 file deposition 725
 file format 19–20
 coordinate section 738–40
 CRYST1 records 738
 header section 737–8
 SCALE records 234, 738
 history 4, 19
 protein disulfide isomerase (PDI) 166
 protein–DNA complexes 64–71, 132–3
 protein engineering 13, 143–8, 175–8, 188–91
 alignment strategies 146–8
 crystallization 143–5
 limited proteolysis 175, 176
 lysine methylation 176–7
 strategies 144–5, 175–8
 surface entropy reduction 150–3
 protein expression see expression
 protein–ligand complexes 122–5, 707–17
 protein maps 522, 529–39
 protein–nucleic acid complexes 64–71, 132–3
 proteins
 anomalous phasing techniques 296
 characteristics 24
 cloning 142–3
 crystal growth 110
 electron density 512–13, 593
 flexibility, concept 24
 folding 166–7
 initial phase acquisition 478–81
 isoelectric point 83
 labelling 16, 43, 125, 171–3, 536–9
 local structure 8, 83
 modifications 144–5, 190
 native and derivative structure factors 476
 peptide bonds 29
 phasing, probability distributions 509–13
 production 142–3
 properties 6–8, 84–7
 purification 157–75
 purity 85–6
 stability 82–3
 stability analysis 179–88
 structural hierarchy 25–6
 structure factor calculation 279–81, 295–7
 tertiary structure 54–8
 torsion angles, peptide bonds 29–32, 629–30
 variability, concept 24
 see also protein structure
 protein sequence alignment searches (*BLASTP*) 146
 protein solutions 83–4, 87–91, 123–5
 protein structure 23–76
 accuracy 657–62
 α -helices 32–4, 677–8
 backbone geometry 28–32
 basics 24–8
 β -strands 35–6
 chirality 27–8
 data-to parameter ratios 627
 deposition 725–7
 determination 8–14, 18
 dimers 213
 disulfide bridges 46–7
 hydration shells 53–4
 hydrogen bonds 33–5
 ligand restraint files 709–13
 low temperature 387
 model building 607–91
 motifs 56–7
 Ramachandran plots 30–2
 side chains 4 9
 solvent coordination 688–70
 solvent interactions 53
 water dynamics 53–4
 see also proteins; secondary structure; structure
 protein structure models
 accuracy assessment 657–62
 hydrogen atoms 27
 hypothesis testing 695
 manual rebuilding 665–73
 pre-crystallography 33
 superposition 565
PROTEUM (computer program) 424
 protonation 100–1
 pseudo dyads 211
 pseudo-merohedral twinning 392
Pseudomonas 161
 pseudo-precession 405
 pseudo-symmetry 392
 negative intensities 344–5
PSI-BLAST see position specific iterated basic-local alignment search tool
 publication 727–32
 low resolution structures 719
 writing articles 728–30
 purification 157–75
 membrane proteins 174–5
 proteins 170–1
 SDS gel 85
Q
 quadrant checking 555
 quality
 analysis 411–17
 Bayes' theorem 335
 correlation coefficients 330–1
 electron density maps 523
 likelihood functions 614–20
 map assessment 534
 model assessment 657–62
 Poisson distributions 319–21
 structure validation 697–8
 quaternary structure 25, 62–4
 quaternion representation 643
 quenching 385–6
 QuickChange™ see single-step PCR mutagenesis
R
 racemic mixtures 234–5
 radiation damage 5, 250, 285, 296, 477
 reduction 79, 372
 synchrotrons 369
 radiation-damage-induced phasing (RIP) 293, 387
 radius of convergence 654
 radius of gyration 183
 Ramachandran plots 30–3
 α -helices 33
 backbone torsion angles 703
 structure validation 699
 Raman spectroscopy 250
 random atom models 347–51
 random errors 322
 random sampling 116–17
 random walks 348
 raw data 410, 411, 696
 raw moments 315
 hemihedral twinning 390–1
 merohedral twinning 354
 Rayleigh scattering 180
 reagents 95–101, 116–17
 real space
 convolutions 444
 cross-validation 626–7
 molecular replacement 565
 reciprocal lattices 238–9
 translational non-crystallographic symmetry 560–2
 real space averaging 566–7, 569
 real space correlation coefficient (RSCC) 17, 331, 704–5, 706
 real space correlation plots 673–4
 real space cycling 498–500
 real space fitting 608, 610–11
 real space grid searches 492–3
 real space probes 573
 real space refinement 441, 610–11
 real space *R*-value (RSR), structure validation 704–5, 706
 real space vectors 244
 receptor occupancy 123–5
 reciprocal lattice points (RLPs) 240, 396
 large unit cells 402
 rotation method 396–7
 reciprocal lattice 237–43, 245
 centrosymmetry 242–3
 construction 239–41
 direction 238–9
 Ewald sphere 270, 271–2
 Miller indices 237–9
 planes 237–9
 three-dimensional 238–9
 two-dimensional 237
 vectors 239–41, 747–8
 reciprocal space 309–10
 centric reflections 303
 chiral space groups 300
 convolutions 444
 diffraction conditions 274
 Ewald sphere 270
 Fourier transformations 441
 metric relations 747
 molecular scattering 266
 non-crystallographic symmetry 561–4, 600–1

- phase restrictions 303–4
 - real space probes 573
 - refinement 461
 - symmetry concepts 307
 - systematic absences 305–6
 - translations 561–2
 - reciprocal space averaging 567–9, 600–1
 - reciprocal space interference function
 - (*G*-function) 449, 566, 568, 583, 625
 - reciprocal space refinement 17, 608
 - reciprocal space restrained refinement 610–11, 620
 - reciprocal space searches 494
 - reciprocal vectors, Ewald spheres 270
 - recombinant DNA techniques 142, 143
 - rectangular tiles 199
 - reduced Chi-squared 326, 410–11
 - redundancy 411–16, 424–6, 430
 - redundancy-independent merging *R*-value 412
 - redundant data collection 424–6
 - reference frames 559
 - refinement 6, 607–91
 - atomic scattering factors 261
 - basics 620–2
 - charge flipping 500
 - computer programs 664
 - convergence 640
 - data-to-parameter ratio 622–45
 - definition 6
 - dummy atoms 573, 655–7
 - end points 682–3
 - fundamental rules 662–4
 - heavy atoms 513–23, 541
 - assumptions 514–16
 - classical 513–14
 - improvements 515
 - maximum likelihood 514–22
 - hydrogen atom restraints 633
 - low resolution structures 719
 - maximum likelihood map coefficients 618–20
 - model building 620–64
 - multi-conformer 655
 - NQH residues 671–2, 701
 - occupancy 262–3, 277, 498–500
 - in practice 665–84
 - protocols 621
 - raw data 411
 - real space 610–11
 - reciprocal space 461, 608, 610–11
 - restrained maximum likelihood 649
 - rigid-body 587–8
 - solvent flipping 504, 525–6
 - target functions 620–1
 - torsion angles 620
 - TRUNCATE* (computer program) 424
 - unrestrained 627, 656–7
 - see also optimization
 - reflections 397
 - absences 454–5
 - acentric, non-isomorphism 478
 - Bragg equation 265
 - capturing 272–4
 - centric 276, 478
 - estimating number 628
 - Ewald spheres 271
 - full 397
 - incommensurate satellite 404–6, 407
 - merging 411–16
 - partial 397
 - phase restricted 276
 - reciprocal space symmetry 303–4
 - satellite, non-crystallographic symmetry 561
 - space groups 230–1
 - split 402
 - REFMAC* (computer program) 411
 - B*-factor restraints 636
 - Fishers information 660
 - ligand restraint files 710–11
 - LINK statements 667
 - macromolecular refinement 642, 645, 648
 - optimization 651
 - register errors 667–8
 - restrained maximum likelihood refinement 649
 - restraint setup 637, 640, 645
 - refractive index 250
 - re-indexing 416–18
 - transformation matrix 745–6
 - see also indexing
 - relative error 320–1
 - relativistic speed effects 377
 - remote data 536–7
 - remote facility access 3–4
 - reporter tagging 169
 - repulsive restraints 632–3
 - rescaling 424
 - reservoir solutions 105
 - residual (free) index (*R*-free)) 17
 - cross-validation 624–5
 - expectation values 660–2
 - residual index (*R*-value) 17
 - anomalous merging 413
 - covariance 330–1
 - cross-validation 626
 - linear merging 412
 - merging 484
 - model building 613–14
 - model refinement 620
 - precision-indicating merging 412–13
 - redundancy-independent merging 412
 - sigma 415
 - upper limits 355
 - residuals, expression 325
 - residues 40
 - chirality/planarity 630–1
 - electron density 47
 - identification 678–9
 - modification 48
 - pK_a* values 48–9
 - real space fitting 610–11
 - surface entropy reduction 150–3
 - see also amino acids; side chains
 - resolubilization 163–4
 - resolution
 - cryocrystallography 386
 - cutoffs 530–1, 532
 - electron density maps 451–3
 - first inspection 400–1
 - importance 395
 - incomplete data 453–7
 - limits 273
 - merging 411–16
 - molecular motion 262
 - peak separation 453
 - signal-to-noise ratio 414–15
 - structure based design 452
 - truncation 448
 - resolution spheres 272–4
 - RESOLVE* (computer program) 481, 522, 527–8, 678
 - resonance 287–8
 - restrained refinement 17, 628, 634–5, 649, 666–7
 - restriction enzymes 154, 156
 - R*-value see linear residual
 - RFCORR* (computer program) 565
 - Rhodobacter capsulatus*, porin 61
 - Rhodobacter sphaeroides* (RS), cytochromes 577
 - rhombohedral centering 217–19
 - rhombohedral lattices 217–18
 - ribonuclease A, β -structure 37
 - β -D-ribose 66
 - ribose-1, 5-biphosphate carboxylase (RuBisCO) 717
 - Rice distributions 358–9, 362–5, 595, 616
 - acentric structure factors 364
 - heavy atom refinement 517
 - Richards box 609
 - riding positions 629
 - riding restraints of hydrogen atoms 633
 - rigid-body refinement 579, 587–8
 - RIP see radiation-damage-induced phasing
 - RLPs see reciprocal lattice points
 - RMSD see root mean squared deviations
 - RMSZ see root mean squared Z-scores
 - robotics 112–13, 383
 - root mean squared deviation (RMSD) 326, 483, 639, 640
 - root mean squared Z-scores (RMSZ) 327
 - rotation axes 203–6, 236
 - rotation images 395–9
 - lunes 396–7, 398
 - rotation matrices 552–5
 - rotation method 395–9
 - fine slicing 398
 - rotations 203–7, 552–7, 581–4
 - Cartesian space 552–5
 - direct function 583–4
 - fast function 583
 - improper non-crystallographic symmetry 551–2
 - likelihood enhanced functions 598
 - locked functions 584
 - matrix operators 223–4
 - maximum likelihood functions 597–8
 - non-crystallographic symmetry 548, 551–2, 560
 - Patterson function 468–9, 549, 581–4
 - real space function 583–4
 - resolution 455–6
 - searches 573
 - self-rotation 584
 - spherical coordinates 556–7
 - tetragonal 204–7
 - two-fold 204
 - ZXZ convention 553
 - ZYZ convention 553–4
 - rotation-translation searches 573, 580–8
 - ROTMAP* (computer program) 553
 - roto-translations 219–23
 - RS see *Rhodobacter sphaeroides*
 - RSCC see real space correlation coefficient
 - R*-sigma 415
 - RSR see real space *R*-value
 - RuBisCO see ribulose-1, 5-biphosphate carboxylase
 - R*-value see residual index
- S**
- SA see simulated annealing
 - Saccharomyces cerevisiae* 164–5
 - SAD see single-wavelength anomalous diffraction
 - SAINT/PROTEUM* (computer program) 405
 - salt bridges 100–1
 - salt crystals 120, 400
 - salting in/out 96
 - salts 87, 96–7, 385
 - salvage strategies 85, 144–5, 401, 458
 - sample distribution 182
 - sample mean 325
 - sampling
 - central limit theorem 323–5
 - crystallization propensities 116–17
 - Nyquist theorem 448
 - sampling density 243, 245
 - sampling probability, Bayes' theorem 318
 - SARS see severe acute respiratory syndrome
 - satellite reflections 406, 407, 561
 - Sayre's equation 496, 527
 - Scaffolding 130, 174
 - SCALA (computer program) 421, 424
 - scalar values 199, 216
 - scale factors 330–1, 355–7
 - SCALE records 234, 738
 - scaling 410, 411, 426
 - anisotropic 483, 641–2
 - data deposition 725
 - local 482
 - scattering 247–311
 - adjacent atoms 263–4
 - anomalous differences 288
 - atomic scattering factors 257–8
 - dispersive differences 288
 - electrons 251
 - free electrons 256–7
 - inelastic 256
 - neutrons 261
 - non-isomorphism 478
 - single atoms 257–61
 - single molecules 266–7
 - small angle 183
 - structure factor summation 275–6
 - summation 267–8
 - X-rays 256
 - see also diffraction
 - scattering diagrams 255–6
 - scattering envelopes 266–7
 - scattering probability 256
 - Schönflies symbols 228
 - scientific illustration 728–30
 - SCOP see Structural Classification of Proteins
 - screening 115–18, 711
 - random sampling 116–17
 - two-tiered approaches 117–18
 - screw axes 219–23
 - enantiomorphic pairs 222
 - space groups 236
 - systematic absences 274
 - screws, nomenclature 34
 - SCRWL* (computer program) 589
 - SD see standard deviation
 - SDS gel 85
 - searches 573–91
 - evolutionary algorithms 573, 575–80
 - molecular replacement 589–91
 - multidimensional 574–80
 - rotation-translation 573, 580–8
 - six-dimensional 573
 - SEC see size exclusion chromatography

- secondary structure 7, 25, 32–9, 187
 α -helices 32–4, 677–8
 α -carbon validation 717–19
 α -turns 38
backbone torsion angles 631–2
 β -bulges 36–7
 β -sheets 36–7
 β -strands 35–6
 β -turns 38
bioinformatics tools 147
circular dichroism 183–5
hydrogen bonds 33–5, 39
irregular sheets 36–7
omega-loops 38–9
protein data bank files 737–8
turns 37–8
second virial coefficient 85, 181
secretion, yeasts 164
seeding see nucleation
selection
combinatorial design 157
dispersive atoms 292–3
wavelengths 289–91
selenium 294
selenomethionine (Se-Met) 16, 43, 125, 171–3, 536–9
self assembly 91–5
self-rotation
locked function 584
non-crystallographic symmetry 563–5
searches 581–4
self-vector peaks 487
Se-Met see selenomethionine labelling
semi invariants, direct methods 496–7
semi-variants, definition 490
sensitive complimentary metal oxide
semiconductors (CMOS) 381
separation of antibodies 131
SEQRES records 725, 737
sequence
binding pockets 715–17
crystallization 144–5
structure 57, 578
surface entropy reduction 150–3
sequence alignment 147–8
sequence file deposition 725
sequence retrieval 146–8
sequential design 144–5
SER see surface entropy reduction
serial extinctions 305
serine 45
serine kinases 715
severe acute respiratory syndrome (SARS) 221
Sf see *Spodoptera frugiperda*
SFALL (computer program) 627
SFCHECK (computer program) 705–6
Shake&wARP (computer program) 590, 656–7
Shake and Bake (computer program) 481, 497
SHARP (computer program) 478
sharpening
electron density maps 526
normalized structure factors 353
Patterson functions 468
sphere of influence method 526
Sheldrick's rule 495
SHELXC (computer program)
electron density maps 504
multi-wavelength anomalous diffraction 537
refinement 424
sulfur single-wavelength anomalous
diffraction 530–1
SHELXD (computer program)
direct methods 495
dual-space direct methods 497
electron density maps 504
multi-wavelength anomalous diffraction 537
occupancy refinement 498–500
refinement 424
substructure solution 481, 482
sulfur single-wavelength anomalous
diffraction 531–2
SHELXE (computer program)
electron density maps 504
Free Lunch 529, 534–5
histogram matching 527
map averaging 569
multi-wavelength anomalous diffraction 537
refinement 424
solvent flipping 526
sulfur single-wavelength anomalous diffraction
532–3, 534–5
SHELXL (computer program)
refinement 629, 634, 635, 640, 645, 651
target functions 621
twinning 389, 394
side chains 24, 47–54
conformations 47–8, 672–3
covalent bonding 50
electron density 47, 671–2
hydration shells 53–4
hydrogen bonding 50–2
hydrophobic interactions 53
ionic bonding 50
polar interactions 52
replacement 665–6
solvent structure 53
structure validation 701
torsion angles 47–8, 672–3
Van der Waals interactions 52–3
water dynamics 53–4
see also amino acids; residues
sigma-A 616–18
computation 617
cross-validation 625
error reduction 359–60
heavy atom refinement 515
phase evaluation 613
sigma-cutoff 484
signal peptides 164
signal sequences 147
signal-to-noise ratio (SNR) 267
data collection 407
fine slicing 398, 402–3
intensity errors 458–9
merging *R*-value 414–15
mosaicity 402–3
sigma-cutoff 484
substructure phasing 484–5
see also noise
Sim distribution 358, 516–17, 595, 616
simplex algorithm 678
simulated annealing (SA) 342, 579, 621, 626, 653–5, 666
Sim-weights 358–9, 514
single-axis goniostat 382
single isomorphous replacement with anomalous
signals (SIRAS) 479, 480, 503–5
combined map averaging 570–1
density modification 503–5
likelihood function 521
Patterson maps 486
single isomorphous replacement (SIR) 476–7, 501–8
density modification 503–5
handedness ambiguity 507–8
phase determination 479, 480
phasing equations 501–2
single molecule diffraction 267
single-step PCR mutagenesis (QuickChange™) 154
single-wavelength anomalous diffraction
(SAD) 290
data collection strategies 409
density modification 503–5
enantiomorph problem 505–6
handedness ambiguity 507–8
likelihood function 520–1
marker atom substructure phasing 477
phase angle ambiguity 293
phase resolution 502–6
phasing equations 502–3
when to use 509
see also sulfur single-wavelength anomalous
diffraction
SIR see single isomorphous replacement
SIRAS see single isomorphous replacement with
anomalous signals
site-directed mutation 142, 150–4
binding pocket prediction 714–15
glycoproteins 178
surface entropy reduction 150–3
site occupancy
B-factors 262–3, 277, 448–50
crystallization 123–5
site prediction 148–9
site-specific viral proteases 168
sitting-drop vapor diffusion 104–5
six-dimensional search methods 573
six-fold screw axes 220–1
size exclusion chromatography (SEC) 179–80
SKETCHER (computer program) 710–11
slab thickness 449–51
slow cooling, of crystals 388
slow cooling protocol 654
small angle scattering 183, 256, 261
small intensity problem 330
small molecules 493–4
SMILES 712
SnB see Shake and Bake
SNR see signal-to-noise ratio
soaking 122–7
solid state enzyme activity 7
SOLOMON (computer program) 522, 526
solubility
pH 89, 99–101
polyethylene glycol 97
temperature 88–9
solubility diagrams 88–9
solubilization, membrane proteins 174–5
solution landscapes 578–9
SOLVE (computer program) 481, 494, 565
solvent 53–4, 82–4, 387
electron density 523–6, 593
Matthews probabilities 549–50
non-water 670
water 53–4, 668–70
solvent building 668–70
solvent channels 7, 83–4, 122–3
solvent contrast 261
solvent correction 719
solvent flattening 504, 523–5, 567–8
solvent flipping 504, 525–6
solvent interactions 39, 53–4, 82–4
solvent masks 504, 523–5, 567
solvent positions 387, 668–70, 681
SOMoRe (computer program) 579
space groups 19–20, 198, 223–36, 245
determination 416, 417, 422–4
extinction rules 230–1
general positions 230
generators 225–6, 229–30
Harker sections 487–9
Hermann–Mauguin symbols 226–8
indexing 753
matrix operators 223–4
origin 228–9
point positions 229–30
preferences 234–6
racemic mixtures 234–5
reflection conditions 230–1
special positions 230
symbolic operators 223
symbols 207
symmetry operations 223–4
unit cell determination 404
spallation neutron sources 261
sparse matrix optimization 651
sparse matrix sampling 116
special positions 209–10, 230, 306–7, 505–6
special structure factors 280, 282
spectroscopic terms 286
speed of light 754
sphere of influence 526
spherical coordinates 429, 556–7, 750
spherical harmonic functions 583
spherulites 111
split reflections 402
Spodoptera frugiperda (Sf) 165
spontaneous nucleation 112
Sporobolomyces salmonicolor (SSCR) 714
spot finding 420
squared structure factor amplitudes 465–9
square tiles 199
squaring method 496
SQUASH (computer program) 522, 527
SRS see sum of residuals squared
S-SAD see sulfur single-wavelength anomalous
diffraction
SSCR see *Sporobolomyces salmonicolor*
stability 82–3, 186, 190–1
 π -stacking 52
standard deviation (SD) 320–1, 325–6
static light scattering 180–1
statistics 8–10, 313–69
anomalous merging *R*-value 413
descriptive 325–7
linear merging *R*-value 412
merging 411–16
pooled coefficient of variation 413
precision-indicating merging *R*-value 412–13
redundancy 411–16
redundancy-independent merging *R*-value 412
twinning descriptors 394
twinning intensities 392–4
Wilson scaling 347–57

- steepest gradient optimization 342, 652
 step functions 449
 stereochemical constraints 627–9
 stereochemical restraints 6, 10, 17, 627–40
 amino acids 630–1
 anisotropic displacement 636
 Bayesian inference 336–7
 Bayes' theorem 646
 B-factors 635–6
 bonding 629–30
 chirality/planarity 630–1
 cross-validation 17
 data-to-parameter ratio 636–40
 dihedral angles 629–30
 estimating number 638
 hydrogen atoms 633
 ligand files 709–13
 likelihood target functions 645–9
 log-likelihood 648
 maximum likelihood 646
 model accuracy 658–9
 model building 611, 627–40
 model error estimation 648
 non-bonded interactions 632–3
 non-crystallographic symmetry 634, 635
 optimization 620
 peptide bonds 29–32, 629–30
 prior probability 646–7
 root mean squared deviation 326
 setup 636, 637–40
 table 637
 weighting 624–5, 639
 stereochemistry
 evaluation 698–704
 structure validation 706–7
 stereographic projections 225, 248, 429, 563–4
 stochastic design 144, 175, 176
 see also combinatorial design
 stochastic optimization 342, 621, 652–5
 stochastic searches 573–80, 652–4
 Stokes–Einstein relation 182
 storage rings 378
 streak seeding 111
 Strep tags 168–9
 stripes, zingers 381
 strong reflections 454–5
 Structural Classification of Proteins (SCOP) 57–8
 structural domains 55–6
 structure
 conservation 57
 heavy atom refinement 513–23
 low temperature 387
 Patterson functions 466–8
 sequence 578
 see also protein structure; secondary structure
 structure based drug design 150–4, 707, 711
 resolution 452
 surface entropy reduction 150–3
 structure determination 8–14, 18
 nuclear magnetic resonance spectroscopy 1
 strategy overview 396
 structure factor amplitudes 6, 275–7, 281–4, 329–30, 347–57
 deposition 696
 determination 276
 error 329–30
 negative intensities 343–5
 normalized distributions 351–4
 reciprocal space refinement 610–11
 squared 465–9
 structure factors 268–70, 277–84, 308–9, 347–65, 476–81
 acentric 350, 361
 anomalous diffraction 295–7
 bulk solvent corrections 591–3
 deposition 725
 distributions 327, 347–65
 epsilon factors 306–7
 equation 268
 error models 360–1
 Fast Fourier Transform 443
 Fourier interpolation 574
 mean *E*-squared minus one computation 354–5
 multiple atoms 360–1
 normalized 278, 351–4, 468, 497
 posterior probabilities 345
 random atom models 348–50
 single atoms 360
 summation 275–6
 unitary 352
 structure-guided drug design 2, 709–17
 structure invariants 496–7
 structure solution, automated 591
 structure validation 17–18, 693–727
 alpha carbon-only 717–19
 backbone torsion angles 631–2
 B-factors 706–7, 709
 binding pocket analysis 712–17
 case studies 720–4
 chemical plausibility 712–13
 computer programs 699
 deposition pre-check 725–7
 electron density 704–7
 geometry 709–13
 as hypothesis testing 694–6
 importance 695–6
 ligand restraint files 709–13
 low resolution 717–19
 multiple side chains 701
 non-crystallographic symmetry 703–4
 NQH flips 701
 property profiling 717
 protein–ligand complexes 707–17
 real space *R*-factor 704–5
 stereochemistry 698–704, 706–7
 torsion angles 717–19
 Z-values 698
 Sturm–Liouville eigenvalue problem 441
 substructure solution 9–10, 302–3, 475–81, 539–40
 isomorphous differences 475–7
 Patterson maps 495
 phase problem 474
 phasing principles 477
 versus *ab-initio* methods 495
 see also marker atom substructure solution
 sulfur, scattering factors 260
 sulfur single-wavelength anomalous diffraction (S-SAD) 293, 417–26, 529–35
 basic steps 530
 data collection strategies 409
 development 506
 Free Lunch 534–5
 map quality assessment 534
 phase 479, 480, 533
 phase extension 534
 SHELXC 530–1
 SHELXD 531–2
 SHELXE 532–3, 534–5
 see also single-wavelength anomalous diffraction
 sum of residuals squared (SRS) 326
 sum rule 317
 superposition 252–5, 564–5
 supersaturation 78, 79, 88–9, 92–3, 112
 superstructure 212–14, 406, 560–1
 surface entropy 83
 surface entropy reduction (SER) 150–3
 symbolic operators 223
 symmetry 202–36
 asymmetry 208–11
 chirality 220
 diffraction limits 272–4
 direction cosine matrix 555
 equivalents 203
 hemihedral twinning 390–5
 hexagonal 207–8
 matrix operators 223–4
 mirror 203, 220, 416
 non-crystallographic 211–14, 551–65
 non-merohedral twinning 388–90
 operations 203–6, 219–24
 point groups 225, 297–9
 publication 731
 reciprocal space 242–3, 297–307
 space groups 223–36, 416
 tetragonal 204–7
 three dimensional 214–23
 trigonal 207–8
 two-fold rotations 204
 unit cells 202–8, 404
 see also Laue symmetry; point group symmetry;
 space groups
 symmetry-related molecules 7, 19–20
 synchrotrons 79, 288, 372, 376–85, 418–19
 charge-coupled devices 381
 circular dichroism 183–5
 coherence length 251
 radiation damage 369
 storage rings 378
 undulators and wigglers 378
 systematic absences, extinction 280
 excluded regions 274
 non-crystallographic symmetry 561
 space group determination 416
- ## T
- Table 1 426, 429–31, 725
 Table 2 683–4
 tagging 167–73
 green fluorescent protein 169
 histidine 85, 167
 intein fusion systems 169
 site-specific viral proteases 168
 thrombin 168
 TA-MD see torsion angle molecular dynamics
 tangent formula, direct methods 497
 targeted protein design 144–55
 surface entropy reduction 150–3
 target functions
 least squares 621
 maximum likelihood 621
 refinement 620–1
 stereochemical restraints 645–9
 TATA box binding protein (TBP) 68
 Taylor expansion
 Euler's formula 749
 log-likelihood 339–40
 optimization 650
 refinement 621
 TBP see TATA box binding protein
 technical review 730
 tedium 680, 682–3
 temperature
 expression 163
 protein structure 387
 solubility 88–9
 see also *B*-factors; cooling; cryo...
 template convolution 679
 tensors
 anisotropy 291, 356, 636, 641
 bond angle calculation 744–5
 metric 233, 744–5
 tertiary structure 25, 54–8
 tetrad symbol 203
 tetragonal crystals, birefringence 120
 tetragonal lattices 217–19
 tetragonal space groups, properties 227
 tetragonal symmetry 204–7
 TEV see Tobacco Etch Virus
TEXTAL (computer program) 678
 TF see ThermoFluor
 thermal vibrations 386
 thermodynamics 87–91
 ThermoFluor (TF) stability assays 179
 thiol residues, disulfide bridges 46–7
 thioredoxin reductase (*trxB*), *Escherichia coli* 162
 thioredoxin (TRX) tagging 169
 Thomson scattering 180, 256–7
 three-dimensional electron density maps 449–51
 three-dimensional lattices 216–19, 238–9
 three-dimensional symmetry 214–23
 three-fold screw axes 220–1
 threonine 45
 threonine kinases 715
 thrombin, fusion tagging 168
 thymidine structure 66
 tight sampling 243, 245
 tile patterns 199–200
 TIM barrel see triosephosphate isomerase barrel
 time-resolved X-ray diffraction 369
 TLS parameterization see translation-libration-screw parameterization
TNT (computer program) 632, 645, 649, 651
 Tobacco Etch Virus (TEV), protease 168
 Tobacco Vein Mottling Virus (TVMV), fusion tagging 168
 topoisomerase cloning 159
 torsion angle molecular dynamics (TA-MD) 654
 torsion angles 26–32
 amino acids 630–1
 carbon backbone 701–3
 deposition pre-check 726–7
 manual model rebuilding 666
 peptide bonds 29–32, 629–30
 protein backbone 631–2
 Ramachandran plots 30–2
 refinement 620, 640, 652–5, 704
 restraints 629
 side chains 47–8, 672–3

structure validation 701–4, 717–19

traces

- alpha carbons 676–7, 717–19
- direction cosine matrix 555

transfection 142–3, 156

transformations

- Cartesian 558–9
- coordinate systems 746–7
- matrices 745
- non-crystallographic symmetry 548, 551–65
- reference frames 559

transition metals 293

translational symmetry, non-crystallographic 213

translation-libration-screw parameterization (TLS parameterization) 8, 620, 638–9, 642–4

translations 213

- fast functions 586
- likelihood enhanced functions 596
- maximum likelihood functions 595–7
- near perfect non-crystallographic symmetry 560
- non-crystallographic symmetry 548
- Patterson space 562
- screw axes 220–3

translation search functions 494, 573

transmembrane helices 147

transmembrane proteins 59–61, 62

trans-peptide bonds 29–30

transport 418–19

transpositions 555, 741–2

triad symbol 203

triclinic lattices 217

triclinic space groups 214–15, 227

trigonal crystal birefringence 120

trigonal space groups 227

trigonal symmetry 207–8

trimming, of search model 577

triphosphate isomerase barrel (TIM barrel) 200–1

triplet relations 483, 495–6

triple vector product 215

TRUNCATE (computer program) 344, 393, 394, 421–2, 424

truncation

- anisotropic 642
- DNA 155–6
- domains 55–6
- electron density 446–8, 450
- heavy atoms 532
- model trimming 577

truncation libraries 156

truncation ripples 448, 498

TRX see thioredoxin

trxB see thioredoxin reductase

tryptophan 45–6

tryptophan synthase 62

tunable X-ray sources 376–9

tungsten 374–5

turns 37–9

- α -turns 37–8
- β -turns 37–8
- γ -turns 37
- π -turns 37

TVMV see Tobacco Vein Mottling Virus

twilight zone, for modelling 578

twinning 94–5, 388–95, 427–8

- acentric reflections 392–3
- centric/acentric distribution 351
- cumulative distributions 322–3, 392–4
- hemihedral 390–1
- holohedry 391
- intensity statistics 392–4
- macroscopic 388–90
- merohedral 390–5, 561
- non-merohedral 388–90
- statistical descriptors 394
- tests 394, 427–8
- Yeates–Padilla plots 393–4

two-axis goniostats 382

two-fold rotations 204

two-fold screw axes 220

two-tiered approaches 117–18

tyrosine 45

tyrosine kinases 715

U

ultraviolet radiation (UV) 67

unconditional probability distributions 347–57

unconditional Wilson limit 364–5

undulators 378

uniaxial, definition 227

unimodal, definition 315

unimodal distribution 324–5

unique axis, birefringence 120

unique reflections 275, 297, 627, 628

unitary structure factors 352

unit cells 81, 200–11, 244, 404

- asymmetric 208–11
- content 231–2, 428
- diffraction non-linearity 275
- general positions 228
- hexagonal 207–8
- large 402
- non-crystallographic symmetry 548–51, 600
- packing 231–2
- projections 228
- re-indexing 416
- rhombohedral 218
- symmetry 202–8
- triclinic 214–15
- trigonal 207–8
- two-fold rotations 204
- volume 215, 548

unit lattices 199–200, 215–16

univariate, definition 315

unmerged data 411

unrestrained maximum likelihood refinement 656–7

unrestrained refinement 627

upper limits 355

uracil 66

usage bias 97

UV see ultraviolet radiation

V

validation see structure validation

valine 42

Valium® see diazepam

van der Waals (vdW) forces 52–3, 82, 631–2

vapor diffusion 78–9, 102–5

variability 24

variance 320–1, 325, 349–50, 598

- inflation 520

vdW see van der Waals forces

vectors 162–3, 215, 244

- basic algebra 740
- Cartesian space 552
- Harker sections 486–7
- indexing 403, 405
- matrix operations 742–3
- multiplication 741
- Patterson maps 485–94
- protein expression 160, 161–5
- reciprocal lattices 239–41
- to atomic positions 489

verify3D (computer program) 717

vibrations, cryocrystallography 386

virtual ligand screening (VLS) 707, 715–16

viruses 26, 108

viscotoxin (VTA1) 418–27

vitreous states 387

VLS see virtual ligand screening

VTA1, ribbon model 536

W

water

- clathrates 90
- coordination 53–4
- dynamics 53–4
- molecules 669–70

wavelength

- anomalous diffraction 297
- Bijvoet differences 293
- large unit cells 402
- relationship with energy 249
- selection, X-ray absorption 289–91
- see also energy

wave vector, definition 252

wedges, of diffraction data 297, 455–6

- Friedel pairs 299–301
- symmetry generation 299–301

weighted averages 332–3

weighting

- free *R*-value 624–5
- restraints 624–5, 639

Weiss indices 237

WHAT-CHECK (computer program) 640

white line peaks 173, 286–7

wigglers 378

Wilson distributions 366–7, 595

- acentric 350
- central limit theorem 324
- centric 349–50
- electron density map refinement 461

normalized 353

- random atom models 347–51
- unconditional limit 364–5

Wilson-like maximum likelihood rotation function (MLRF) 597

Wilson plots 355–7, 427, 706

Wilson scaling 284, 351, 355–7, 366–7, 482

- TRUNCATE* (computer program) 421–2

Wilson statistics 494, 613

Woolfson distributions 363–5, 616

X

XANES see absorption near edge structure

XAS see absorption edge fine structure

XDS (computer program) 405

Xengen (computer program) 405

xenon derivatization 126

Xhercules (computer program) 492–3

xor see exclusive or statements

XPLOR (computer program) 632, 634, 648, 651–4

XPREP (computer program) 411, 422–4, 537

X-rays

- absorption 284–97
- anomalous diffraction 250
- brilliance 378
- characteristic radiation 373–4
- coherence length 251
- detectors 379–81
- discovery 248
- emission 372–3, 376–7
- energies for atomic numbers 293
- exposure time 401
- focusing 250
- free radicals 250
- generators 374–5
- intensity 275–84
- phasing 250
- properties 249–55
- radiation damage 250
- scattering 247–311
- spectra 373
- synchrotrons 376–9

X-ray sources 372–9

- Bremsstrahlung 372–3
- brilliance 378
- characteristic radiation 373–4
- emission 372–3, 376–7
- synchrotrons 376–9

X-ray terms 647–8

Xtal/View (computer program)

- manual model rebuilding 665
- Patterson searches 492–3
- register errors 667–8

Y

yeasts 164–5

Yeates–Padilla plots 393–4

Z

zinc-finger DNA binding motif 68

zingers 381

- α -zingers 381

zonal extinctions 305

zone 270

Z-values 322, 698

ZXZ convention 553

ZYZ convention 553–4

