

## Index

“1.13.12.4” 112, 115

### a

*ab initio* methods 76

*ab initio* modeling 55

abiotic 447

absorption 5, 135, 178, 240, 333, 359

acceptor 16, 68, 118, 178, 181, 190,  
249, 263, 264, 269, 270, 279, 299,  
301, 302, 318, 322, 347, 428, 453  
*see also* hydrogen-bond  
acceptors

accessibility 101, 182, 210, 285, 292,  
367, 516

accessible surface area 294

ACD/MS Fragmenter 151, 375

ACD software 143, 156

ACD structure elucidator 154, 155

acetylcholinesterase inhibitors 418

Achilles project 198, 199

acid dissociation constant (p*K*<sub>a</sub>) 54,  
73–76, 349, 456

acidity 11, 53, 456

activation energy 121

active analog approach 263

active pharmaceutical ingredients  
(APIs) 453, 573

active sites 179, 283–292, 298–304,  
315, 317, 367

activity cliffs 320

ADABoost 26

adaptive neuro-fuzzy inference system  
(ANFIS) 350, 352

adaptive soft sensors 576–578, 582

additivity schemes 56–58, 62f, 70

adenosine monophosphate (AMP)  
121–123

adipose 240

ADME (absorption, distribution,  
metabolism and excretion) 272,  
333, 359, 448

ADME-Tox 166, 178ff, 272, 350–353,  
544

adrenaline 261

ADRIANA-Code 338–347

adverse drug reactions (ADRs) 398

aem-thiolate proteins 366

*Aerococcus viridans*, 128

aflatoxin 445

Aggregated Computational Toxicology  
Resource (ACToR) 431

agonists 167, 225, 361, 375

agricultural research 417ff

agrochemical industry 6, 313

air-water contact angle 553

alanine 95, 128

albumin 349, 350

alcohol and aldehyde dehydrogenases  
363

aldehydes 175, 363, 378, 511

aldose reductase-2 (ALR-2) 240

algorithmic complexity 268

alignment 24

multiple sequence 285, 291, 298

structure 178

alignment-independent 3D QSAR

methods 24

aliphatic carboxylic acids 73, 75

- Allen scheme 62
- allosteric sites 284
- allosterism 413
- Almond 24
- ALOGP 57, 65
- ALOGPS 65f
- alpha-hydroxy-isocaproate 126
- alpha shapes 287
- ALR2 inhibitors 240, 242
- alternating least squares (ALS) 492
- AM1, 66, 367
- AMBER 319
- Ames test 432
- p*-aminobenzenesulfonamides 260
- $\beta$ -amino-phenylpropanoicmimic 242
- amorphous forms 55, 69–72
- $\alpha$ -amylase 275
- $\alpha$ -amylase inhibitor 276
- anaerobic gut bacteria 362
- analytical chemistry 7, 469–493
- animal studies 188, 429, 441
- anisotropy 144, 149
- annotated genomes 123, 125
- annotations 198
  - active site 293
  - binding site 284
- antagonism 260
- antagonist 167, 260, 275, 361, 369, 409, 413
- anti-cancer effects 224
- ant colony optimization (ACO) 316, 492
- anti-inflammation 535, 538
- anti-inflammatory compounds 221, 224, 227, 240, 373
- anti-influenza 226
- antibacterial treatment 125
- antibiotics 170
- antibody markers 565
- anticonvulsant effect 514–516
- antidepressant 517
- antipsychotic agent 374
- antitarget 220
- anti-T2D compound database (ADB) 239
- anti-T2D drug target 238
- antiviral agents 272
- anti-wrinkles/anti-ageing 538
- apoprotein 428
- applicability domain (AD) 32, 41–43, 46, 66, 334, 365
- application programming interface (API) 449
- APROPOS 287
- AQUASOL 342
- aqueous solubility (log *S*) *see* water solubility (log *S*)
- archazolide A (ArcA) 224
- ARChem-Route Designer*, 99
- Arctander atlas 512
- arctigenin 226
- area under the curve (AUC) 46, 326, 483
- arene oxide formation 381
- arginine (Arg98) 424
- aromatic systems 57, 63, 136, 145, 184, 263, 265–266, 318, 374, 381, 419, 507
- aromaticity 55, 252, 460
- Artemisinin 115f
- artificial intelligence 5, 134, 413
- artificial neural network (ANN) 17f, 28f, 135, 138, 154, 227, 335, 338, 478, 492, 555
- artificial neural network ensembles (ANNE) 350, 352
- ASN.1 format 250
- Aspirin 254
- assay 209, 247
- assay ID (AID) identifier 247
- assay-to-lead attrition 178
- ASSEMBLE 153
- assertional metadata 397
- assertion re-generation 397
- associative neural networks (ASNN) 145
- Asteraceae*, 227f
- atom-based contribution method 57, 60
- atom-centered code 136
- atom counts 250, 507–509
- atomic electronegativity distance vector (VAED) 139
- atomic properties 56, 135, 338

- atomic resolution 110, 112
- atom-to-atom matching 110, 252
- attribute selection 124
- attrition 166, 178, 183
- autocorrelation 16, 173, 177, 186, 346
  - autocorrelation vectors 16, 338
- AutoDock 221, 315f
- automated interpretation 135
- automated synthesis design 102
- automated text mining 398
- automatic information extraction 77
- automatic knowledge extraction 151
- automatic recognition 150
- autoscaling 472
- average absolute error (AAE) 70, 337
- Ayurveda 171
  
- b**
- back-propagation 29
  - error 492
  - neural network (NN) 65f, 154
- backward-elimination regression 21
- bagged decision tree (BDT) 346, 347, 349, 480
- bagging 26, 346, 480
- baicalein 221
- base learners 25f
- baseline toxicity 185
- basis set 476
- Bayes' rule 577
- Bayes' theorem 28
- Bayesian methods 552, 554
- Bayesian regularized artificial neural network (BRANN) 29
- Beilstein Handbook 96
- benchmarking 66, 210
- Benson scheme 61
- benzodiazepine agonists (BDA) 173, 174
- benzoic acid 456, 457
- benzyloxybenzene 418
- beta-secretase 408
- big data 77, 413, 495, 549
- binary classification 45, 347, 397
- bindability 292, 294
- binding affinity 69, 181, 210, 265, 317, 319, 320
- binding motif 323
- binding pocket 179–181, 189, 221, 225, 226, 428
- binding pose 209, 230, 316, 425, 428
- Bingo 449
- binned nearest neighbors (BNN) 483
- bioactivation 361f
- bioactive polymers 561–564
- bioactivity 13, 198f, 211, 226, 361, 395f
- bioassays 240
- bioavailability 63, 209, 274, 293, 333, 336, 353
- biochemical assay 418, 431
- biochemical databases 375
- biochemical on-chip assay 408
- biochemical pathways 106–115, 566
- biochemical reactions 85, 106, 110, 125, 171
- biochemical synthesis 375
- biocompatibility 551
- BioCyc 111
- biodegradation 533
- biodistribution 413
- biodiversity 208
- bioinformatics 2, 108, 123, 125, 166, 168, 170, 195, 407, 527
- biological activities 10, 11, 17, 18, 190, 408, 442–44
- biological affinity 361
- biological analogs 448
- biological data 14, 20, 25, 166, 229, 553
- biological testing of matching molecules 272
- biology files 386
- biology-oriented synthesis (BIOS) 209, 412
- biomarker 128, 195, 199
- biomolecules databases 505
- BioPath.Database 109–128
- BioSM 375
- biotechnology 175, 246, 313
- biotic 447
- biotransformation 359, 361, 362, 368
- BIOVIA Direct 449
- BitterDB 505, 509
- bitvectors 251f

- BLAST 297f
- BLASTP 126
- bleaching 418
- BLOCKS 298
- blood–brain barrier (BBB) 334, 342–346
- Boehm's function 320
- Boltzmann's equation 419
- bond additivity 62
- bond angle strain 63
- bond-type E-state descriptors 65
- Boolean array 15
- boosted trees 480, 487
- boosting 26
- bootstrapping 31, 37–38, 45, 294, 491
- breast cancer drug 87
- BRENDA 126
- brewing 511
- broker model 200
- BSAlign 301
- building blocks 240, 391, 409, 412
- C**
- Caco-2 cell line 350
- Caco-2 cell permeability 349, 350
- CACTVS 387, 389–391
- CADEX method 35, 36
- calibration 11, 320, 486
- Cambridge Structural Database 319, 390
- CAMEO program 97
- cancer 87, 196, 198, 199, 386, 445, 518, 556
- cancer cell line encyclopedia (CCLE) 199
- canonical variables 479
- carbinolamine 378–381
- carbocyclic coformycin 122, 123
- carbohydrates 106, 505
- carcinogenicity 336, 429, 431, 434, 435, 442, 443
- Carcinogenic Potency Database (CPDBAS) 434
- cardiotoxicity 350
- Cartesian coordinates 135, 137
- Case Ultra 430
- CAS numbers 253
- CASPER program 144
- CAST 286, 287
- catalysts 263, 278, 549, 554, 558
- catalytic cycle 366
- catalytic site 275, 283, 365
- catechol 381
- CATH 298
- CavBase 299, 301
- CCR8, 408
- CDK 449
- CDK2 complex 268, 270, 297
- cDNA microarray analysis 536
- cell
  - adhesion 533, 535, 551
  - communication 534
  - extracellular matrix interactions 534
  - migration 534
  - proliferation 536
- cellular and molecular processes 106, 536
- cellular disease models 199
- Center for Food Safety and Applied Nutrition (CFSAN) 443, 506
- centering 19, 472
- central metabolism 106, 108
- central nervous system (CNS) 172, 342
- ceramics 554
- Cerius2, 347
- cetirizine 73
- Chamming 27
- charge density 55
- charge distribution 24, 248, 507
- CHARGE program 144
- ChEBI database 111, 112
- CheMagic.org 388
- Chematica 100–101
- ChemAxon 400, 449
- ChemBank 198
- ChEMBL database 13, 196, 198, 395
- ChemDraw/SymxyDraw 253
- Chemical Abstract Services (CAS) 386
- Chemical Abstracts 96, 255, 386
- Chemical Activity Predictor (CAP) 391
- chemical descriptors, *see* descriptors
- chemical environment effect 135, 136, 141, 149, 293, 301, 338, 367

- chemical identifier resolver (CIR)
  - 387–388
- chemical information 3, 134, 137, 168, 385, 506, 511
- chemical properties 5, 10, 11, 53, 135, 300, 587
- chemical reactors 572
- chemical shifts 136, 141–149
- chemical space 34, 95, 171, 292, 322, 334, 365, 462–464, 506–510, 549
- Chemical Structure Lookup Service (CSLS) 388, 389
- chemical subgraphs and reaction mark-up language (CSRML) 453, 457
- chemical systems biology 125, 588
- CHEMICS 153
- ChemInform 99
- ChemNavigator iResearch™, 391
- ChemOffice 143, 144
- chemogenomics 171, 199
- chemome 239
- chemometrics 2, 17, 471–496
- chemoselectivity 92–93, 360
- ChemoText 399, 400
- ChemoTyper 58, 187, 188, 454
- chemotypes 187, 239, 240–243, 445, 453–459
- ChemScore 320
- ChemSpider project 14, 256, 400
- Chinese herbal medicine 172, 221, 237–243
- CHIRON computer program 100
- chlorpromazine 179
- cholestasis 397
- cholesterylester transfer protein (CETP) 223
- chorismate 112, 114
- chromatography 93
- chromosome 316, 486
- cinnamyl acid 240–243
- circular fingerprints 459, 461
- cityblock distance 42, 252
- classification 18–20, 25, 28, 293, 333, 346, 400, 475
  - activity 210
  - blood brain barrier permeability 343
  - models 11
  - random forest 293
  - supervised 479
- classification and regression trees (CART) 480
- click chemistry 90
- clinical trials 188, 219, 549
- clique detection 299, 301, 316
- Cliquer 301
- CLOGP 65, 347
- cluster(ing) 17, 27, 36, 293, 397, 447
  - analysis 150, 477
  - genome 123–125, 129
  - hierarchical 124, 270
  - structure-based 430
- cluster-based methods 35, 36
- COCOA 154
- CODESSA 555
- coenzyme Q10, 486
- co-factors 121, 266, 360, 363, 364, 427
- cohesive energy 558
- collision-induced dissociation (CID) 151
- column distillation 579–581
- combinatorial chemistry 53, 134, 141, 166, 175
- combinatorial libraries 172, 175, 183, 513
- COMBINE program 153
- CoMFA 22–25, 181
- comparative molecular field analysis (CoMFA) 22, 365, 420, 421
- comparative molecular moment analysis (CoMMA) 24
- comparative molecular similarity indices analysis (CoMSIA) 24, 181, 420, 421
- COMPASS 24
- compatible solutes 528, 529, 533
- compound databases 13, 225, 239, 246
- compound identifier (CID) 246, 249
- compound libraries 153, 171, 182, 202, 219, 272, 313, 423, 506 *see* libraries
- compound-mediated toxicities 199
- computational chemistry 3, 7, 150, 208, 334, 440, 588

- computational tools 86, 102, 208, 211, 220, 228, 229
- computer-aided drug design (CADD) 259, 385–391
- computer-aided pharmacophore modeling and screening 278
- computer-aided structure elucidation (CASE) 153–156
- computer-aided synthesis design (CASD), *see* computer-assisted synthesis design
- Computer Assisted Evaluation of industrial chemical Substances According to Regulation (CAESAR) 435
- computer-assisted molecular design 406
- computer-assisted structure elucidation (CASE) 3, 133–157, 587
- computer-assisted substance identification 139
- computer-assisted synthesis design (CASD) system 5, 84, 94, 96, 100, 101, 587
- computer-assisted synthesis planning 409
- computer automated structure evaluation (CASE), MCASE 430
- computer graphics 99
- ConCavity 288
- conductivity 551–558
- conductor-like screening model (COSMO) 55
- conformational ensemble methods 316–317
- conformational flexibility 137, 269, 316, 533
- conformational search, systematic 419
- conformational space 24, 181, 365, 367
- conformations 16, 55, 63, 211, 243, 249, 269–272, 291, 315–317, 419, 423, 428, 529
- conformer generation 316
- confusion matrix 45
- CONGEN 153
- congeneric series of compounds 20, 58, 64
- connection tables 89, 110, 137
- connectivity map concept 200
- Connolly surface 287, 299
- consensus model 72, 433, 434
- consensus scoring 288, 320
- conservation 208, 285, 287, 364, 503
- constraints 95, 153, 267–268, 323, 375, 425
- contiguous blocks 489
- continuum solvation model for real solvents (COSMO-RS) 55
- contour maps 421
- CORINA 47, 110, 112, 121, 122, 137, 138, 172, 339, 389, 464
- corosolic acid 222
- correction factors 57, 64, 65
- correlation 135, 337, 552
  - analysis 335, 485
- correlation coefficient 20, 335, 421
- concordance (CCC) 40
  - Kendall 485
  - Pearson 321, 485
  - Spearman 485
- correlative structure-activity relationship methods 429
- cosmetics 7, 350, 441, 452, 525–541, 586
- COSMOS 445, 449, 464
- COSMOS DB 449
- COSY spectra 154
- cross-validation 30, 31, 36–37, 44, 186, 335, 398, 400, 421, 433, 485, 491, 555
- crystals 69, 71, 320
- crystallization 72, 93
- CSI-FingerID 153
- CTD2 project 198, 199
- curation 9, 13–14, 201
- curcumin 242, 513
- custom development project 253
- cyclooxygenase-2 (COX-2) inhibitor 373
- cyclopeptides 533–541
- cytochrome , 360, 363–367

**d**

- DARC-EPIOS 153
- data analysis 17, 18, 150, 472
- data augmentation 249
- data avalanche 196
- databases 34, 96, 99, 100, 142, 144, 151, 386, 391
  - BRENDA 126
  - ChEMBL 395
  - chemical shift 142
  - ConSurf-HSSP 287
  - drug 171
- external 178, 247, 388, 392
  - Food additives 505
- Fragrance and Flavor 505
  - HDB 238
  - KEGG REACTION 111
  - mining 200, 272
  - monitoring 578
  - Natural products 215
  - PAFA 452
  - NCI 386
  - PEDANT 123
  - Pocketome 297
  - PubChem 175, 245, 247
  - reaction 91, 96–97, 110
  - Regulatory 505
  - searching 142, 143
  - SIDER 401
  - storage 249
  - toxicity 448
  - toxicological 431
  - VigiBase 398
- data compression 17
- data curation 13, 14
- data cycle 189
- data-driven 195
- data mining 17, 134, 166, 175, 443, 464, 513–521
- data modelling 20, 449–453
  - methods, non-linear models *see* non-linear models
  - non-linear models
  - regression-based QSAR approaches *see* regression, analysis
  - 3D QSAR *see* 3D QSAR
- data reduction 372, 474
- data silos 201
- data splitting 32
- dataset 21, 26, 32–34, 71, 119, 135, 137, 181, 183, 334, 338, 489, 512, 549, 552
- DataWarrior 520
- DAVID 199
- Daylight DayCart 449
- N*-dealkylation biotransformations 378
- deamination of AMP 122, 123
- death-associated protein kinase 3 (DAPK3) 409, 411
- decision tree (DT) 18, 25–27, 138, 147, 227, 335, 347, 444, 552
- decoys 226, 273
- Deductive Estimation of Risk from Existing Knowledge (DEREK) 430, 432
- deep learning 200, 396, 495
- degrees of decomposition 55
- dehydrogenase 363
- Delaunay triangulation 287
- delocalization stabilization of charge 119
- O*-demethylation 376, 379
- denaturation 529
- DENDRAL Project 5, 134, 153
- dendrogram 477
- denitration 578
- de novo* design 101, 169, 179, 182, 276, 407–409, 413, 423
- density functional theory (DFT) 55, 142, 367
- dereplication 209, 219
- descriptors 14, 19, 20, 58, 59, 224, 293, 317, 335, 443
  - 1D 15
  - 2D 71
  - 3D 16, 137
  - 3D Zernike 300
  - binding site 284
  - chemical descriptors 13, 119, 121, 135, 144, 347, 365, 400, 555
  - Dragon 434
  - fragment-based 135
  - geometric 16–17, 144
  - GRIND 16

- descriptors (*contd.*)
  - herbal prescription 238
  - mathematical 551
  - molecular, *see also* molecular descriptors
  - pharmacophore 365
  - physicochemical 119, 121, 144, 347, 365
  - quantum-chemical 555
  - selection 552
  - shape 346
  - spectral property 150
  - topological 16, 144, 338, 555
  - uninformative 551
  - whole-molecule 65
- design of experiments (DOI) 553
- detoxification 361
- Developmental Therapeutics Program (DTP) 386, 387
- diabetes 222, 225, 237 *see also* type 2 diabetes
- dibenzofuran 445
- dibenzo-p-dioxin 445
- Dice 252
- 2,6-dichlorophenol 187
- dietary supplements 486, 516
- Difference of Gaussian (DoG) 286
- diffusion 167, 343, 347, 533, 554
- dihydrofolate reductase enzyme 260, 261
- para*-dihydroquinone 379
- dimension reduction 476, 477
- dimethylsulfide 128
- DIOS database 222
- 1,2-diphenylethane 418
- dipole and quadrupole moments 24, 54, 346, 550, 558
- discriminant analysis 294, 480
- discrimination functions 19, 227, 293
- disruptive technology 548
- dissolving process 69, 336
- distance-based methods 42
- distance, Manhattan 487
- distribution 5, 14, 24, 30, 34, 42, 170, 185, 186, 274, 333, 349, 359, 507
- diverse libraries 178
- diversity 67, 506
- Django 449
- DNA methyltransferase (DNMT) 509, 518–521
- DOCK 221, 230, 276, 315, 327
- docking 16, 168, 179, 221–225, 240, 274, 287, 296, 315–317, 367, 406, 423
- DoGSite 286
- DoGSiteScorer 293, 294
- Dolabriferol 90
- domain of applicability 336, 552
- domestic substance list (DSL) 441, 452
- donor 16, 68, 178, 249, 263, 264, 268, 279, 299–301, 318, 347, 430, 507, 519
- dopamine agonists (DAA) 173, 174
- D-optimal design 23, 36
- DRAGON software 400, 432, 516, 555
- drug approval 167, 190
- DrugBank 277, 400, 508, 514
- drug design 165–168, 179, 276, 385–391, 406–13 *see* computer-aided drug design
- drug discovery 5, 165–190, 333, 371, 405, 586
  - applications 501
  - data-driven 201
  - indication expansion 200
  - target mining 196
  - toxicity prediction 199
- druggability 198, 284, 288, 292–296
- druggability dataset (DD) 294
- drug2gene 196, 198
- Drug Information System (DIS) 386
- drug like density (DLID) 294
- drug likeness 171, 178, 274, 387, 521, 522
- drug metabolism 360, 361
- drug metabolism and pharmacokinetics (DMPK) 371–372
- drug-metabolizing enzymes 360, 363
- drug permeability 350
- DrugPred 293, 294
- drug-receptor interactions 261, 262
- drug targets 13, 170, 171, 196, 198
- DrugScore 319
- DrugSite 287, 288



- DUPLEX algorithm 36  
dynophores 276–278
- e**
- EC number 108, 111, 112, 117  
ecotoxicology 184, 429  
EC-PDB databases 113  
ectoine 528–533  
edge of chaos 414  
EDIA 321  
effective core potentials (ECPs) 142  
Eigenvectors algorithm 490  
Elaboration of Reactions for Organic Synthesis (EROS) 97–98, 139  
electron density 24, 321  
electron impact (EI) mass spectra 150, 151  
electronegativity 119, 144, 173, 346, 368  
electronic effects 23, 119, 342, 346, 456  
electronic health records 201  
electronic laboratory notebooks 102  
electrophiles 186  
electrophoresis, single cell gel 474  
electrospray soft ionization (ESI) 151  
electrostatic field 22, 421  
electrostatics 23, 24, 319  
  potential 528, 533  
electrotopological state (E-states) 430  
embryonic stem cells (ESCs) 562  
empirical scoring functions 318–320, 423  
enantiomers 248, 261  
enantioselectivity 93  
encoding 98, 143, 147, 248–250, 302, 566  
endocrine-disrupting chemicals (EDCs) 429, 544  
endogenous metabolism 106, 171  
endoplasmic reticulum 367  
englerin A 412  
enrichment 199, 269, 272, 324, 536  
enrichment factor (EF) 274, 324  
Ensembl 201  
ensemble docking (ED) 317  
ensemble learning 25, 26, 576  
enthalpy ( $\Delta H_f^\circ$ ) 60, 181, 318, 321  
entity-attribute-value model 450  
Entrez 246, 250, 255  
entropy ( $S^\circ$ ) 60, 179, 181, 265, 318, 320, 326  
enumeration 134, 243  
environmental fate 429, 447  
enzymes 11, 106, 108, 111, 118–124, 167, 284, 367  
epalrestat 241, 242  
(-)-epigallocatechin gallate (EGCG) 518  
epigenetics 516–521  
epoxide hydrolase (EH) 363, 365  
equilibrium solubility 69  
Eribulin/Halaven 87  
error back-propagation algorithm 29  
E-state indices 71, 338  
esterases 363  
estradiol 261  
estrogenic agent 261  
eTOX project 189, 200, 449, 452  
Euclidian distance 27, 36, 224, 252, 464, 473, 486  
European Chemical Agency (ECHA) 447, 448  
European Food Safety Authority (EFSA) 444  
EU Scientific Committee of Consumer Safety (SCCS) 444  
Everything Added to Food in the United States (EAFUS) databases 506, 510, 520, 522  
evolution 13, 21, 208, 503  
evolutionary algorithms 29, 101  
exclusion volumes 267, 268, 270  
excretion 184, 333, 349, 359, 364  
expectation maximization (EM) 489  
expert systems (ES) 134, 135, 138, 154, 368, 429, 431  
EXPIRS 138  
explicit water 321, 428  
extensible markup language (XML) 250  
extracellular matrix (ECM) 535, 538, 539

**f**

- factor analysis (FA) 19
  - factorial design 559
- false negatives (FN), positives (FP) 45, 273, 324, 343, 370, 483
- Farnesyl-diphosphate 115, 116
- FAst MEtabolizer (FAME) software 368
- Fasudil 409, 411
- FATCAT 298
- feature bitvector 251
- feature extraction 27
- feature selection 347, 552, 557, 565, 566
- federated database system (FDBS) 449
- fibroblasts 535, 536, 540, 541
- file formats 248, 253, 388, 390
- filtering 178, 211, 220, 274, 322, 334, 485
- FINDSITE 287
- fingerprints 15, 147, 176, 251, 299, 369, 454, 459, 507
  - bitvectors 251
- chemical 153
- dynamic 459–461
- extended connectivity 459, 461, 507, 508
  - MACCS 400
  - pharmacophore-based 300
  - radial 508
- first-in-class drugs 195, 196
- first order approximation 56, 61
- Fisher criterion (F value) 485
- fitness function 271, 316, 411, 486
- fitness landscapes 407, 409, 411
- FITTED 317
- fitting 552
- flagging 58
- FLAP 300
- flattened protoporphyrin IX 428
- flavin adenine dinucleotide (FAD) 121, 424, 427, 517
- flavin monooxygenases (FMO) 363, 365
- flavonoids 240
- flavor cliffs 511–512, 522
- flavor compounds 125, 126, 128
- flavor-forming pathways 125–128
- Flavornet 506, 509
- FlexX 315, 316, 317, 424
- FlexX-Pharm 425
- Flory Huggins parameters 557
- FlowerPower 298
- food additives 444, 502, 505
- food analysis 492
- food-contact substances 443
- Foodinformatics 502
- food-related chemogenomic space 513, 521
- food science 501–522
- force field 16, 137, 319, 418, 428
  - HINT interaction 320
  - OPLS-2005, 530
- force field based scoring functions 319
- forensic toxicology 372, 374–375
- forest model 368
- formal reaction generators 97
- forward search 97
- forward-selection regression 21
- forward synthetic route 99
- Fpocket 287, 293
- fractional factorial design 23
- fragment 15, 25, 58, 135, 138, 263, 335
  - constant approach 64, 65
  - fragmentation 316, 343
    - approaches 58
    - MS patterns 375
- fragment-based *de novo* design 276
- Fragment Reduced to an Environment that is Limited (FREL) 135
- FRED 315, 316
- free binding energy 320, 424
- free energy 11, 14, 23, 58, 91, 110, 181, 265, 317, 321
- free energy perturbation (FEP) 262, 321
- Free-Wilson method 11
- frequent hitters 58
- Fructus Lycii* (Gouqizi) 238, 240
- Fructus Schisandrae* (Wuweizi) 238, 240
- FSSP/Dali 298
- Fullerenes 554, 555

- functional groups 23, 54, 57, 65, 91,  
135, 143, 266, 337, 362–364, 369,  
560
- FuzCav 300
- fuzzy data 154
- fuzzy logic 138
- g**
- Gaucher disease 254
- Gauge-Invariant Atomic Orbital (GIAO)  
method 142
- Gaussian 142  
function 301  
processes 59, 432
- Gaussian radial basis function 481
- GEN 154
- GenBank 246
- gene expression 199, 535, 564
- GeneGo cellular processes 536
- Genentech dataset 199
- Generalized Born Surface Area (GBSA)  
181, 320
- generally recognized as safe (GRAS)  
452, 502
- generative topographic mapping (GTM)  
algorithm 509
- gene set enrichment analysis 199
- gene signatures 200
- genetic algorithm (GA) 17, 18, 21, 123,  
154, 175, 179, 316, 335, 347, 486,  
555, 557, 572
- genetic algorithm-based process  
variables and dynamics selection  
(GAVDS) 572
- genetic algorithm for multiple molecule  
alignment (GAMMA) 123,  
179
- genetic function approximation (GFA)  
47, 347, 353
- genetic linkage 198
- genetic programming 540, 557
- GENIUS 154
- GENOA 153
- genome clustering 123–125, 129
- genomic(s) 106, 166, 199, 304,  
407
- genotoxicity 443, 474–475
- geometrical features 144, 560
- geometric methods 42
- GERM 24
- ghecom 288
- Gibbs free energy ( $\Delta G$ ) 317
- Gibbs–Helmholtz 318
- GIF Creator 389–390
- glass transition temperature 553, 554,  
557, 558
- Glide 315, 316, 426
- glucose 222, 240
- glucuronidation 363, 376, 379
- glutamate 112, 113, 124, 180, 516
- glutamate racemase (MurI) 180–181
- glutathione conjugation 363, 364
- glycans 143, 144
- glycation mechanisms 240
- glycine 128, 533, 534
- glycoprotein 350, 540
- glycoside 240, 242, 243, 509
- Glycyrrhiza glabra* L. (Fabaceae) 226
- GlyNest program 143
- GoFigure 298
- GOLD 315, 316, 327
- GoldScore 319
- GOLPE 23
- goodness of prediction 39–41, 421
- G-protein coupled receptor (GPCR)  
272, 409, 423
- gradient boosted trees (GBTs) 346,  
347, 349
- gram-positive 124
- GraphicsMagick 389
- graph theory 14, 16, 137, 173, 251,  
299, 301, 421, 460
- GRAS compounds 506, 508, 510, 513,  
517, 520
- green chemistry 71, 413
- GRID 17, 23, 24, 269
- grid-based algorithm 285
- GRIND descriptors 16
- group additivity 61–63
- group contribution methods 63,  
337–338 *see also* group additivity
- guanidine 240, 266
- GUSAR 391

**h**

- halophilic organisms 528, 529
- Hammett equation 456
- Hamming distance 172
- Hartree–Fock 142
- hash codes 249, 250, 252, 369
- hash-coding algorithm 15
- hash function 299
- HazardExpert 431
- HDon\_O 347, 349
- heat capacity ( $C_p^\circ$ ) 60, 61, 558
- heat of adsorption 560
- heats of atomization ( $\Delta H_a$ ) 62
- heats of formation ( $\Delta H_f^\circ$ ) 60–63
- heats of reactions 98
- Helicobacter pylori*, 180
- hemiacetal 97
- hemoproteins 363
- Henry's Law, coefficient 566
- hepatic metabolism 376
- hepatotoxicity 376, 378, 379, 397, 398, 431
- herb-chemome-MOA network (HCMN) 239, 243
- herbs 239–242
- heterocyclic systems 63
- heuristics 97, 99, 153, 301, 316, 388, 406, 488
- hierarchical cluster analysis (HCA) 119, 124, 227, 270, 477
- Hierarchical Ordered description of the Substructure Environment (HOSE) 136, 143, 144, 147
- hierarchical trees 73
- highest occupied molecular orbital (HOMO) 16, 550
- high production volume (HPV) 446, 452
- HINT interaction force field 320
- histidine degradation 125
- histogram*, 300, 301, 324, 325, 456, 459
- histone acetyltransferase p300, 224
- histone deacetylases (HDACs) 517–518
- historical Hungarian coins 480–483
- HiT QSAR 14
- hit rate 172, 229, 274, 292, 293, 325, 326, 412, 459
- HIV inhibitors 101
- HIV-1 protease 297
- HMBD 375
- holoprotein 428
- homology 143, 168, 261, 284, 291, 313, 315
- HOSE code 136, 143, 144, 147
- host-microbial co-metabolism 128
- hot spot diagram 287, 368, 371
- HSQC and HMBC spectra 154
- Hudlicky's analysis of syntheses 96
- HumanCyc 375
- human genome 106, 170
- human health 7, 429, 431, 442, 517, 586, 588
- human intestinal absorption (HIA) 334, 346–350
- human oral bioavailability (HOBA) 349, 353
- human plasma protein binding (PPB) 343, 349, 350, 353
- human serum albumin (HSA) 349, 350, 353
- human skin permeability 349, 350
- hybridization 60
- hydantoins 175–177
- HYDE 320
- hydrogen-bond acceptors 16, 270, 302, 338, 339, 347, 428, 430, 464, 519
- hydrogen-bonding 176, 177, 261, 264, 318, 321, 343, 349
- hydrogen-donor feature 270
- hydrogen encoding 248
- hydrolases 117–119, 121, 363
- hydrophobic contacts 226, 264–265, 320, 424
- hydrophobicity 24, 176, 184, 264, 293, 294, 296, 318–320, 336, 346, 350, 353
- 11 $\beta$ -hydroxysteroid dehydrogenase 1 (11 $\beta$ -HSD1) inhibitors 222, 223
- HyperChem 142
- hyperplane 19, 29
- hyperstructure 154
- hypothetical activity models 166

- i**
- IC<sub>50</sub>, 221, 222, 225, 240, 241, 247, 374, 429, 535
- ICH M7, 441, 444
- ICM 315
- ICSynth 99–100
- IGOR 97
- ill-conditioned problem 476
- impact resistance 557
- impurities 72, 441, 444, 445
- InChI 91, 112, 249, 253, 387, 388, 450
- InChI (Chemical Identifier) 89, 91, 112, 249, 253, 387, 388, 450
- InChIKey 112, 387, 388
- increment-based methods 143–144
- incubation 373, 376, 378, 536
- index
- database monitoring (DMI) 579
  - E-state 71, 338
  - Tanimoto 112
  - topological 16, 71, 338, 430, 558
- indication expansion 195, 196, 200–201
- indoleamine 2,3-dioxygenase 226
- indomethacin 373
- indoyle 240
- induced fit 317, 426, 428
- induced fit docking (IFD) 317, 426
- inductive effect 75
- inductive learning 84
- inflammation 200, 274, 275, 535, 536, 538, 540, 541, 544
- inflammatory bowel disease (IBD) 200
- InfoChem 100
- infrared (IR) spectrum 135, 137–140
- inhibitor 101, 121–123, 129, 167, 222, 226, 242, 284, 353, 420, 426, 510, 517, 519, 520
- inner salts 67
- Innovative Medicine Initiative (IMI)
- eTOX project 451
- innovative syntheses 96
- inosine monophosphate (IMP) 121–123
- in silico* design and data analysis (ISIDA) 58, 400
- in silico* inspired synthesis 97
- in silico* toxicology 417, 429, 432–435
- insulin 240
- integrins 534, 535, 539, 540, 542
- interactions 318
- cation- $\pi$ , 265, 266
  - cis-trans isomer 136
  - drug-drug 365
  - energies 55
- ionic 266, 423
- ligand-receptor 264
  - $\pi$ - $\pi$ , 318
  - protein-ligand 317
  - protein-protein 189
- interactive computer graphics 98–99
- intercellular adhesion molecule-1 (ICAM-1) 530
- internal validation 31–33, 36, 43–45
- International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH M7) 441, 444
- interpolations 41, 143, 582
- interval PLS (iPLS) 486
- intestinal absorption 333, 334, 346–347, 353
- IntOGen 198
- intralaboratory reproducibility 55
- intrinsic solubility 69
- inverse Boltzmann technique 423
- inverse soft sensor-based feed forward (ISFF) control method 582
- in vivo* animal studies 441
- in vivo/In Silico* Metabolites Database (IIMDB) 375
- in vitro* tests 184, 459, 535
- ion channel 167, 423
- ionic liquids 71, 554
- ionization 68, 73–76, 151, 456
- Iris dataset 35, 36
- ISAC approach 320
- ISIDA/Duplicates 14
- IsoCleft 299
- isomerases 117
- isomer generator software 153
- isomeric hydrocarbons 61
- isostere 260

iso-surface 269  
 isotope 249, 250, 252  
 IspD 428  
 iterative stochastic elimination 181

**j**

jackknifing 485, 489  
 JavaScript 253  
 JChem 449  
 Joint FAO/WHO Expert Committee on  
 Food Additives (JECFA) 444,  
 505, 506, 516  
 JSME 112, 389  
 Just Exploring Druggability at protein  
 Interfaces (JEDI) 296

**k**

kaempferol 277–278  
 KEGG 112, 375  
 Kennard-Stone algorithm 35–36  
 keratinocytes 530, 535, 536, 541  
 kernel function 29, 481  
*k*-fold cross-validation 36, 37, 335  
 kinase-inhibitors 220, 409  
 kinetic solubility 69  
*k*-nearest neighbor (kNN) 27, 138,  
 145, 147, 335, 432, 482, 577  
 knowledge-based expert systems  
 368–369, 431  
 knowledge-based scoring functions  
 319, 423  
 knowledge extraction 84, 151  
 Kohonen maps 173, 174, 478  
 Kohonen neural network 17, 19–20,  
 119, 138, 173  
 kosmotropic 533  
 Kulczynski 252  
 Kyoto Encyclopedia of Genes and  
 Genomes 111

**l**

lab-on-a-chip 408  
 lactate-2-monooxygenase 126  
 lactic acid bacteria (LAB) 126, 128  
 Laidler scheme 62  
 Langerhans cells 529, 530

latent TGF- $\beta$  binding protein (LTB,P1)  
 539  
 latent variables 19, 22, 476, 487  
 lattice energy 70, 336  
 LC50-value 184  
 LD50-value 184  
 lead compounds 178, 183, 313, 333,  
 371, 435, 527, 542  
 lead finding 167, 195  
   ligand-based drug design (LBD)  
   171–175  
   structure-based drug design (SBD)  
   179–182  
 lead hopping 172, 174, 183  
 lead identification 183, 417, 423  
 LeadIT 316  
 lead optimization 167, 182, 195, 417  
   ADMET properties 183  
   toxicity 184–187  
 leadscope 430, 431  
 lead structure 167, 172–175, 182, 190,  
 272, 279, 283, 418, 588  
 learning 11 *see also* classification  
   methods; non-linear models;  
   regression analysis; 3D QSAR  
   statistical 29  
   supervised 18, 28, 411, 492  
   unsupervised 17, 173, 492  
 least absolute shrinkage and selection  
 operator (LASSO) 486–488,  
 572  
 leave-many-out (LMO) 491  
 leave-one-out (LOA) 37, 181, 421, 433,  
 489, 491  
 legacy encoding 248  
 Lennard-Jones potential 24, 319  
 leoligin 223  
*Leontopodium alpinum*, 223  
 leucine 126  
 L-glutamate 108, 109, 112, 180  
 LHASA 98–100, 391  
 L-histidine 125  
 libraries  
   combinatorial 172, 175, 183, 513  
   corporate compound 171  
   design 195, 337, 338  
   diverse 178

- focused 172, 178, 240
  - screening 209, 240, 241, 513
- LIBRARY mode 66, 68
- lichen 208, 221
- licorice 226
- life cycle assessment 96
- ligandability 292, 294, 296
- ligand-based approach 270, 273, 409, 419–422, 436
- ligand-based drug design (LBDD) 169–179
- ligand conformers 270, 272
- LigandScout 263, 268–270, 275, 276, 278
- ligand shape 267–268
- ligand/target binding mechanism 259
- ligases 117, 121
- lignan 223, 226
- LIGSITE 285, 287
- linear discriminant analysis (LDA) 19, 138, 227, 479
- linear free energy relationship (LFER) 11, 20, 58, 59, 64, 65, 73, 184
- linear regression 20, 59, 65, 71, 293, 433, 487
- Lipinski's rule 94, 210, 294, 347
- lipophilic contacts 264, 265
- lipophilicity 53, 63, 64, 178, 184, 342, 361, 365, 367, 369, 508
- lipoprotein 350
- liquid chromatography–mass spectrometry (LC-MS) 151, 227, 441, 448
- L-lactate oxidase (LOX) 126, 128
- loading vectors 476, 485
- logical rules 138, 397
- logistic regression (LR) 21
- loquat 222
- lowest unoccupied molecular orbital (LUMO) 16, 550, 558
- LSD 154, 156
- LUDI 269, 270, 423
- lyases 117
  
- m**
- MACCS key 507–510, 517
- machine learning 26, 29, 30, 59, 71, 76, 77, 99, 144, 149, 157, 227, 495
- macroconstants 73
- magic constants 64
- magnetic field 142
- magnolol 225
- Mahalanobis distance 42
- maitotoxin 87, 102
- majority voting 26
- Mannich bases 139
- mapping methods *see* classification, methods
- Mass Frontier 151, 152, 156
- mass spectrometry (MS) 150, 151
- mastic gum 225
- matairesinol 226
- matching 297
  - atom-by-atom 110, 252
- materials science 553–566
- matrix,
  - confusion matrix 45
  - decomposition 476
- loading 19
- metalloproteinases (MMPs) 541, 542
- Matthews correlation coefficient (MCC) 45
- Maximal Affinity Predicted for Passively absorbed Oral Drug (MAPPOD) 293
- maximal electroshock seizure test 515
- maximum common subgraph 299, 301
- mean absolute error (MAE) 31, 41, 145, 147
- mean centering 19, 472
- mean molecular polarizability 59–60, 338, 339
- mechanism of action (MOAs) 185, 186, 238, 239, 242, 418
- mechanistic analysis 97
- medicinal chemistry 166, 219, 259, 260, 303, 365, 371, 373, 395, 406–409, 413
- MEDLINE 397
- melting point (MP) 54, 55, 70–72, 337
- membrane bioreactor (MBR) 573
- membrane partition coefficients 442, 456

- membrane transport 11, 336
  - MeSH 246, 400, 401
  - Mestrelab 147
  - MetabolExpert 368
  - metabolic pathways prediction 125–128
  - metabolics tree 369, 372
  - metabolism 11, 106, 333, 359, 376, 413
  - metabolites 110, 117, 125, 145, 153, 208, 219, 260, 365, 370, 371, 374, 375, 378, 444
  - metabolome 360, 375
  - metabolomics 106, 108, 151–153, 209, 227, 372, 375, 412, 441, 448, 453, 535
  - MetaCore™ 535, 536
  - metadata 397–398
  - MetaDrug 368
  - metagenomics 209
  - metaheuristic algorithm 495
  - metal complexation 248, 266–267
  - metal ions 265, 266, 295
  - metalloproteases 266, 541
  - metal organic frameworks (MOFs) 548, 560f
  - MetaPocket 288
  - MetaSite 367, 373
  - Meteor Nexus 368, 369, 376, 377, 379, 381
  - methanogenesis 124
  - methotrexate 261, 388
  - methylparaben 516
  - methyltransferase 518–521
  - metric, distance 27, 483
  - Metropolis criterion 315
  - microarrays 535, 536, 564–566
  - microbial cell factories 128
  - microconstants 73, 74
  - microfluidics 408, 409
  - microsomes 376, 432
  - microstates analysis 350
  - mixture
    - multicomponent 219
    - non-ideal 57
  - MMFF 319
  - model
    - acceptability criteria 41–43
    - degradation 574, 576, 577
    - just-in-time (JIT) 576
    - molecular 366
    - moving window (MW) 576
  - performance 334, 335, 340, 344, 345, 348, 351
  - pharmacophore 268
  - quantum mechanical 366
  - validation 30–31, 36, 209, 400, 433, 574
- mode of action (MoA) 185, 186, 266, 270, 418
  - Modgraph's NMRPredict 143
  - moisturizer 528–530, 542
  - MoKa program 76
  - molecular databases 209, 220, 228, 395, 502–506, 512, 513, 521
  - molecular data handling 134
  - molecular descriptors 10, 11, 14, 135–137, 172, 334, 549
  - molecular docking 274–276, 315, 515
  - molecular dynamics (MD) 149, 240, 272, 276, 277, 291, 296, 320, 367, 407, 428, 529–531
  - molecular features 101, 134, 412, 419
  - molecular informatics 2, 407
  - molecular interaction field (MIF) 23, 24, 76, 269, 275, 367
  - molecular libraries initiative* project 246, 395
  - molecular mechanics (MM) 137, 181, 316, 319, 320, 367, 428
  - molecular modeling 166, 168, 211, 278, 366–368, 385, 418, 439, 548
  - 3D molecular models 135
  - Molecular Operating Environment (MOE) 263, 278, 508, 509
  - molecular property (P)*, 54, 56, 61, 388, 449
  - molecular refraction 57
  - molecular scaffolds 412, 507, 508, 520
  - molecular shapes 268
  - molecular surface 16, 55, 176, 177, 186, 224, 285, 320
  - molecular weight 57, 112, 178, 249, 250, 284, 292, 338, 370, 379, 405, 430, 507



- 3D-molecule representation of  
structures based on electron  
diffraction (3D-MoRSE) codes  
16
- Molfiles 253, 389ff
- MolSql 449
- molybdenum oxygenases 363
- moment, dipolar 560
- monoamine oxidases 171, 185–187,  
238, 363, 418
- monooxygenase enzymes 112, 114,  
363, 366, 374
- Monte Carlo method 181, 316, 491,  
560, 561
- Moore–Penrose 484
- morphine 96
- MOSES 353, 449
- multi-class classification 483
- multidrug resistance (MDR) 353
- multilayer perceptron (MLP) 335
- multi-learning approaches 77
- multi-linear regression (MLR) 11, 18,  
20–22, 61–65, 139, 147, 335, 338,  
350, 353, 420, 484, 555
- multiple sequence alignments 285,  
291, 298
- multiplicity 141, 153
- multi-protic 73
- multivariate classification 150
- multivariate curve resolution (MCR)  
492
- multivariate analyses 150, 471
- MurI inhibitors 180f
- muscle relaxants 179
- mushroom 208
- mutagenicity 183, 429, 431–433, 441,  
445
- mutation 196, 198, 432
- MutSigCV 198
- mutual overlap 288
- Mycobacterium smegmatis*, 126
- m/z* values 137
- n**
- NADP *see* nicotinamide adenine  
dinucleotide (NAD)
- naive Bayes (NB) classifier 27–28
- nanomaterials 548, 550, 551, 553–557
- nanotechnology 548
- nanotubes 554
- narcosis 185
- National Cancer Institute (NCI) 6,  
385–391
- National Center for Biotechnology  
Information (NCBI) 175, 201,  
246, 250, 253, 255, 256
- National Institutes of Health (NIH) 6,  
13, 175, 246, 385, 395
- natural products 151, 172, 207–212,  
215, 220, 223–228, 411
- NCI Database Browser 386, 387, 392
- negative contoured maps 23, 573
- neural networks 19, 26, 59, 144, 553  
architecture 559  
artificial 28, 135, 138, 502, 511,  
571  
back-propagation (BPG) 154, 338  
counter propagation (CPG) 29, 138,  
139, 145, 186, 224, 434  
deep 77  
feed-forward 145, 147, 151, 492,  
555
- general regression (GRNN) 29  
multilayer feed-forward 558
- neuraminidase (NA) inhibitors 226
- neuron 28
- new approach methods (NAMs) 448,  
453, 462
- new chemical entities (NCEs) 166f,  
406
- new drug application (NDA) 452
- new molecular entities (NMEs) 167,  
198, 407
- Newton optimizer 179
- nicotinamide adenine dinucleotide  
(NAD) 121, 517
- Nipagin 516
- Nipasol 516
- NMR chemical shifts 142–145, 147
- NMR coupling constants 142
- NMRPredict 143
- NMRShiftDB database 145
- NMR spectra 134, 136, 141

- NMR spectroscopy 134, 140, 141, 150, 313  
  automatic structure elucidation 141  
  machine learning methods 144, 145, 147, 149  
no effect level (NOEL) 444, 465, 543  
NOESY 154  
Nomenclature Commission of the International Union of Biochemistry and Molecular Biology (NC-IUBMB) 117  
non-electrolyte activity 57  
non-hydrogen atoms (NHA) 66, 67, 136, 154, 512  
non-ideal mixtures 57  
non-linear approaches 71  
non-linear iterative partial least squares (NIPALS) 487  
non-linear mapping (NLM) 19  
non-linear models 20, 25–30, 556, 560, 562  
norethindrone 318  
normalization 44, 249, 451, 473, 536  
*Notopterygium incisum*, 225  
nuclear magnetic moment 142  
nuclear receptor modulators 272  
nuclear spin energy 142  
nucleic acids 106, 144, 407, 528  
  database 390  
nucleosides 390  
nutriepigenomics 517
- O**  
obesity 275  
obligate anaerobe 124  
OCSS, 98, 99  
octanol/water distribution coefficient (log D) 67–68  
octanol/water partition coefficient (log P) 54, 63–67, 184, 333, 335, 337, 550  
odorants 503, 505, 512, 513, 521  
off-target effects 13, 199, 517  
oleoresin 225  
olfactory system 509, 512, 513  
olivatoric acid 222  
OMEGA 316  
oncogenes 196, 518  
OncoLogic 431  
oncology 196  
Online Chemical Modeling Environment (OCHEM) 48, 71  
OntoBrowser project 451  
ontology 298, 397, 443, 451, 536  
Ontology Lookup Service 451  
open access 102  
open circuit photovoltage 557  
open data 48, 102  
Open3DQSAR 24, 47  
open-source 24, 305, 389  
opentargets.org 196, 200  
Optical Structure Recognition Application (OSRA) 388–389  
OptiSim 36  
oral bioavailability 63, 293, 349, 353  
OrChem 449  
ordinary least squares (OLS) 47, 484, 488  
organic synthesis 94, 97, 99, 102, 129, 175, 182, 408, 409  
Organization for Economic Co-operation and Development (OECD) 41, 54, 431, 445  
organ-on-a-chip devices 408  
osteoporosis 565, 566  
outlier 17, 397, 485, 553, 573, 574  
overdosing 363  
overfitting 25, 27, 29, 38, 482, 488, 552, 554, 574  
overtraining 455, 553  
oxidoreductases 117, 119, 121
- P**  
PaDEL 459  
PAFA (Priority-based Assessment of Food Additives) 452–464  
PAIRS 138  
*p*-aminobenzoic acid 260f  
*Panax quinquefolius* L., 227  
parachor 57  
parallel synthesis 53, 134  
parsing 252, 391  
partial charges 16, 98, 119, 145, 187, 368, 457, 460, 555

- partial least squares (PLS) 18, 21–23, 73, 147, 181, 294, 335, 420, 479, 502, 511, 571  
 discriminant analysis (PLS-DA) 480  
 regression (PLSR) 181, 420, 485ff
- particle swarm optimizer (PSO) 21
- partition coefficients 11, 55, 63–67, 320, 338, 347, 442, 456, 520
- partitioning, recursive 480
- PASS 286, 288, 387
- passenger alterations 198
- PAST 298
- PATENTS dataset 72
- pathogen 170, 274, 516, 540, 562–564
- pathological mechanisms 200
- pathways 111, 375  
 biochemical 106  
 metabolic 228  
 synthetic 86
- patient stratification 196, 199
- pattern recognition 17, 135, 138, 462, 475–480
- peak intensity 150
- Pearson 252, 321, 485
- PEDANT database 123, 124
- penicillin 166
- periodontal disease 124f
- perlatolic acid 222
- permeability 342–347, 349, 350
- peroxidases 363
- perturbation 142, 198, 199, 262
- pesticides 4, 431, 444, 453, 459, 465
- petrochemical process 572, 582
- PFAM 298
- P-glycoprotein (P-gp) 343, 514, 515
- pH 67–69, 266, 349, 506
- pharmaceutical and food preservatives 514–516
- pharmacodynamic effects 359, 381
- pharmacognosy 219–220, 230
- pharmacokinetics 167, 183, 190, 359, 365, 371–372
- pharmacophore 11, 16, 24, 169, 178, 221, 224, 259–279, 320, 419
- Pharmacovigilance 398–401
- PharmDock 276
- phase I and II biotransformations 362–364
- phenols 186–187, 376
- PhenomicDB 196
- phenotype 124, 198, 418, 462, 586
- phenylethyl amide 373
- phenylpyrazole inhibitor (INH) 424f
- phloretin 221
- photo-ageing 538
- photovoltaic cell 556f
- Phydbac 298
- Phyllanthusengleri*, 412
- phylogeny 298
- physicochemical properties 73–76, 135, 186, 349
- physiologically-based pharmacokinetic (PBPK) models 543
- physiological properties 349
- physodic acid 222
- phytochemicals 222, 226–228
- phytotherapy 230
- Pipeline Pilot 400, 432
- $\pi$ - $\pi$  interaction 265, 266
- PIQOR™ 536
- Pistacia lentiscus*, 225
- Pistoia Ontologies Mapping project 201
- $pK_a$  54, 68, 73, 75, 76, 349, 350, 457
- Plant Protection Products Regulation 429, 435
- PLANTS 315, 316
- plasma protein binding (PPB) 343, 349, 350, 353
- platform technologies 547
- pleiotropic 220
- PM3, 66
- POCASA 288
- POCKET 285
- pocket detection 285, 288
- PocketMatch 300
- PocketPicker 285, 288, 293
- polarity 294, 336, 346, 509
- polarizability 59–60, 75, 98, 144, 338, 339, 346, 550
- polarization 55, 149
- polar surface area 347, 349, 430
- polyacetylenes 225, 226

- polyhalogenated dibenzo-p-dioxins 445
- polymers 554, 557, 558
- polymerization 561
- polymorphic forms 55, 69, 71
- polymorphisms, genetic 363
- polypharmacology 171, 303, 379, 407, 411
- poremean curvature 560
- posees 275, 315–317, 321, 425, 428
- positive contoured maps 23
- potential energy 16, 419, 428, 531
- potential of mean force (PMF) 319, 423
- Power User Gateway (PUG) 255
- PPAR $\gamma$  partial agonists 225
- precision medicine 406, 409–411
- preclinical and clinical trials 188
- preclinical data science 196
- preclinical research 199, 201
- preclinical testing 167
- prediction 10, 18, 25, 39, 387, 421
  - accuracy 335, 343, 574, 578
  - active site 284
  - activity 391
  - bioactive molecules 273
  - druggability 292
  - error 489
  - physicochemical properties 53
  - polypharmacology 411
  - pose 317
  - property 333
  - reaction 84
  - reliability 143
  - spectra 135
  - structure 139
  - target 406
  - toxicity 199
- predictive error of sum of squares (PRESS) 39, 488
- preferential exclusion model 528, 531
- pre-processing methods 19, 475
- PrGen 420, 422
- primary cancer cells 199
- principal component analysis (PCA) 17, 19, 35, 42, 150, 227, 335, 420, 462–464, 476, 487, 502, 511, 558
- principal component regression (PCR) 18, 22, 487, 488, 571
- principal components 19, 22, 35, 420, 462, 476, 477, 491, 559
- principal moments of inertia 24
- PRINT 298
- prior, Gaussian 555
- privileged structures*, 219
- probabilistic neural network (PNN) 29
- ProBis 299
- PROCAT 298
- process analytical technology (PAT) 573
- process control 7, 571, 581
- pro-drug 361, 381
- projection 21, 35, 36, 294, 462, 463, 472
- projection of latent structures (PLS) 18, 21–24, 147, 335, 420, 486–488, 571
- promiscuity 305, 364
- property prediction 10, 11 *see also* QSAR/QSPR
- proportional-integral-derivative (PID) controller 581f
- proprietary methods 143
- propylparaben 516
- PROSHIFT 147, 149, 157
- PROSITE 298
- prostaglandin E2 synthase1 (mPGES-1) inhibitors 221
- ProSurfer 299
- Protein Data Bank (PDB) 285, 389, 390, 423
- protein-ligand binding 428
- proteins 106, 108, 143, 144, 147, 264, 266, 269, 276
  - flexibility 291, 303, 317
  - fold 298
- proteins-based pharmacophoric filters 323
- protein-solvent-protein (PSP) 285, 287
- proteomics 106, 108, 166, 170, 535
- protonation states 326
- protoporphyrin IX 366, 419–428
- protoporphyrinogen 419–428
- Pseudomonas aeruginosa* (PA) 562

- pseudoreceptor model 422  
 Pseudo-Rotational Online Service and Interactive Tool (PROSIT) 298, 390  
*pseudo*-synthesis 409  
 PubChem 13, 112, 175, 245, 391, 395, 512  
 PubMed 126, 246, 250, 375, 396, 400  
 pulmonary hypertension 221  
 purities of compounds 55  
 pyrazolopyrimidinediones 180  
 Python 449
- q**  
 3D QSAutogrid 24  
 $q^2$ -GRS method 23  
 Q-SiteFinder 287  
 qualitative structure–property relationship (QSPR) 333, 548, 585  
 quality by design (QbD) 573  
 quality control 227–228, 493, 543, 585  
 quality criteria 32, 39–41, 294  
 quantitative high throughput screening (qHTS) 441  
 quantitative structure–activity relationships (QSAR) 10–46, 183, 221, 365, 395, 442, 484, 543, 551, 585  
 quantitative structure–odor relationships 512–513  
 quantitative structure–property relationship (QSPR) 10–13, 59, 71, 333, 342–349, 548, 549, 551, 554, 571, 588, 589  
 quantitative structure–spectrum relationships 139  
 quantitative weight of evidence assessment 447  
 quantum chemistry  
   calculations 138  
   descriptors 66  
   methods 55  
   prediction of NMR properties 142  
 quantum efficiency 557  
 quantum mechanical (QM) methods 97, 137, 142, 367
- molecular mechanical methods (QM/MM) 367  
 quantum mechanics 54, 142  
 queries 138  
   data 250  
   processing 254  
 quetiapine 374–375
- r**  
 radial basis function (RBF) 29  
 radial distribution function (RDF) 16, 135–145, 224, 339  
*Radix Astragali* (Huangqi) 238, 240  
*Radix Ginseng* (Renshen) 240  
*Radix Ophiopogonis* (Maidong) 238, 240  
*Radix Puerariae* (Gegen) 238, 240  
*Radix Rehmanniae* (Dihuang) 238, 240, 242  
*Radix Rehmanniae* (H02) 241  
*Radix Trichosanthis* (Gualou) 238, 240  
 Raman spectrum 138  
 Random forest (RF) 17, 18, 26–27, 68, 144, 147, 149, 293, 335, 368, 400, 432, 433, 480, 487  
 randomization tests 271, 490  
 random sampling 34  
 random splitting 34  
 random subsets 27, 489  
 range-based methods 42  
 rapid automated materials and processing (RAMP) 549  
 Rapid Overlay of Chemical Structures (ROCS) 226  
 RApid Pocket MAtching using Distances (RAPMAD) 301  
 rational selection methods 34  
 RDKit 449  
 reactions 83–91  
   biochemical 106  
 reaction center 91, 111, 125, 365, 367, 370  
 reaction databases 84, 86, 91, 96–97, 110, 111, 125, 128  
*Reaction InChI (RInChI)* 91  
 reaction mechanisms 90, 92, 119  
 reaction pathways 95, 97, 113

- reaction planning 84, 86
- reaction prediction 87–97
- reaction retrieval 111
- reaction sites 110, 111, 123
- reaction tree 412
- reactivity 90, 92, 93, 102, 261, 365, 445
  - chemical 10, 11, 20, 58, 97, 365, 372, 445, 447
- Reactome 111, 197
- Read-Across (RA) 442, 445–448, 543
- real time release testing (RTRT) 573
- Reaxys 96
- RECAP 175
- Receiver Operating Characteristic (ROC) curves 45, 226, 272, 274, 323, 483
- receptor 167, 361
  - binding 11, 166, 178
  - protein 506, 534
  - surface 24
- receptor-based deduction 269
- receptor-based pharmacophores 269–270
- recoding structural features 248
- recursive partitioning 25, 430, 480
- redocking 323, 324
- refractive index 554, 557, 558
- regenerative medicine 548
- regiochemistry 92, 93, 375
- Registration, Evaluation, Authorization and Restriction of Chemicals (REACH) 441, 446, 586
- regression
  - analysis 20–22
  - backward-elimination 21
  - ensemble online support vector (EOSVR) 577
  - forward-selection 21
  - ill-posed 552
  - linear 20, 71, 293
  - multi-linear, *see* multi-linear regression analysis
  - multiple linear 420, 555
  - ridge 486
  - support vector 29, 571
  - tree 480
  - univariate 484
- regression/correlation models 11
- regulatory and metabolic capabilities 123
- regulatory databases 247, 505
- regulatory science 439–464
- relational database management system (RDBMS) 449
- repeated double cross-validation 491
- repositories 196
- representational state transfer (REST) 449
- rescoring 320
- Research Institute for Fragrance Materials (RIFM) 505
- residual error 484
- residual sum of squares 39
- resonance effect 58
- response randomization 38
- retrieval system 111
- retroaldols 97
- retrosynthetic analysis 94ff
- reverse docking approach 224
- reverse pathway engineering (RPE) 125–128
- Rhea 113
- Rhizoma Anemarrhenae* (Zhimu) 238, 240
- Rhizoma Dioscoreae* (Shanyao) 238, 240
- rho kinase inhibitors 220, 221
- ribonuclease 261
- ridge regression 486
- ring effects 63
- risk assessment 350, 417, 441–448
- ROBIA program 97
- robustness 336, 421
- ROESY 154
- root mean squared error of
  - cross-validation (RMSECV) 488
- root mean square deviation (RMSD) 324
- root-mean-square error (RMSE) 41, 486, 555, 577
- rotatable bonds 316, 430
- rotation forest 27

- R squared (coefficient of determination)*, 554
- R statistical package 27
- rule-based systems 133, 368, 429
- Russel 252
- Ruta graveolens*, 223
- rutamarin 223
- RXN00173, 112
- S**
- Salmonella* reverse mutation assay 432
- Salmonella typhimurium*, 432
- salt bridges 318
- saponins 227
- SARpy 459
- scaffold 365, 430
  - hopping 262, 272
  - molecular 507
  - Murcko 507
- scaling 19, 472–474
- scatterplot 150
- Schrödinger's equation 92, 142
- SciFinder 96
- SCOP 298
- score-based metabolic reconstruction 124
- score histogram 324, 325
- scoring,
  - binding affinity prediction 317
  - consensus 320
  - function 181, 276, 294, 299, 315, 317–330, 407, 423
- scPDB 303, 304
- scrambling 554
- SCREEN 293
- screening 181, 245, 251, 298, 323, 391
  - commercial libraries 513
  - experimental random 422
  - in silico* 292
  - NMR-based fragment 292
  - phenotypic 405
  - shape-and feature-based 274
  - similarity 226
  - virtual 172, 209, 211, 226, 240, 423
- scree plot 477
- SDF-format 248, 389, 390, 396
- search(ing)
  - full structure 91, 112, 250
  - reaction 91
  - similarity 91, 172, 252
  - substructure 251, 387
  - superstructure 251
- secondary metabolites 125
- second order approximation 56, 61
- selection 211, 486
- selectivity 177, 183, 263, 273
- self-organizing map (SOM) 17, 19, 28, 119–121, 173, 228, 293, 335, 338, 343, 478
- semantics 397
- sensitivity 45, 324, 370, 432
- sequence homology 143
- sequence search algorithms 297
- serotonin 224, 254
- SESAMI 154
- sesquiterpene lactones (STLs) 224, 228
- Setubal principles 336
- shake algorithm 531
- shape-matching 406
- shared encoding 250
- side effects 188, 199, 298, 326, 343, 361, 401, 540
- SIENA 297
- SIFTER 298
- signal-to-noise ratio 488
- similarity 10, 19, 250, 397, 446
  - analysis 41
  - maps 512
  - searching 252
  - Tanimoto 369
- similarity ensemble approach (SEA) 199
- simplified molecular-input line-entry system fingerprint (SMIfp) 509
- SIMPLS 22
- simulated annealing 17, 21, 315, 316, 430, 495
- simulation
  - molecular dynamics (MD) 530
  - spectra 133, 138
- single nucleotide polymorphisms 363
- SiteAlign 300
- SiteBase 299
- SiteEngine 299

- SiteFinder 287
- SiteMap 287, 293
- site of mechanism (SoM) , 176, 177, 367, 369, 377
- sketcher 253, 254
- skin aging 528, 529, 542
- skin sensitization 431, 443
- SLN strings 252, 253
- smallest set of smallest rings (SSSR) 63
- SMARTCyp algorithm 367
- SMARTS 253, 254, 367, 445, 459
- SMILES 112, 252, 387, 396, 450, 459
  - canonical 249
  - translator 389
  - unique 389
- soft sensors 571–582
- solar cells 548, 556, 557
- sole suspect 398
- solubility 54, 69, 72, 334, 336, 361, 551, 554
- solvent
  - accessibility 285, 301
  - supercritical 554
- solvent accessible solvent area (SASA) 76
- SONNIA 173, 176, 186
- SOPHIA 97
- SPARTA+, 147, 149
- spectra 133–156
- spectral data 5, 133, 134, 150, 461, 473, 483
- spectrum prediction and comparison 134
- spectrum–structure correlation 135
- sphere exclusion 36
- spherical volume 425
- spin–spin couplings 154
- SPINUS 145
- splitting, data 32
- SQL 450
- $\pi$ -stacking 265
- standard deviation (SD) 38, 61, 65, 66, 144, 149, 172, 287, 335, 451, 472
- standard deviation error of prediction (SDEP) 41
- standard error 38, 554, 558, 563, 564
- standardization 201, 247–250, 255, 413, 472–475, 478, 503
- Staphylococcus aureus* (SA) 562
- StarDrop P450, 367
- static fingerprints 459
- statistical analysis 178, 269, 319, 429, 442, 447, 533
- statistical modelling 23, 30, 34, 76, 200, 561, 571
- statistical significance analysis 271
- steady-state 342, 372
- stereochemistry 110, 136, 154, 211, 248, 249
- stereoselectivity 93
- steric clash 267
- steric contours 23, 24
- steric effects 58
- steric hindrance 75
- steroids 445
- sterol 224
- Stevens–Johnson Syndrome (SJS) 398–401
- stochastic methods 315
- stratification 34
- stratum corneum 529
- StromBone™, 565
- structural identity 140
- structural keys 15
- structure-activity relationships (SAR) 4, 11, 260, 418, 419, 442
  - quantitative, *see* quantitative
  - structure-activity relationships
- structure-based approaches 422–429
- structure-based drug design (SBD) 168, 179–182
- structure-based pharmacophore model 269
- structure-based virtual screening (SBVS) 313–326
- structure elucidation 133–135, 140, 209
- structure-flavor relationships 511
- structure generator 110, 172
- structure ID (SID) identifier 246, 387
- structure–metabolism relationships (SMRs) 368



- structure–property relationships (SPR),
    - see quantitative
    - structure-property relationships
  - structure query 253
  - structure representation 248
  - structure searching 91, 112, 250
  - structure-spectra correlation 133, 137
  - structure validation 134
  - subgraph 456
  - substance database 246
  - substrate 167, 360
  - substructure recognition 150
  - substructure-subspectrum database 136
  - sulfotransferases 277
  - sulphonation 363
  - sulphone-di-oxygenation 374
  - sulphotransferase(SULT) 365
  - sulphoxide-mono-oxygenation 374
  - sum of ranking differences (SRD) 474
  - SuMo 299
  - superfeature 277
  - superimposition 123, 179, 419
  - SuperScent 506, 509
  - SuperStar*, 269
  - superstructure search 251
  - SuperSweet database 505, 509
  - supervised learning 18, 335, 475
  - support vector machine (SVM) 18, 29–30, 59, 119, 144, 147, 294, 335, 343, 400, 432, 480, 488, 560
  - support vector regression (SVR) 29, 571
  - surface 181
    - hydrophobic 327
    - molecular 224
    - GBSA 181, 320
    - protein 283
  - SURFNET 286
  - sweeteners 514
  - SYLVIA 101, 182
  - SynChem 100
  - SynGen 99
  - SYNOPSIS 101
  - synthesis
    - biology-oriented (BIOS) 412
    - continuous flow 408
    - in silico* 375
    - short 96, 407
    - total 87
  - synthesis design 84, 86, 94–102
  - synthesis planning programs 99
  - synthesis routes 407
  - synthetic accessibility 101, 182
  - Synthetically Accessible Virtual Inventory (SAVI) 391
  - System for Organic reaction Prediction by Heuristic Approach (SOPHIA) 97
  - systems biology 201
- t**
- tailored/target-specific scoring functions 320
  - Tanimoto coefficient 36, 112, 172, 252, 369, 370, 510, 517
  - targetability 292
  - target-based *drug* discovery 405
  - targeted/focused libraries 178
  - target fishing 198, 223
  - target identification 167ff, 196
  - target-mediated toxicities 199
  - target mining 196–198
  - target validation 170
  - taste 503
  - tautomerism 55, 249, 252, 326, 428, 445
  - TCGA database 196
  - Tenascins 540
  - TESS 299
  - test set 17, 334, 490
  - 2,3,4,5-tetrachlorophenol 187
  - Tetrahymena pyriformis*, 433
  - tetrazole 409
  - text mining 198, 396–398, 400, 401
  - Theonella swinhoei*, 224
  - thermal stability 151
  - thermodynamic integration 321
  - thermodynamic properties 60–63
  - 3-methylbutanoic acid 126
    - threading algorithm 287
  - three-point contact model 261
  - 3R philosophy 429
  - Threshold of Regulation (TOR) 443

- threshold of toxicological concern  
     (TTC) 443, 444, 446, 543  
 Tikhonov regularization 487  
 TIMES 368  
 tissue inhibitor of metalloproteinases  
     (TIMP-1) 541  
 tizanidine 179  
 TOCSY spectra 154  
 Toll-like receptors, subtype 2 (TLR2)  
     274, 275  
 tolperisone 179  
 top-down approach 442  
 Topiramate 200  
 topoisomerase 540  
 topological autocorrelation 173, 186  
 topological descriptors 16, 144, 338,  
     555  
 topological distances 73  
 topological indices 16, 71  
 topological polar surface area (TPSA)  
     347, 349  
 topological properties 553  
 topological spheres 73, 75  
 topomer 25  
 torsional energy 319  
 total body clearance 349  
 total synthesis 87  
 totrain 320  
 Tox21 algorithmic groups 200  
 toxalerts 58  
 ToxCAST<sup>TM</sup> 395, 431, 441  
 toxicity 11, 58, 183, 184, 361, 372, 391,  
     442  
     aquatic 433  
     assessment 441  
     chronic 431  
     genetic 431  
     prediction 199  
*toxicity prediction by komputer assisted  
     technology TOPKAT* 430  
 Toxicity Reference Database  
     (ToxRefDB) 432  
 toxic modes of action 185  
 toxicological alerts 187  
 toxicology 14, 177, 184, 200, 254, 350,  
     365, 370, 372, 374–375, 398, 417,  
     429, 431–435, 441, 586  
 ToxPrint 58, 187, 453–458  
 ToxTree 431, 445  
 trachelogenin 226  
 Traditional Chinese Medicines 171,  
     238 *see also* Chinese herbal  
     medicine  
 training set 11, 17, 145, 200, 264, 334,  
     555  
*trans*-diethylstilbestrol 261  
 transepidermal water loss (TEWL)  
     528  
 transferases 117, 363  
 transition states 121, 123  
 transmembrane protein 534  
 transport system 167, 208  
 tripeptoid library 175  
 Triton-X100, 426  
 TrixP 302  
 TrixX 316, 317  
 true actives 324  
 true negatives 45, 273, 324, 343  
 true positives 45, 273, 324, 343, 483  
*t*-test 485, 536  
 tumor suppressor 198, 518  
 tumor therapy 353  
 turnover number 554, 558, 559  
 Tversky 252  
 Tylenol 254  
 type 2 diabetes (T2D) 222, 225, 237
- u**
- ultra high-throughput screening  
     (u-HTS) 166  
 uniform design method 35  
 uninformative descriptors 551  
 UNQUAC Functional-group Activity  
     Coefficients (UNIFAC) 57  
 univariate regression 484  
 unsupervised learning 17–18, 119,  
     173, 335, 475  
 uridine 5'-diphospho-  
     glucuronosyltransferase (UGT)  
     365  
 uropathogenic *Escherichia coli* (UPEC)  
     562  
 US Food and Drug Administration  
     (FDA) 238, 405, 443, 502

**V**

valency states 248  
 validation 11, 30, 31, 271, 323, 334, 335, 400  
   applicability domain 41, 42  
   data compilation 32–37  
 external 30–32, 37, 41, 43, 44, 442, 492  
   goodness of prediction 39  
 valproic acid 517  
 van der Waals (vdW)  
   energy 16, 287  
   radii 260, 285  
 variables 472–488  
 variable importance (VIP) 486  
 variable selection methods 23, 44, 485  
 variable subset selection (VSS) 488  
 variance analysis (ANOVA) 474ff  
 VAST 298  
 VB model 248  
 vector 135  
   score 476  
 venetian blinds 489  
 vibrational spectroscopy 137  
 VigiBase 398, 400  
 virtual hits 182, 274  
 virtual organic reactions 409  
 virtual screening 10, 101, 166, 175, 177, 210, 211, 220, 272, 278, 313  
   *see also* structure-based virtual screening (SBVS)  
 virulence factors 170  
 viscosity 554, 557  
 VolSurf 16, 24, 267  
 VSN algorithm 536

**W**

Waikato Environment for Knowledge Analysis (WEKA) 27  
 wall chart 106  
 water-ectoine mixture models 529ff  
 water-glycerol complex 531ff  
 WaterMap 321  
 water-binding activity 528

water solubility (log S) 55, 57, 69–71, 336–342  
 weak polar interactions 318  
 weighted averaging 26  
 whole-molecule descriptors 65  
 wisdom of crowds concept 26  
 Workbench for the Organization of Data for Chemical Applications (WODCA) 99  
 World Drug Index 432

**X**

xenobiotic metabolism 359–375  
 xenografts 199  
 Xiaoke 238–240, 242  
 XLogP 57, 65, 346, 464  
 X-ray  
   crystallography 168, 321, 323, 423, 425, 428  
   structure 168, 180, 269, 411, 418  
 X-Score 320  
 xyz-format 390

**Y**

Yalkowsky's general solvation equation (GSE) 70  
 yield  
   of actives 274  
   of reaction 93  
 Y-permutation 38  
 Y-randomization 31, 32, 38–39, 45  
 Y-scrambling 30, 38–39, 490  
 Yule 252

**Z**

zeolites 559  
 zeolitic imidazolate framework (ZIF) 560  
 zero-order approximation 56  
 ZINC databases 514  
 Z-test 38, 39  
 zwitterions 67, 75, 528



























