## Index

Acetolactate synthase, 263 Acetyl-CoA, 168, 252, 285 Activation, cassette-type, 172 Adaptation, 10-11 Affymetrix GeneChips, 142 Aldolase, 262 Algorithms alignment, 229 elementary mode analysis, 256-257 **MACAW**, 136 for motif discovery, 135-140 for protein categories, 239 sequence alignment, 265 AlignACE, 129, 136–142 Alignment algorithms, 229 of metabolic pathways, 259-263, 265 Amino acid production, 59 Amphiphilic molecules, 268 Ancestry, and homology, 6, 7 Anemia, hemolytic, 279-280 Annotation five step approach, 24 of new genome (E. coli), 103-104 of pathways, in genomes, 263-267 pitfalls, 20-21 specific systems, 21-24 vocabulary, 33 Antigens, cell surface, 163 Apoptosis and Boolean network, 197, 201-202 and cancer cells, 212 as cell state, 183

and Ras, 189 Archaea glycolysis, 263 proteomes, 26, 34 Arginine biosynthesis, 133 Arrays. See Microarrays Attraction, basins of and cancer, 211 and cell state change, 201, 203, 204-205 description, 197, 199-200 Attractor states, 199-202, 203-205 and cancer, 210-212 pseudo, 208-209 B. burgdorferi, 266–267 B. subtilis, 121, 124 purine biosynthesis, 132 Bacteria. See also specific bacteria chemotaxis, 280-281 DNA-binding regulators, 114 DNA regulatory motifs, 139-142 glycolysis, 262-263 operon prediction, 121-124 proteomes, 26-27, 34-35 transcriptional units, 116-117 Bacteriophage lamda, 282-283 Basic Local Alignment Search Tool (BLAST), 223, 229 Bayes theorem, 89 Binding sites predicting, 87 for transcription factors, 94, 98, 129 Biochemical analysis, 260-263

BioKleisli, 57-58 Biological noise, 208-209 Biomechanics, 6 Biopathways Consortium, 213 **Biosynthesis** cholesterol, 167-169 heme, 162-163 modeling, 64 nucleotide, 263 purine, 132 Birds, wings, 4 BLAST. See Basic Local Alignment Search Tool Boltzmann equation, 88-89 Boolean networks architecture, 194-196, 205-207 attractor states, 199-202, 203-205, 208-209, 210-212 basins of attraction, 197, 199-200, 201, 203, 204-205 and cancer, 181, 189, 209-212 and cell states, 196-198, 200-209 directionality, 199 dynamics, 196-198 and expression profiles, 213 limitations, 212-213 on-off switching, 192-194 pleiotropy, 205-207 protein-gene interaction, 213 proteolysis, 195-196 state space, 197, 198-200, 203, 214 trajectories, 199-200, 202 unstable states, 198, 199, 203 updating, 199 BRENDA, 49, 57, 66, 252 Burns, 267 Butterflies, eyespots on, 3

*C. acetobutylicum*, 132 *C. glutamicum*, 263 Cadherins, 231 *Caenorhabditis elegans* comparative analysis, 36–41 repeating domains, 40 Cancer, and Boolean networks, 181, 189, 209–212 Carbon dioxide transport, 279 Cassette-type activation, 172 Catalysts, 268 Celera Genomics, 76 Cell membrane and cholesterol, 160 in simulated cell, 274, 278, 279 Cell(s) construction of, 59 virtual, 277-280 (see also E-CELL) Cell Signaling Networks Database, 213 Cell states. See also Differentiation; Signal transduction pathways in Boolean network, 196-198, 200-209 and cancer, 209-212 and context, 208-209 definitions, 182-183 and gene network hierarchy, 172-173 perturbations, 189-190, 201-209 robustness, 202 in rule-based model, 60 Cell surface antigens, 163 Chance, 6, 7, 8 Chemical kinetic simulation, 164-167 Chemotaxis, 280-282 Cholesterol, 155-156, 158-160 mathematical model, 167-169 Cleavage sites, predicting, 27 Clustering as analysis approach, 27-32 coinheritance groups, 231 databases, 27-28 DNA regulatory motifs, 140 and expression profiling, 213 hierarchical, 29 on mRNA expression, 131 by regulatory region, 234 of related enzymes, 260 and transcription regulation, 116 Clusters of Orthologous Groups (COGs), 27-30, 260, 265 CluSTr, 27-32, 34 Co-A transferase, 133 Coinheritance groups, 228-231 Communication processes, 64-65. See also Signal transduction pathways Comparative analysis and elementary modes, 257, 263

on eukaryotic proteomes, 34-42 of genomes, 103-104, 232, 233 and RNAP binding, 110-117 Concentration rates, in models, 63, 65 velocities, 166-167 Congruence, 117-120 Conservation of DNA regulatory motifs, 141 of genes in operons, 122-124 and phylogenetic space, 240 Context and cell states, 208-209 and protein function, 223-224, 225, 226-234, 239-240 Contingent events, 7 Convergence and homology, 6, 7, 8 in signal transduction, 187-189 Cooperativity, 193 CORBA (Common Object Request Broker Architecture), 74, 76 Database Management Systems (DBMS), 51 - 52Database of Interacting Proteins (DIP), 238 Databases biochemical, 49, 252, 261 classification, 29-32 for clustering, 27–28 vs. DBMS, 50-52 enzymes, 54 EST, 235 for functional groups, 134–135 gene network, 150 gene regulation, 54 genomic neighbors, 231 integrating, 54-58, 69-76 listing, 54 microarray, 235 pathways, 49, 54, 213-214, 238 promoters, 234 protein interactions, 238 quality control, 55 redundancy, 29-30 remote access, 73 Saccharomyces, 33 search algorithms, 28

sequence annotation, 20–25 sequences, 27-28, 49, 53, 54, 228, 264 transcription factors, 49 transcriptome experiments, 105 user queries, 30-32 Data merging, 55 Data Warehouse, 57 DBMS. See Database Management Systems Differentiation and Boolean network, 197, 200-202 as cell state, 182-183 gene network control, 160-163 induced, in culture, 190 vs. quiescence, 183 Digitalization. See Boolean Networks Dihydroxyacetone kinase, 265 DIP. See Database of Interacting Proteins Distal-less gene, 4, 10 Distance, intergenic and coinheritance, 229 and functional relatedness, 116, 121, 122, 124, 132, 229, 233-234 in regulatory motif search, 139-140 in S. cerevisiae, 142 from start codon, 139-140 Distribution, hypergeometric, 139 DL-diaminopimelate, 263 DNA-binding proteins, 87-93, 98. See also Weight matrices DNA microarrays, 235 DNA regulatory motifs, 139 DNA replication factors, 241 DNA sequences motif discovery within, 135-140 similarity, and homology, 5 Domain fusions, 225-228 Domains annotation, 25, 34 C2H2-type zinc finger, 37-38, 40, 41 classification, 29 collagen triple helix repeat, 39 comparative distribution, 38 composition, 41 C-type lectin, 39 C4-type steroid receptor zinc finger, 39 EGF-like, 40, 41 fibronectin type III, 40

Domains (cont.) immunoglobulin, 40 LDL-receptor, 40–41 ligand-binding, of nuclear hormone receptor, 39 major histocompatibility complex, 40 nonspecific, 34 repeated across sequence, 40 Rosetta Stone links, 225–228 *Drosophila melanogaster* comparative analysis, 36–41 domain repetition, 40–41 Dyad-detector method, 112

E-CELL cell models, 277-280 gene regulation model, 282-283 mitochondria model, 283-285 scope, 273-275 signal transduction model, 280-282 software, 59 EcoCyc, 238 Electroneutrality, 279 Elementary modes, 255-259, 263 EMBL. See European Molecular Biology Laboratory EMPATH, 257 Encephalopathy, mitochondrial, 285 Energy. See also Glycolysis binding, 87-89, 90-93 and Boolean networks, 198-199 and enzyme types, 252 and mitochondria, 285 multicellular organisms, 181-182, 198-199 Engrailed expression, 3, 10 Entner-Doudoroff pathway, 262 Entrez, 22-23, 231 Entropy, relative, 89, 93 Environmental modulation, 208-209 ENZYME database, 54, 252 Enzymes. See also specific enzymes and cholesterol, 159-160, 168 databases, 54 defined, 60 elementary modes, 255-259, 263 heme biosynthesis, 162-163

hierarchies, 263 Michaelis-Menten kinetics, 193 modeling, 59, 66-67 nitrite reductase, 227 pH dependence, 279 types, 252-253 EPD. See Eukaryotic Promoter Database Erythrocytes as irreversible process, 160-163 models, 169-171, 278-280 and pyruvate kinase deficiency, 279-280 Erythroid progenitor cells, 154 Erythropoietin, 160, 170-171 Escherichia coli acetate Co-A transferase, 133 acetate synthesis, 263 adaptation, and congruence, 118-119 chemotactic response, 280 coregulated genes, 112-113, 119-120 DNA regulatory motifs, 141 and domain fusion, 227 flux conditions, 259 gene conservation, 123 gene regulation simulation, 282 glycolysis, 262, 282 lactose, 182 metabolic model, 78 phosphorylation, 281 promoters, 107-116 purine biosynthesis, 132 transcription, 104, 113-114, 116-117 EST. See Expressed Sequence Tags Eukaryotes and operons, 133 phylogenetic diversity, 228 Eukaryotic Promoter Database (EPD), 54, 234 Eukaryotic proteomes cluster data, 29 comparative analysis, 35-41 complete sets, 26-27 domain distribution, 38 phylogenetic classification, 27-28 RNA binding, 38 European Molecular Biology Laboratory (EMBL), 49, 53, 54 E-values, 265

Events, reaction vs. regulatory, 152–153, 155-156 Evolution. See also Phylogenetic profiles and Boolean network, 205-207, 208 and transcription regulation, 105, 121, 124 ExPASy. See Expert Protein Analysis System Expectation-maximization (EM) method, 96 Expected values (E-values), 256 Expert Protein Analysis System (ExPASy), 54, 261 Expert systems, 59 Expressed Sequence Tags (EST), 235 Expression basic elements, 282 of distal-less gene, 4, 10 E-CELL model, 282-283 mRNA, 130-131, 142-143, 235-236 profiling, 213 and promoter specificity, 87 and protein function, 234-237 from proteomes, 236-237 RegulonDB search, 117 Eye, homology, 8-9 Evespots, of butterflies, 3 False positives, 106, 109, 111–112 Feedback and Boolean network, 193 cholesterol, 158-160, 168-169 erythrocytes, 161, 162, 171 positive and negative, 172 Flight, 11 Flowers, petals of, 5 FlyBase, 33 Footprinting, 120, 135, 140 Fossils, Burgess shale, 7 Functional dynamics, 163-167 Function(s). See also Protein functions and DNA motifs, 129 of network types, 156-163 relatedness, 133-135 and transcription regulation, 114 Fungal protein, 38 Fusion, domain, 225-228

Galactose utilization, 142 GATA1, 170-171 GATA1-p, 154, 158, 161, 162 GDB. See Genome Database GenBank, 54, 228 GeneNet, 49, 150-158, 168 Gene Ontology (GO), 33, 34 Genes. See also Expression coexpression, 112 context, 225, 226-234, 239-240 coregulated, 112-113, 119-120, 140-141 (see also Regulons) distal-less, 4, 10 distance between, 116, 121, 122, 124, 132, 229, 233-234 functionally related, 133–135 homeobox, 10 homology, 8 within operons, 117-118, 121, 122-123 regulatory, 8 relative positions, 231-233 signaling, 184 transition-initiating, 207 Genomes. See also Proteomes comparative analysis, 35 human, 35 pathway annotation, 263-267 and protein function, 225-234 protein networks in, 240-243 relative positions in, 231-233 signal transduction portion, 184 starting new, 103-104 Genome Database (GDB), 54 Gibbs' sampling, 96-97, 112, 136 in AlignACE, 136-137 Gluconeogenesis, 267 Glucose, lactose, RNA-polymerase, 63 - 64Glucose-6-phosphate, 60-61 Glycolysis E. coli simulation, 282 elementary modes, 258-259 pathway alignment, 262-263 rule network, 67-68 in simulated cells, 278-279 G-protein coupled receptor, 38 Greedy algorithms, 95

Growth and development, 160-163 Growth factors, 183-184, 189 Haemophilus influenzae, 116, 259 Heat shock response, 142 Hedgehog protein, 3 Helicobacter pylori, 262 Helix-turn-helix, 114, 121 Hemoglobin, 193, 279 Hemolysis, 279 Hemolytic anemia, 279-280 Hidden Markov Models (HMMs), 23 Homeobox genes, 10 Homeostasis, 158-160, 167-169 Homology benefits, 11–12 definitions, 2-3, 5-6 at differing levels, 3-4, 9-10 and dissimilarity, 5 distal-less gene, 4, 10 DNA sequences, 5 gene expression patterns, 4 of gene vs. end product, 8-10 as hypothesis, 3, 6-8 limitations, 223-224 vs. paralogy, 6 of regulatory circuits, 1-2 serial, 5-6 and surrounding parts, 6 Homology-derived secondary structure of proteins (HSSP), 27, 31 HTML. See HyperText Markup Language Human genome, 35 Human Genome Project, 53 Human Genome Sciences, 76 HUSAR, 57 Hypergeometric distribution, 139 HyperText Markup Language (HTML), 53, 73 Immunoglobulin domain, 40 **INCYTE Genomics**, 77 Information fusion, 56, 74

Informax, 77 Insect cuticle protein, 38 Internal congruence, 119 InterPro and CluSTr, 34 for comparative analysis, 35, 37-41 controlled vocabulary, 33-34 description, 23 and domain composition, 41 and GO, 34 protein analysis, 27 user interface, 33 Jaccard coefficient, 239 JAVA, 73-75, 156 JDBC (Java DataBase Connectivity), 58, 73 - 74KEGG. See Kyoto Encyclopedia of Genes and Genomes Key word recovery, 238-239 Kullbach-Liebler distance, 89, 93 Kyoto Encyclopedia of Genes and Genomes (KEGG) and database integration, 57 and DNA regulatory motifs, 141 and functional relationships, 238 interface, 53 and metabolic pathways, 49, 134-135, 252, 261 url, 54 Lactate dehydrogenase, 253

Lactic acidosis, 285 Lactose, 63–64, 182 LASSAP, 29 Leigh syndrome, 285 LexA, 111–112, 113 LIGAND database, 54 Limbs, 4, 5 Lion Bioscience, 77 Lipidation, 237 Lipids biosynthesis, 266–267 metabolism, 155–156 Liver, 267 Low-density lipoproteins (LDLs)

Information system(s)

signal transduction as, 181–182, 186–188,

defined, 52

205-206

domain, 40-41 role, 160, 167-168 Lysine, 263 Lytic-lysogenic switch, 282-283 MACAW. See Multiple Alignment Construction and Analysis Workbench Major histocompatibility domain, 40 Mammals, 172-173 MAP (mitogen-activated protein) kinase, 185, 187, 193 cascades, 208 MAP score, 138 MARGBench. See Modeling and Animation of Regulatory Gene Networks Markov models, hidden (HMMs), 23 Mating type, 142 Matrices. See Elementary modes; Weight matrices MEME. See Multiple EM for Motif Elicitation Metabolic flux space, 259 Metabolic networks diagrams, 59 glucose-6-phosphate, 60-61 glycolysis pathway, 67-69 and homology, 223 MARGBench example, 56, 69-76 mathematical models, 58-59 Metab-Sim simulation, 58, 66-69, 71 in multicellular organisms, 182 rule-based modeling, 60-66, 76-79 simulators, 163-167 Metabolic pathways alignment, 259-263, 265 boundaries, uncertain, 267 branched and interconnected, 252-253 catabolic and anabolic, 252 defined, 252-253 genome analysis, 263-267 identification elementary modes, 255-259, 263 by synthesis, 255 and organism complexity, 268 Metabolism comparative analysis, 41-42

proteome proportion, 41–42 Metabolites identification, 257-258 in models, 60, 62-63, 65 MetabSim, 58, 66-69, 71 and MARGBench, 75-76 Methanococcus jannaschii, 263 Metrics, of protein function, 238 Mevalonate pathway, 159-160 MGD. See Mouse Genome Database Michaelis-Menten kinetics, 66-67, 165, 167, 193 Microarrays, 235 Millipedes, 5 Minimal upstream regions, 116 MIPS. See Munich Information Centre for Protein Sequences Mitochondria, 283-285 Modeling and Animation of Regulatory Gene Networks, 56, 69-75 application, 75-76 Models. See also Boolean networks; Simulation chemical-kinetic, 164-167 of cholesterol biosynthesis, 167-169 gene regulation, 65 mathematical, 150, 191-192 of metabolic pathways, 267-268 (see also Metabolic pathways) rule-based, 60-66 Modularity, 190-191 Molecular databases, 53-58 Morphogenesis, 160–163 Motifs common. 112 discovery process, 129, 130 DNA-binding, 114 DNA regulatory, 135-140 overlapping, 112-113 palindromic, 140 RNA-binding, 38 Mouse Genome Database (MGD), 33 mRNA expression, 130-131, 142-143, 235-236 Multiagents, 57 Multicellular organisms, 181-182, 209-212

Multiple Alignment Construction and Analysis Workbench (MACAW), 136 Multiple EM for Motif Elicitation (MEME), 136 Munich Information Centre for Protein Sequences (MIPS), 134-135, 142, 238 MURS. See Minimal Upstream Regions Muscle development, 9 Mutations and Boolean networks, 210-212 in simulated cell, 281 Myc, 189, 208 Mycobacterium tuberculosis, 244-245 Mycoplasma genitalium, 265, 277-280, 282 Mycoplasma hominis, 262 Mycoplasma pneumoniae, 264–265, 266 Myopathy, mitochondrial, 285 Nematodes, 38 Neostructuralists, 6 Network(s). See also Metabolic networks cholesterol biosynthesis, 167-169 components, 172 congruence, 119 control, 152 defined, 49, 149 diversity, 163-164 elementary structures, 151 functional dynamics, 163–167 functional types, 156-158 gene regulation, 282 homeostasis-maintaining, 158–160 and irreversible processes, 160-163, 169-171 lytic-lysogenic, 282-283 mammalian, 172-173 in multicellular organisms, 182 object oriented analysis, 151-158 organization, 150-151, 163, 172-173 protein interaction, 240-243 signal transduction, 188, 190-191 (see also Boolean networks) transcription initiation, 104, 106-117, 124 Nitrite reductase, 227 Noise, biological, 208-209 Nucleotides, 263, 278

Object-oriented systems, 59, 66 for gene networks, 151, 163, 164-167, 172 Object Query Language (OQL), 74 ODBC. See Open Database Connectivity Oligonucleotides, 136 Open Database Connectivity (ODBC), 73 Open Reading Frame (ORF), 103–104, 139 Operator sites, 106-107 Operons in bacteria, 121-124, 132, 141 in E. coli, 104, 116-117 in eukaryotes, 133, 231 and evolution, 122-124 genes within, 117-118, 121, 122-124 lac and ara, in E. coli, 282 and protein function, 231-233 and regulatory motifs, 141 OPM, 57 OQL. See Object Query Language ORF, ORFs. See Open Reading Frame Organisms, multicellular, 181-182, 209-212 Organs, morphogenesis, 160–163 Orthologues, 38, 116. See also Clusters of Orthologous Groups (COGs) Osmosis, 279 Oxidation, 237 Oxygen transport, 279 Palindromes, 140 Paralogy, 6 Pathways. See also Signal transduction pathways databases, 54 liver antioxidant, 267 MAP kinase, 185, 187, 193 metabolic (see Metabolic pathways) modeling, 65 novel, 244-245, 253 ribulose, 266 PDB. See Protein Data Bank Pearson correlation, 140 PEDANT, 57 Pentose phosphate cycle, 258-259, 262, 278, 282 Peptides, signal, 27

Petri nets, 59 pH, 279 Phosphofructokinase, 59, 262 Phospholipid biosynthesis, 274, 278 Phosphorylation and Boolean networks, 195-196, 198-199 and external stimuli, 280-282 and metabolic pathway, 252 and protein modification, 237 Phylogenetic footprints, 120, 135, 140 Phylogenetic profiles, 115, 134, 228-231 Phylogenetic space, 240 PIR. See Protein Information Resource P13K-Akt sequence, 185 Pleiotropy, 187-189, 205-207 Prediction of cell regulative disorders, 214 of protein-binding sites, 106 of protein functions, 237-239 of regulatory network, 104, 106-117 of regulons, 130-135 of signal peptides, 27 Predictive value, 109 Profiling, gene expression, 213 Proliferation, 181 Proliferation, cellular, 197, 211-212 Promoters and discretization, 194 in E. coli, 103, 107–117 predicting, 106-107, 109 and RNAP, 106-117 specificity, 87, 94, 98 PROSITE database, 22 Protease, sterol-regulated, 155, 160 Protein Data Bank (PDB), 31, 54 Protein functions categories, 34, 41, 239-240 and expression, 234-237 and gene position, 231-233 measuring, 237-239 metrics, 238 molecular vs. cellular, 224 phylogenetic profiles, 228-231 Rosetta Stone approach, 225–227 structure-function relationship, 266 Protein fusion, 225-228

Protein-gene interactions, 114, 213 Protein Information Resource (PIR), 49, 54 Protein interaction networks, 241-243 Protein kinases, 37-38 Protein-protein interactions in Boolean networks, 195-198, 199 and homology, 223-224 Proteins. See also Yeast annotation, 20-25 chicken, 154 classification, 26-34, 41 constraint sharing, 225 DNA-binding, 87-89 eukaryotic (see Eukaryotic proteomes) fungal transcription, 38 fusion, 225-228 Hedgehog, 3 human, 155 insect cuticle, 38 lengths, 36-37 master, 208 modifications, 237 multidomain, 41 Myc, 189, 208 Ras, 189, 208, 241 reading frames, 264 regulatory, 106, 189 rhodopsin-like, 38 RNA-binding, 38 secreted, 27, 37 species-unique, 38 SREBP, 155, 159-160, 168 synthesis simulation, 278 transition-causing, 208 transmembrane, 27, 37 Proteolysis, 195-196 Proteomes. See also Comparative analysis; Eukaryotic proteomes analysis, 25-33 annotation, 20-25 of bacteria, 26-27, 34-35 classification, 25-33 comparative analysis, 34-41 expression profiles, 236-237 functional analysis, 34, 41 sequencing history, 19-20

ProtoMap database, 28 Pseudo attractors, 208-209 PSI-BLAST, 265 Purine biosynthesis, 132, 133 Purine metabolism, 59 Pyruvate kinase, 262, 279-280 Quality, of data, 55 Queries, 30-33, 55, 57-58. See also Searches Ras, 189, 208, 241 Reaction events, 152, 155 Reading frames protein- vs. RNA-coding, 264 reannotating, 265 Reannotation, 264-267 Receptors, 7-helix G-protein coupled, 38 Redox balance, 257-258 Redundancy in databases, 29-30, 51-52 in signaling, 187 Regulation, in multicell organism, 182. See also Feedback; Transcription factors Regulatory circuits, 1-2, 172 Regulatory events, 152-153, 155-156 Regulatory genes, 8 Regulatory regions, 234 RegulonDB database, 54, 105, 110 expression regulation, 117 and protein gene regulation, 112 and transcriptional units, 104 Regulons and Boolean networks, 207-208 defined, 132 prediction methods, 130-135 purine biosynthesis, 133 and transcriptional units, 116-117 Replication factors, 241 Reverse engineering, 213 RFC1-5, 241 Rhodopsin-like G-protein-coupled receptor (GPCR), 38 Ribosylation, 237 Ribulose uptake pathway, 266 RNA-binding motif, 38 RNA-polymerase (RNAP), 63-64, 106-117

RNP-1, 38 Rosetta Stone method, 225-228 RuleBase, 22, 24, 25 Rule-based modeling, 60-66 Saccharomyces cerevisiae. See also Yeast comparative analysis, 36-41 DNA regulatory motifs, 139-140, 142 mRNA expression, 131 repeated domains, 41 Saccharomyces Genome Database (SGD), 33 SAGE, 237 Searches, 30–33, 55, 57–58 RegulonDB, 117 SQL, 73, 75 SYSTER, 28 Semi-Thue system, 60 Sensitivity amplification, 193 Sequence Retrieval System (SRS), 57 Sequences. See also DNA sequences alignment, 260 annotation, 20-25 binding specificity (see Specificity) coding regions, 2 databases, 49 DNA, 5, 135-140 domain repetition, 40 P13K-Akt, 185 regulatory network, 104, 106-117 similarities, 229, 265 specific, 87 Serum, growth factors in, 183 Sigma factor, 106 SignalP, 27, 37 Signal transduction pathways annotation, 185, 186, 188 basic concept, 184 as Boolean network, 204–209 cascades, 193, 204-205, 208 for chemotaxis, 280-282 conflicting signals, 203 and context, 208-209 convergence, 187 cooperativity, 193 erythrocytes, 160-162

homology, 223 modularity, 190-191 perturbations, 189-190 simulation, 280-282 subcellular, 212-213 Similarities explanations, 6-8 nonhomologous, 5 in phylogenetic profiles, 229 statistical significance, 28-29, 265 Simulation. See also Models of cell (see E-CELL) chemical kinetic, 164-167 E. coli chemotaxis, 281 essential data, 285-286 metabolic pathways, 268 of networks, 163-167 signal transduction, 191-192, 214 software for, 275-277 stiffness problem, 276 Simulators, 49-50, 58 Size, of proteins, 36-37 Sodium transport query, 30-32 Software, simulation, 275-277 Specificity definition, 109 of DNA-binding protein quantitative aspect, 87-89 weight matrix models, 89–97 RNAP transcription, 106–107, 110–117 to species, 263 Specificity score, 138-139 SPTR database, 26, 28 SQL. See Structured Query Language SREBP proteins, 155, 159-160, 168 Stanford Microarray Database, 235 State space, 197, 198-200, 203, 214 Statistical analysis, 27, 31 Statistical significance of similarities, 28-29 Sterol-regulated protease, 155-156, 160 Stiffness, 276 Structure-function relationships, 266 Structured Query Language (SQL), 73, 75 SWISS-PROT annotation, 21-23, 24

and clustering, 28 and GO, 34 and protein functions, 238, 266 and proteome analysis, 26 controlled vocabulary, 33 database, 54 Synchronous congruence, 119 SYSTERS (SYSTEmatic Re-Searching), 28 T. pallidum, 266 Thermotoga maritima, 266 TIGR. (The Institute for Genomic Research), 261, 264 TIM barrels, 266-267 Tissue dynamics, 210 Tissues, morphogenesis, 160–163 TMHMM, 27, 37 Transcriptional units (TUs) in bacteria, 116-117 boundary genes, 116, 121, 122, 124 Transcription factors

binding sites, 94, 98, 129

and cholesterol, 155, 159

and cis-regulators, 213

site recognition, 234

in bacteria. 114

Transcription regulation

and gene function, 114

Database (TRRD), 54

TRANSFAC database, 54

Transition complexes, 193

annotation, 21-23, 24

and clustering, 28

Transmembrane proteins, 27

initiation, 104, 106

Transcriptomes, 2

TRANSPATH, 49

TrEMBL

and Boolean networks, 208, 213

of erythrocyte differentiation, 162

activators vs. suppressors, 114-115

false positives, 106, 109, 111-112

Transcription Regulatory Regions

Gene-Net depiction, 154, 155

for purine biosynthesis, 132

evolutionary origin, 105, 121

Index

controlled vocabulary, 33 and GO, 34 and proteome analysis, 26 TRRD. *See* Transcription Regulatory Regions Database Tus. *See* Transcriptional Units

Von Willebrand factor, 36

WD repeat, 38 Weight matrices and DNA regulatory motifs, 139 of *E. coli* promoter, 107, 108–110, 113 expectation-maximization (EM), 96 Gibbs' sampling, 96–97 greedy algorithms, 95 limitations, 110 network method, 97 in RegulonDB, 111 as specificity model, 90–93 Wings, 4, 5 WIT database, 54, 140–141, 231, 261

Yeast. See also Saccharomyces cerevisiae and domain fusion, 227 in network, 241–242, 243 phylogenetic profile, 230 Yeast Protein Database (YPD), 135, 142