Atmospheric pressure thermal desorption ionization (APTDI), 20
Automated Edman degradation, 322
Automated ligand identification system (ALIS), 259–263
affinity ranking in mixtures, 261–263
competition-based binding mode determination, 261
ligand binding affinity measurement by ALIS, 261
stages of, 259
Automatic gain control (AGC), 76
Backbone hydrogens, 176
Beta-endorphin, 395
Bifunctional crosslinkers, 199
Bioactive peptides, 394
Bioinformatics, 102, 119, 140, 151, 214, 231–251, 258, 385
to analyze glycoproteomes and phosphoproteomes, 352
data analysis with, 416–419
database searching, 231–251
Biomarkers, 158
Bipartite-graph based parsimony, 246
Blackbody infrared radiative dissociation (BIRD), 51
BLAST protein database, 234
Blood-brain barrier, 437
β2-microglobulin, 373, 385
Bond dissociation energy (BDE), 51
Bottom-up approach, applications, 216
Bottom-up/top-down approaches, 199
Bovine fetuin, partial mass spectra for, 9
Bovine insulin, 127I-PDMS spectra of, 5
Bovine serum albumin (BSA), analysis of, 17
Bradbury–Nielsen gate, 65
Breast cancer, stages, 132
Caco-2 permeability, 436
Caenorhabditis elegans, 406
Californium isotope, 4
Capillary electrochromatography (CEC), 407
Capillary electrophoresis—mass spectrometry, 264, 410–411
Capillary isoelectric focusing (CIEF), 17, 407
MS analysis, 17
Capillary zone electrophoresis (CZE), 327
Carbohydrate-deficient syndrome, 327
Carboxylation, 322
Cell–cell signaling, 394
Cell-culture development, 290–294
Cellular secretion profile, 158
CE-MALDI-TOF MS hydrophobic peptides, analysis of, 411
CEM Discover Benchmate microwave system, 221
Central nervous system (CNS), 394
CE separation modes—capillary zone electrophoresis (CZE), 407
Chemical crosslinking, 198–201, 270
drawbacks, 199–201
benefits, 198
protein structure characterization strategies, 200
Chemical footprinting: chemical crosslinking, 198–201
drawbacks, 199–201
for determining protein properties, and interactions, 175–206
experimental procedures, 178–182
global hydrogen–deuterium exchange, 178–179
HDX at peptide level, 179–182
fast photochemical oxidation of proteins (FPOP), 197
Fenton chemistry oxidation, 194–196
hydroxyl radicals, radiolytic generation, 196–197
stability of proteins from rates of oxidation (SPROX), 198
HDX, EX1 and EX2 rates, 176–178
hydrogen–deuterium amide exchange fundamentals in proteins, 176
hydrogen–deuterium exchange, 175–178
selective and irreversible chemical modification, 201–205
cysteinethioldervatization, 203
footprinting, FMO protein, in photosynthetic bacteria, 203–205
lysine acetylation, 202
potential pitfalls, 205
Chemical ionization (CI), 4
Chemical labeling approaches, 119
Chemical labeling reagents, 111
Chemical noise overlap minimization, 147
Chemical-tagging strategies, 116
Chip-based nanospray system, 268
CHO-derived interleukin-4 (CHO IL-4), 329
containing two potential glycosylation sites fulfilling, 331
positive-ion ESI mass spectrum, 334
positive-ion nESI mass spectrum, 330
tryptsin-treated, LC-ESI MS analysis, 333
Chromatographic separation, 193
CID process, 233
Circular dichroism (CD), 13
Class II MHC polymorphism, 374
Cleavable isobaric labeled affinity tag (CILAT), 113
Cluster analysis, 152
Cobalt-loaded Dynabeads (TALON), 267
Collisionally activated dissociation (CAD), 48
amino acid preferences, 57
high-energy, 49
mobile proton model, 48
Collision cross sections (CCS), 147, 150, 156
Collision-induced dissociation (CID), 48, 142, 182, 191, 232
Combining separation techniques, 159
Commassie-stained SDS-PAGE gels, 219
Comparative proteomics, 129, 130
conventional, 130–131
histology-directed protein profiling for, 132
using imaging MS, 131
Conjugation of small endogenous molecules, 436
Continuous flow screening (CFS), 272
Continuous flow system advantage, 273
for inhibitors detection, 273
Core plus building block approach, 260
Cross-correlation-based XCorr score, 241
Cross-linked peptides, 201
Culture-derived isotope tags (CDITs), 107
α-Cyano-4-hydroxycinnamic acid
Cyclic growth regulating factor (GRF), 437
Cyclic polypeptides, characterization, 215
CYP P450 enzyme, 436
Cysteine-containing peptides, 112
Cysteine (C) oxidation, 321
Cytochrome C
ESI spectra, 26, 223
MALDI mass spectra, 220
MALDI mass spectrum, 218
tryptic peptides, 218
tryptic fragments, MALDI mass spectrum, 217
Cytochrome (CYP) P450 enzymes, 436
Cytokines, 393
Cytoplasmic membrane (CM), 203
D-amino acids, 437
Data analysis, 257
Databases
Immune Epitope Database, 374
search algorithms, 234
SYFPEITHI, 374
2D DIGE separation, 130
Denaturing methods, 232
Density functional theory (DFT) methods, 151
Deprotonated dimers, DFT calculations, 152
Desorption atmospheric pressure chemical ionization (DAPCI), 20
Desorption electrospray ionization (DESI), 3, 20, 21–24, 156
analytical performance, 23
cold-ion formation, 22
definitions of, 22
detection of proteins, 24
ESI-like spectra, 23
ionization mechanisms, 21–23
ionization source, 21
Mass spectra of bovine serum albumin (BSA), 23
for protein analysis, 23–24
soft ionization method, 21
source, 22
Desorption ionization (DI), 5
Desorption/ionization process from porous silicon (DIOS), 275
Detection limits, current mass spectrometers, 119
Deuterated peptide, tandem MS, 192
2D HILIC-RP LC, 406
Diepoxybutane, 250
Difference gel electrophoresis (DIGE), 109
Diketopiperazine pathway, 49
Dipeptide ions, 152
Dipeptidyl peptidase IV (DPP-4), 261
Direct analysis in real time (DART), 20
Direct detection techniques, 257, 258
Direct ESI-MS analysis, of protein, 267
Direct tissue analysis comparative proteomics using imaging MS, 131–136
biomarker discovery, breast cancer, 131–133
conventional comparative proteomics, 130–131
using imaging mass spectrometry, comparative proteomics, 129–137
Dissociation techniques, 233
Disulfide bond detection, 347
disulfide mapping, 347–350
MS detection, 347
Disulfide mapping, 347–350
Dithiothreitol (DTT), 289
3D microcapillary LC system, 407
DNA molecule, 202, 251
2D PAGE-based quantitation, 108–109
3D quadrupole ion trap schematic cross-sectional view of, 72
Drift cell, 148
Drift tube design, inherent simplicity, 142
Drift tube IM-MS, 143
Drift tube ion mobility (DTIM), 141
electrostatic for, 142
Drift velocity, 148
Drosophila melanogaster, 406
2D RP-RP LC, 406
Drug-based treatment, 158
Drug discovery, 435
affinity selection mass spectrometry (AS-MS), 256–258
noncovalent protein–ligand complexes, 257, 258
challenge for, 255
enzyme activity assays using MS for screening/confirming, 271–276
application of MALDI to high-throughput enzyme assays, 274
continuous flow screening, 272–273
desorption/ionization process off of porous silicon (DIOS) and, 275
immobilized enzyme reactor (IMER), 273–274
MALDI–triple quadrupole mass spectrometry (MALDI-3Q), 276
MS to measure substrate turnover, 272
multicomponent measurements, 272
overcoming low serial throughput by, 276
ratiometric assays using MALDI, 275
self-assembled monolayers for MALDI-MS (SAMDI), 275
gas-phase interactions, 267–271
protein-ligand complexes mass spectrometry-based screening and characterization, 255–277
solution-based AS-MS AS screening technologies, 258–267
automated ligand identification system (ALIS), 259–263
emerging technology, 266–267
frontal affinity chromatography–mass spectrometry (FAC-MS), 265–266
indirect detection AS-MS, 266
speedscreen, 263–264
ultracentrifugation coupled to mass spectrometry, 264–265
Drug metabolism and pharmacokinetics (DMPK) groups, 436
Drug–protein receptor interactions, 159
Drug screening process, 158
2D SCX-RP LC system, 406
DTIM cells, 144
DTIM instruments, 147
Ductal carcinoma in situ (DCIS), 132, 133
Edman degradation, 109, 231, 322, 338, 346, 372
Electron-capture dissociation (ECD), 55, 92, 182, 232, 233, 333, 345, 379, 386
amino acid preferences, 57
CAD method, 55
implementation of, 55
mechanism for, 56
N–Cα bond cleavage, 57
Rydberg state, 55
Electron-detachment dissociation (EDD), 57–59
Electron-ionization dissociation (EID), 57, 58
Electron microscopy, 158
Electron-transfer dissociation (ETD), 57, 58, 182, 192, 222, 233, 290, 333, 379, 386
cold fragmentation, 58
ion–ion interactions, 58
of peptides is a proton-transfer reaction (PTR), 58
reverse, 59
Electron-transfer tandem mass spectrometry, 191
Electrospray spray, 269
Electrospray spray ionization (ESSI), 3, 17–20
gas nebulizer, 19
ion formation, 19
protein–ligand systems, 19
Electrospray-assisted laser desorption ionization (ELDI), 3, 20, 27
human tears, mass spectra of, 28
insulin, disulfide reduction of, 28
ionization process of, 29
liquid, protein analysis, 27–28
reactive, 29–30
solid, protein analysis, 27
Electrospray ionization (ESI), 140, 232
development, 176
principle of, 13
Electrospray ionization, ion-mobility measurements, 157
Electrospray ionization (ESI) technologies, 3
fused-droplet electrospray ionization (FD-ESI), 3
in hybrid qTOF mass spectrometer, 290
mass spectrometric, 129, 405
MS-MS, 192
Orbitrap mass spectrometers, 289
quadrupole ion trap, 289
TWIM-MS/MS, 145
Electrostatic field, 148
Endogenous cell–cell signaling peptides, 393
Endoproteases trypsin, 216
Entrez databases, 237

Enzyme activity assays
using MS for screening/confirming drug candidates, 271–276
application of MALDI to enzyme assays, 274
continuous flow screening, 272–273
desorption/ionization process off of porous silicon (DIOS) and, 275
immobilized enzyme reactor (IMER), 273–274
MALDI–triple quadrupole mass spectrometry (MALDI-3Q), 276
MS to measure substrate turnover, 272
multicomponent measurements, 272
overcoming low serial throughput by, 276
ratiometric assays using MALDI, 275
self-assembled monolayers for MALDI-MS (SAMDI), 275
Enzyme-linked immunosorbent assay (ELISA), 439
ESI experiment, 179 (also see Electrospray ionization)
Estrogen receptor (ER), 203
1-Ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride (EDC), 204
Exchange rate constants, 177
EX2 kinetics, 177
Exponentially modified protein abundance index (emPAI), 119
Extracted ion counting (XIC), 116
Extractive electrospray ionization (ESI), 20
False discovery rates (FDR), 243, 244
FASTA database, 238
Fast atom bombardment (FAB), 4
Fast photochemical oxidation of proteins (FPOP), 197
Fc fusion protein, 288
Fenna–Matthews–Olson (FMO) antenna protein, 203, 204
Field asymmetric waveform ion-mobility (FAIMS) devices, 142, 144
Field desorption (FD), 4
FlashQuant™ system, 276
Fluorescent isotope-coded affinity tag (FCAT), 110
Footprinting methods, 196
Footprinting protein/DNA interactions, 194
Förster resonance energy transfer (FRET), 256
Fourier transform ion cyclotron resonance (FT-ICR), 9, 21, 44, 51, 74, 140, 257
high-energy activation, 66
mass analyzer
Fourier-transform limited mass resolving power of, 75
mass spectrometers, 74, 76
analysis time, 77
principles of, 75
Fragmentation process, 192
Fragment ions, 233
Fragment mass tolerance specification, 241
Free-radical-initiated peptide sequencing (FRIPS), 59
Frontal affinity chromatography–mass spectrometry (FAC-MS), 265
Fused-droplet electrospray ionization (FD-ESI), 24–27
ionization source, 25
for protein analysis, 25–27
Fused-droplet electrospray ionization mass spectrometry (FD-ESI-MS), 25
Gaseous ions, 16
Gas-number density, 149
Gas-phase interactions, 267–271
Gas-phase intermolecular folding forces, 145
Gas-phase kinetics theory, 144
Gas-phase peptide sequencing, 47
Gas velocity, 148
Gaussian shaped peaks, 44
Gel electrophoresis, 194
Gel electrophoresis experiments 1D and 2D, 250
Gel heterogeneities, 108
GEMFILEKGEYPR model, 232
product-ion spectrum, 233
Global-scale proteomics approach, 116
Glu-Fibrinopeptide B, tandem-TOF photodissociation of, 53
Glycans
analytical approaches for separation and analysis, 332
chains, nature of, 329
characterization, 331
classification, 327
heterogeneity, 327–329
modifications, 333
role of, 329
Glycated hemoglobin HbA1C, microwave-assisted enzymatic digestion, 217
Glycine ethyl ester (GEE), 204
Glycoforms, 329
variants, 327
Glycoproteins
analysis of, 327
challenges, 327
comparative MS mapping of, 331
high mannose-type, 328
hybrid-type, 328
in-gel digestion, 219
mapping by LC-ESI and MALDI tandem MS, 329
Mr determination, 329
MS detection, 323–327
oligosaccharide moieties, 216
structural characterization, 329
Glycosylated peptides, 384
Glycosylation, 322–323, 384
site quantitation, 336–338
sites, 329
GPC spin columns, 264
Graphical user interface (GUI), 245
GroEL complex, 14
MS of, 15
Guanidine hydrochloride (GdnHCl), 289
HCK Src Homology 2 (SH2) domains, 268
H/D exchange, 176 (also see hydrogen/deuterium exchange)
HDX approaches, 190 (also see hydrogen/deuterium exchange)
HDX experiments, 177, 178, 193 (also see hydrogen/deuterium exchange)
automated system, 182
drawbacks, 182
HDX extent, 188
HDX kinetics, 178
HDX MS, 176
HDX MSMS, 192
HDX rate constants, change in, 183
HDX technique, functional labeling, 188
Hemoglobin (Hb), 188
Hepatocyte gel, 130
Herceptin, for HER2 receptor treatment, 133
High-abundance proteins, 119
disadvantage, 119
High field asymmetric waveform ion-mobility spectrometry (FAIMS), 141
High-performance liquid chromatography (HPLC), 46, 129, 372
High-resolution image analysis, 131
High-resolution IM measurements, 155
High-throughput screening (HTS), 186, 256, 267
High-throughput screening protocol, 187
His-tagged proteins, 267
Histology-directed approach, 131
Histology-directed protein profiling, 131
Homogeneous time-resolved fluorescence (HTRF), 256
Housekeeping proteins, 102
HPLC gradients, 194
HPLC-MS system, 265
Human epidermal growth factor receptor 2 (HER2), 133
Human estrogen receptor protein, 268
Human telomeric repeat binding factor 2 (hTRF2) interaction, 189
HX-Express programs, 181
Hybrid qTOF mass spectrometer, 290
Hydrogen-bonding network, 176
Hydrogen-deuterium amide exchange
(also see HDX), 176, 223, 270
Hydrophilic interaction chromatography (HILIC)-RP, 406
Hydroxylated drug molecule, 436
Hydroxyl radicals, 196
ICR trap, 74, 76, 78
IDPicker, 243, 244
parsimony analysis, 245
software, 231, 235
IgG1 monoclonal antibody, 294
IL-1β protease inhibitors, 440
structures, 440
Imaging mass spectrometry (IMS), 136
advantage, 134
development, 129
Immobilized enzyme reactor (IMER), 273
Immobilized metal affinity chromatography (IMAC), 382
IM-MS experiment time scale, 149
topical listing, 155
IM-MS separations, advantage, 144
Immune Epitope Database, 374
Immunobiology, 372–374
Immuno-precipitation (IP), 250
IM protein complex, 158
In-cell labeling, 105–107
15N metabolic labeling, 105–106
stable isotope labeling by amino acid (SILAC), 106–107
In-cell quantitative labeling, 107
Infrared laser (IR) MALDI, 269
Infrared multiphoton dissociation (IRMPD), 51
Integral membrane proteins, 260
Intensity fading (IF) MALDI, 269
Interferon (IFN) α-2b, 213
Interleukin-1β (IL-1β) converting enzyme (ICE), 440
Intra-molecular vibrational energy redistribution (IVR), 48
Invasive mammary cancer (IMC), 132
Iodoacetamide, 289
Iodoacetic acid (IAA), 203
Ion dispersion, 69
Ion-evaporation model (IEM), 13
Ion fragmentation, 80
Ionization imaging mass spectrometry (IMS), 7
experimental design for, 7
Ion mobility combined with mass spectrometry (IM-MS), 139, 156
components, 140
block diagram, 141
critical factor, 142
principles and operation, 140
role in, 152
Ion-mobility device, 80, 81
Ion-mobility mass spectrometry (IMS), 269
Ion mobility measurements, 156
Ion movement theory, 147
Ion-neutral collisions, 147
Ion oscillation, 78
Ion packet, 74
Ion peak intensities, 117
Ion trapping, 77
Ion-trapping capability, 69
Iron cations, 382
IR/UV photons, 46
Isobaric interferences, limitation of, 158
Isobaric tags for relative and absolute quantitation (iTRAQ), 113
Isoelectric focusing (IEF) experiments, 250
Isotope-coded affinity tag (ICAT) technology, 110–112
Isotope-coded protein label (ICPL), 110
Isotopic coded affinity tag (ICAT) labeling, 249
Kingdon trap, 77
Kintek QF-3 instrument, 184
KrF excimer laser beam, 197

Label-free methods, 119
Label-free quantification software QuasiTel, 248
L-amino acids, 437
Laser ablation electrospray ionization (LAESI), 20
Laser capture microdissection (LCM), 131
Laser desorption/ionization (LDI) mass spectrometry, 9
Laser-induced liquid bead ion desorption (LILBID), 269
Laser irradiation, 6
Laser spray ionization (LSI), 20
LC-ESI MS, 410
analysis of IL-5Rα tryptic digest, 333
useful for detecting several glycoforms and, 336
LC-MS analysis, 291–293, 298, 299, 303, 305, 309, 312, 322, 350
of recombinant IgG4 Fc fusion protein, 310
LC-MS/MS analysis, 242, 244
for metabolite identification, 437–439
Ligand-dependent nuclear receptor, 182
Limits of detection (LODs), 23
Linear quadrupole ion trap (LIT), 70
ion-trapping device, 71
Linear time-of-flight mass analyzer principles of, 61
schematic of, 63
Liquid chromatography (LC), 140 (also see HPLC)
Liquid chromatography ESI-MS (LC-ESI-MS), 214
applications, 214
Liquid chromatography LC-MS/MS product-ion scan, 69
Liquid chromatography-mass spectrometry, (LC-MS)-based techniques, 256
Local pool error test (LPET), 119
Lock–key and receptor–ligand theories, 255
Lorentz force, 73
Low-density microwave energy, 215
Low-molecular-weight analytes, 266
Low-temperature plasma (LTP), 20
LTQ ion fragmentation, 80
LTQ-Orbitrap XL instrument, 78, 79
Lysine C enzymes, 216

Mac Mini computers cluster, 248
Magnetron frequency, 74
Major histocompatibility complex (MHC), 371
Edman degradation, 372
electrospray ionization and MALDI, development of, 372
mass spectrometry, for mapping MHC peptidomes, 372
peptides bound directly to MHC molecules, 372
sequence of class I and class II MHC peptides, 372
studies, brief history of, 371–372
use of tandem mass spectrometry (MS) to sequence, 372
X-ray crystal structure of MHC complex, 372
Malachite Green (MG) assay, 272
MALDESI source, 29
MALDI mass spectrometry, 129, 131, 219
microwave-assisted ingel digestion, 219
MALDI-TOF mass spectrometry, 183, 289
(see Matrix-Assisted laser desorption ionization) advantage of, 331
analysis of glycopeptides, 331
loss of the trimethylamine group in, 416
utility of, 274
Mascot database searching program, 384, 385
Mascot generic file (MGF) format, 237
structure, product-ion spectrum, 236
Mass accuracy, 45
Mass resolving power (RP), 44
Mass spectra, 195
Mass spectrometry (MS), 43, 129, 214, 288, 372
application to antigenic peptide study, 381–385
in-cell labeling, 105–107
$^{15}$N metabolic labeling, 105–106
stable isotope labeling by amino acid (SILAC), 106–107
label-free quantitation, 116–119
nanostructure-initiator MS(NIMS), 3
protein, history of, 4–5
quantitation via isotopic labeling on peptides, 112–116
absolute quantitation, 114–116
ICAT, 110
isobaric tags for relative and absolute quantitation (iTRAQ), 113
SoPIL, 113–114
quantitation via proteins isotopic labeling, 107–112
2D PAGE-based quantitation, 108–109
proteolytic labeling using $^{18}$O water, 109–110
quantitative labeling by chemical tagging, 110–112
quantitative proteomics, 101–119
sample preparation for, 395, 397
collecting peptide release, 400, 402, 403
direct-tissue profiling, 397–399
extraction-based sample preparation approach, 401
extraction-based strategies, 399–400
POMC, processing of, 396
solid-phase extraction (SPE), 402
stretched sample preparation method for MSimaging, 398
Mass spectrometry-based HDX in practice, 182–193. See also Chemical footprinting
functional labeling, and multiple proteases, 188
HDX and tandem mass spectrometry analysis, 191–192
optimizingHDIX, with high pressure, 192–193
PLIMSTEX, application, in protein–DNA interactions, 189–191
proteinfootprinting via free-radical oxidation, 192–193
Mass spectrometry (MS)-based proteomics, 101
Mass spectrometry imaging (MSI), 399, 411
sample preparation for, 403–405
Mathieu equation, 67
Matrix-assisted laser desorption electrospray ionization (MALDESI), 3
hybrid atmospheric pressure ionization method, 30
for protein analysis, 30
Matrix-assisted laser desorption ionization (MALDI), 3, 214, 232, 322
based screening system, 270
experiments, 179
ionization sensitivity, 6
limitations, 276
structures of, 6
use, 274
Matrix-assisted laser desorption/ionization imaging mass spectrometry (MALDI-IMS), 7
Matrix metalloprotease (MMP3) protein, 266
Maxwellian distribution function, 148
Melanocyte protein Pmel 17, 381
Membrane proteins, 372
Message passing interface (MPI), 214, 248
Metabolic labeling, in-cell labeling, 105
Metabolic pathway, for Z-Val-Ala-Asp-TPP, 444
Metabolite identification, 437–439
Metal-coded affinity tag (MeCAT) approach, 111
Metalloenzymes, 395
Metastable-atom dissociation (MAD), 59
Metastable-atom fragmentation (MAF), 59
Met-enkephalin, 395
Methionine-containing peptides, 198
Methionine (M) oxidation, 321
MHC peptide analysis, 376–381
data analysis, 379
HPLC separation, 377
mass spectrometers, 377–379
MHC peptide analysis (Continued)
proteomics applied to antigenic peptides, 380
sample preparation, 376–377
MHC-peptide complex, 382 (see Major histocompatibility complex)
Michaelis–Menten constants, 272
Microchannel plate (MCP), 61
discharge of electrons, 62
β2-Microglobulin, 192
Microwave-assisted acid hydrolysis (MAAH), 221
applications, 221
uses, 222
Microwave-assisted acid proteolysis, applications, 222
Microwave-assisted enzymatic digestion, 220
Microwave-enhanced approach, 217
Microwave induced organic reaction enhancement (MORE), 214
Microwave technology
protein analysis acceleration, 215–223
Akabori reaction, 215–216
intact proteins, extraction from, 219–220
microwave-assisted proteolysis application using, 220–221
microwave digestion of proteins from, 219
protein characterization by, 216–217
proteins with microwave irradiation, acid hydrolysis, 221–222
temperature and microwave irradiation effects on, 217–218
Mobile proton models, for b/y cleavages, 49
Modeling protocol, 150
Modern quadrupole mass analyzers, 67
Molecular dynamics packages, 151
Molecular operating environment, 150
Monoclonal antibody, 287, 288
Mot1P complex, 250
MS-based assays, 268, 277
MS-based peptidomics, 393
MS-based proteomics, 119
MS-based strategy, for characterization of recombinant proteins, 288
MS ionization efficiency, 117
MS/MS analysis, 233, 250
MS protein characterization, 289, 290
MS² scans, 385
Multidimensional scaling (MDS), 133
Multiple LC-MS/MS experiments, 246
Multiple overlapping fragments, 188
Multiple reaction monitoring (MRM) mode, 70
Multivariate hypergeometric (MVH), 241
score, 243
threshold, 244
Murine class II MHC, 373
family of antigenic peptides, 375
Myoglobin, microwave-assisted enzymatic digestion, 220
MyriMatch database search engine, 231
comparing candidate spectra with experimental spectra and evaluating matches, 240–242
improvements to, 248–249
parallel processing, 248–249
protein modification analysis, 249
selecting candidates from databases, 239–240
spectrum preprocessing, 239
MyriMatch filters, 239
MyriMatch-IDpicker pipeline, applications, 250–251
DNA-protein crosslinks, characterization, 250–251
protein–protein interactions, characterization, 250
yeast proteome on diverse instrument platforms, characterization, 250
MYRIMATCH-ID picker protein identification pipeline, 235–246
MyriMatch database search engine, 239–242
peptide identification reporting, 242–243
post-processing of search results using IDPicker, 243–246
protein sequence databases, 237–239
raw data file formats, 235–237
MyriMatch results file snapshot, 242
MyriMatch semitryptic search times, 249
MyriMatch software, 248
MyriMatch tests, 249
N-Acetylglucosamine (GlcNAc), 328
Naïve protein identification algorithm, 244
Nanoelectrospray ionization (nESI), 14, 324, 325
Nano-ESI techniques, 271
Nanospray-MS methods, 268
Nanostructure initiator mass spectrometry (NIMS), 11
ionization process, 12
nanostructured silicon surface, 11
SEM image of, 12
National Institute of Standards and Technology (NIST), 250
15N-containing peptide, 106
Nd:YAG laser, 52, 269
Neprilysin, 395
N-ethylmaleimide (NEM), 289
Neurolysin, 395
Neuromodulation, 394
Neuropeptides, 393, 394, 403
biosynthesis of, 394
Neuropeptide Y, 395
Neuropeptidomics, 394, 407
N-Glycanase, 331
reaction, 331
N-Glycans, 328
N-Glycosylation, 327, 328
Nicotinoyloxysuccinamide, 110
N-Linked carbohydrate structures, 328
N-Linked deglycosylation, 331
N-Linked glycosylation sites, 294, 298, 299, 301, 328, 331
N-Linked oligosaccharides, 288
NMR spectroscopy, 175, 195, 268, 270
Non-ribosomal peptide synthetase (NRPS), 272
Nucleic acid–based products, 287
Nyquist theorem, 45

O-GlcNAc glycosylated proteins, 327
O-Glycosidase, 288
O-Linked glycosylation sites, 328, 331
O-Linked oligosaccharides, 288
Open reading frames (ORFs), 277
Open-tubular system, 272
Optimized CDK2 ligands, identification, 262
Orbitrap mass analyzer, 45, 439
Orbitrap mass spectrometer, 77
Ovalbumin, 328
Overlapping peptides, deuterium uptake, 190

Oxonium ions, 333
Oxytocin, 394
Parkinson’s disease, 8
 Parsimony, 245
Paul trap, 72
PDB databases, 237
PEGylated protein drugs, 437
Peptidases, 395
Peptide
amino-acid sequence, 242
identification, with database searching, 235
Peptide amide hydrogens
intrinsic exchange rate constant, 179
Peptide and protein analysis
applications, 158–159
bioanalyses, separation selectivity in, 145–147
IM-MS to peptide and protein characterizations, 152
ion structures, fundamental studies, 152–157
protein complex characterization, 157–158
instrumentation, 140–145, 159
ion migration and data dimensionality, 142
ion-mobility–MS/MS, fragmentation, 144–145
ion source selection, fundamental considerations, 141–142
time and space dispersive ion mobility arrangements, 142–144
ion mobility–mass spectrometry, 139–140
structures, characterizing and interpreting, 147–152
calculating collision cross sections, considerations, 148–149
interpretation, computational approaches for, 149–152
ions motion within neutral gases, 147
using ion mobility–mass spectrometry, 139–159
Peptide-bond hydrolysis, 443
Peptide characterization, via mass spectrometry, 407
data analysis
with bioinformatics, 416–419
Peptide characterization (Continued)
qualitative analyses, 407
capillary electrophoresis–mass spectrometry, 410–411
direct analysis, 407–408
hyphenated analysis, 408–409
liquid chromatography–mass spectrometry, 409–410
mass spectrometry imaging, 411–413
relative quantitative analyses, 413–416
Peptide-drug metabolism, 436–437
Peptide identification
with database searching, 234–235
filtering, 244
Peptide-matching score summation (PMSS), 119
Peptide–MHC class II complexes, 384
Peptide-MHC complexes, 382
Peptide-N-glycosidase (PNGase F), 288
PeptideProphet, 244
Peptide-protein assembly, 244–246
Peptides, 372
fragmentation rules, 240
from hemoglobin identification, 189
interpreting spectra, 199
and proteins model
biophysical studies, listing of, 153–154
scores, 241
Peptide-spectrum match (PSM), 247, 248
Peptide tandem mass spectra sequence ions, nomenclature for, 47
Peptidomics, 394
Peroxisome proliferator-activated receptor (PPARγ), 270
P-glycoprotein interaction, 436
Phase II metabolic reactions, 436
Phase I oxidative metabolism, 436
Phosphopeptides, 384
quantitation, 346–347
Phosphorylated peptides, enrichment, 340
chemical tagging methods, 341
hydrophilic interaction chromatography, 341
immobilized metal affinity chromatography, 340
immunopurification (IP), 340
metal oxide affinity chromatography, 340–341
strongcation exchange chromatography, 341
Phosphorylation peptides, neutral phosphoric acid, 70
Phosphorylation
MS detection, 338–339
site identification, 341–346
Photodissociation (PD), 50–55, 71
femtosecond laser-induced dissociation, 54–55
FTICR mass spectrometers, 51
infrared multiphoton dissociation, 51
ion/ion interaction, 50
ultraviolet photodissociation, 51–54
P450 inhibition, 436
PKA enzyme titration, 274
Plasma desorption, 4
Poisson distribution, 197
Polyamino-amine (PAMAM) generation-4 dendrimer, 114
Polycyclic aromatic hydrocarbons (PAHs), 59
Polycyclodimethylsiloxane (PCM-6) ions, 79
Polyethylene glycol (PEG), 437
Polyketide synthase (PKS), 272
Polymorphism of MHCs, 373
Post-source decay (PSD), 45, 65, 333
Post-translational modifications (PTMs), 47, 249, 290, 294, 321, 393, 395
Precursor ion, 46
Precursor-mass tolerance (PMT), 240
Preprohormone, 394, 395
Probability factor, 177
Product-ion spectrum, 195, 239, 382 (also see MS/MS)
in MGF format, structure, 236
representation, 237
for Z-Val-Ala-Asp-TPP, 443
Product-substrate ratio, 273
Prohormone, 395
Proline effect, 49
Proopiomelanocortin hormone, 395
Proopiomelanocortin (POMC), processing of, 396
Protein-affinity column (PAC), 267
Protein analysis, 5
Protein analysis acceleration
microwave technology to, 215–223
Akabori reaction, 215–216
intact proteins extraction from, 219–220
microwave-assisted proteolysis
application using, 220–221
microwave digestion of proteins
from, 219
protein characterization by microwave
irradiation and MS, 216–217
proteins with microwave irradiation,
acid hydrolysis, 221–222
temperature and microwave irradiation
effects on, 217–218
Protein biomarkers, identification, 213
Protein complexes IM studies, listing, 157
Protein–DNA complex, 188, 202
Protein–DNA interactions, 188
Protein drugs, 437
Protein-expression analysis, 118
Protein GPR128, 385
Protein identification report, 247
Protein kinase A (PKA), 274
Protein-labeling strategy, 110
Protein-ligand binding, 175
Protein-ligand complexes, 179, 257, 260, 266
dissociation, 267
HDX, determination procedure for, 180
mass spectrometry-based screening and
characterization, 255–277
separation, 263, 266
stability, 257
structure, 205
Protein–protein complexes
applications for, 269
Proteins
digestion efficiency, 222
identification, 102, 213
laser-based ionization methods
atmospheric pressure matrix-assisted
desorption/ionization (AP-MALDI), 8–9
matrix-assisted laser desorption/
ionization (MALDI), 5–8
nanostructure initiator mass
spectrometry (NIMS), 11–12
surface-enhanced laser desorption/
ionization (SELDI), 9–11
mass spectrometry (MS), history of, 4–5
microwave-assisted enzymatic
digestion, 220
microwave irradiation, 217
spray-based ionization methods
electrospray ionization (ESI), 13–14
sonic spray ionization (SSI), 14–17
Proteins enrichment. See Phosphorylated
peptides, enrichment
Protein sequence databases, 238
Protein tumor necrosis factor alpha
(TNF-alpha), 214
Proteolytic cleavage, 437
Proteolytic labeling, using 18O water,
109–110
Proteome, drug-induced changes in, 135
Proteomics, 393
Proteotryptic peptides, 116
Proton-transfer reaction (PTR), 58
PTM analysis of proteins, 322, 327

mass resolving power, 44
quadrupole mass analyzer, 66–69
scan speed, 45–46
tandem MS analysis, 46
time-of-flight mass analyzer, 60–66
triple-quadrupole mass spectrometers,
69–73
orbitrap, 77–80
radical-induced fragmentation
methods, 59
tandem MS analysis, 46
fragmentation, 46–48

Protein–protein complexes
applications for, 269

Proteins
digestion efficiency, 222
identification, 102, 213
laser-based ionization methods
atmospheric pressure matrix-assisted
desorption/ionization (AP-MALDI), 8–9
matrix-assisted laser desorption/
ionization (MALDI), 5–8
nanostructure initiator mass
spectrometry (NIMS), 11–12
surface-enhanced laser desorption/
ionization (SELDI), 9–11
mass spectrometry (MS), history of, 4–5
microwave-assisted enzymatic
digestion, 220
microwave irradiation, 217
spray-based ionization methods
electrospray ionization (ESI), 13–14
sonic spray ionization (SSI), 14–17
Proteins enrichment. See Phosphorylated
peptides, enrichment
Protein sequence databases, 238
Protein tumor necrosis factor alpha
(TNF-alpha), 214
Proteolytic cleavage, 437
Proteolytic labeling, using 18O water,
109–110
Proteome, drug-induced changes in, 135
Proteomics, 393
Proteotryptic peptides, 116
Proton-transfer reaction (PTR), 58
PTM analysis of proteins, 322, 327

mass resolving power, 44
quadrupole mass analyzer, 66–69
scan speed, 45–46
tandem MS analysis, 46
time-of-flight mass analyzer, 60–66
triple-quadrupole mass spectrometers,
69–73
orbitrap, 77–80
radical-induced fragmentation
methods, 59
tandem MS analysis, 46
fragmentation, 46–48

Protein–protein complexes
applications for, 269
Pulsed Q dissociation (PQD) scheme, 71
Pulsed ultrafiltration-MS (PUF-MS), 264
Pump/probe experiment, 197
PVDF membranes, 216

Q peptides concatenations (QCAT), 115
Q-TOF instruments, 240
Quadro-logarithmic distribution, 78
Quadrupole, in a/q space
  stability diagram of, 68
Quadrupole ion trap (QIT) mass
  spectrometer, 44, 72
Quadrupole-linear ion trap (QTRAP) mass
  spectrometers, 438
Quadrupole mass analyzer
  cylindrical rods, schematic of, 66
  principles of, 68
Quadrupole mass filter (QMF), 66
  collision cell setup, 76
Quadrupole time-of-flight (Q-TOF) mass
  spectrometers, 21, 257, 439
Quantitation in drug metabolism
  studies, 439
Quantitation technique, 102, 116
Quantitative determination, of larger
  molecular weight peptides, 439
Quantitative labeling methods, 105
Quantitative MS-based proteomics, 102
Quantitative proteomics, 101–119
  approach, 105, 119
  implementation, 102
Quantum theory, 151
Quenched protein, 183
Quench-flow labeled peptic peptide
  isotopic distribution, 185
Quenching process, 178

Radio-chemical detectors, 439
Radiochromatogram
  for Z-Val-Ala-ASP-TPP, 443, 444
RAW files, binary data in, 235
Recombinant DNA technology, 213, 214,
  216, 287
Recombinant hormones, 287
Recombinant human insulin, 287
Recombinant human interferon α-2b
  (rh-IFN- α-2b), 216
Recombinant IgG4 Fc fusion protein, 292,
  294
analytical RP-HPLC chromatograms, 295
deconvoluted ESI mass spectra, 292, 293
identification of a pyruvic acid
  modification, 295
LC-MS analysis, 310
LC-MS glycosylation profiling, 29, 294
LC-MS TICs of tryptic digest of, 296
LC-UV chromatographic profiles, 314
mechanism of reaction of pyruvic acid
  with N-terminus of, 297
produced using an NS0 cell line, 312
product comparability assessment,
  311–313
Recombinant proteins, 287
Recombinant therapeutic proteins, 288
Recombinant vaccines, 287
RefSeq databases, 237
Reversed-phase (RP) capillary LC, 405 (also
  see HPLC)
Rifampin (RIF), 135

SCX chromatography, 250 (also see strong
  cation exchange)
SCX column, 406
SCX-RP in peptidomic studies, 406
SDS PAGE analysis, 322
SDS-PAGE gels, 219
Selected reaction monitoring (SRM), 70, 272
Self-assembled monolayer (SAM), 50
Self-assembled monolayers for MALDI-MS
  (SAMDI), 275
Separation methods, 405–407
Sequest and Mascot limit fragment, 241
Shared peak count (SPC) reports, 240
Shotgun proteomics study, results, 246–248
Side-chain fragment ions, 47
Sieber amide polymer matrix, 112
Signal-to-noise ratios (S/N), 221
Single-point analysis, 186
Size-exclusion chromatography (SEC), 259,
  268
Slope sigmoidal dose–response curve, 261
Small-molecule labeling, 103
  isotope incorporation, 103
  purification mechanisms, 103
Soft ionization technique, 269, 271
Solid-phase based peptide synthesis, 114
Solid-phase extraction (SPE), 276
Solid-phase reagent, 112
Solution-based AS-MS AS screening technologies, 258–267
automated ligand identification system (ALIS), 259–263
emerging technology
proton affinity column (PAC)—SPE-LC-MS platform, 266–267
two-dimensional turbulent flow chromatography—LC-MS platform, 266
frontal affinity chromatography—mass spectrometry (FAC-MS), 265–266
indirect detection AS-MS, 266
speedscreen, 263–264
ultracentrifugation coupled to mass spectrometry, 264–265
Solution-phase hydroxyl radicals, 195
Solution-phase oxidized peptide, tandem MS spectra, 196
Somatostatin, 395
Sonic spray ionization (SSI), 3, 14
analysis of, 17
by ESI, 16
fused-silica capillary, 14
ion formation, mechanism of, 15
typical schematic of, 16
SoPIL, approach to quantitative proteomics, 113–114
Space-charge effects, 69
Spectral counting method. See also Spectrum sampling (SpS) method
advantage, 118
Spectrum sampling (SpS) method, 118
SpeedScreen technology, basic principles, 263
SPE-LC systems, 267
S-Pro system, idealized SUPREX curves, 187
Stability of proteins from rates of oxidation (SPROX), 198
Stability of unpurified proteins from rates of H/D exchange (SUPREX), 184
curve, 186
Stable isotope dilution method, 114
Stable isotope labeling by amino acid (SILAC), 106–107
advantage, 107
media designed for, 106
Stable isotope labeling in plants (SILIP), 106
Stable isotope standard with capture by antipeptide antibodies (SISCAPA), 116
Standard gel electrophoresis, 129
STEM imaging, 203
Strong cation exchange (SCX) chromatography, 250, 406
Substrate-to-product ratios, 275
SUPREX approach, to screening of protein ligands, 184–187, 270
Surface-enhanced affinity capture (SEAC), 9
Surface-enhanced laser desorption/ionization (SELDI), 3, 9
ProteinChip® System, 10
TOF-MS, 10
Surface-enhanced neat desorption (SEND), 9
Surface-enhanced photolabile attachment and release (SEPAR), 9
Surface induced dissociation (SID), 50, 144, 233
Sustained offresonance irradiation (SORI), 76
Swiss-Prot databases, 237
Synchrotron-generated oxidation, 196
Tandem mass spectrometry, 194, 214, 231–233
peptide fragmentation, 232–233
protein sequencing, 231–232
Tandem mass tags (TMT), 113
Tandem TOF instrument schematic of, 65
Target proteins, 89–99
bottom-up proteomics, 90
GeLC-MS/MS, 93–94
peptide mass fingerprinting (PMF), 91
shotgun digests, 94–96
mass spectral approaches, 89–90
next-generation approaches, 98–99
top-down approaches, 96–98
T cells, 383
assay, 381
mediated adaptive immunity, 371
Temperature IM-TOFMS, 159
Temperature protocols, 151
TFTICR mass spectrometer, 232
T glycopeptide, 333
Therapeutic monoclonal antibodies, 288
<table>
<thead>
<tr>
<th>Term</th>
<th>Page(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ThermoLCQDeca ion trap mass spectrometer</td>
<td>382</td>
</tr>
<tr>
<td>Thermospray ionization (TSI)</td>
<td>6</td>
</tr>
<tr>
<td>TIC of tryptic digest of the Fc fusion protein</td>
<td>333 (also see total ion current)</td>
</tr>
<tr>
<td>Time-of-flight (TOF)</td>
<td>6</td>
</tr>
<tr>
<td>delayed extraction (DE) scheme</td>
<td>62</td>
</tr>
<tr>
<td>mass analyzers</td>
<td>6</td>
</tr>
<tr>
<td>mass resolving power of</td>
<td>62</td>
</tr>
<tr>
<td>orthogonal TOF (oTOF)</td>
<td>64</td>
</tr>
<tr>
<td>schematic of reflectron</td>
<td>64</td>
</tr>
<tr>
<td>secondary emission multiplier (SEM)</td>
<td>61</td>
</tr>
<tr>
<td>Time-of-flight (TOF) analyzer</td>
<td>64</td>
</tr>
<tr>
<td>Time-to-digital converter (TDC)</td>
<td>62</td>
</tr>
<tr>
<td>TOF-TOF mass spectrometer</td>
<td>6</td>
</tr>
<tr>
<td>Total ion current (TIC)</td>
<td>239</td>
</tr>
<tr>
<td>Trans-Golgi network</td>
<td>395</td>
</tr>
<tr>
<td>Traveling wave ion mobility (TWIM)</td>
<td>141, 142</td>
</tr>
<tr>
<td>TrEMBL databases</td>
<td>237</td>
</tr>
<tr>
<td>Trifluoric acetic acid (TFA)</td>
<td>114</td>
</tr>
<tr>
<td>Trimethylammonium butyrate (TMAB)</td>
<td>418</td>
</tr>
<tr>
<td>Tripeptide Z-Val-Ala-Asp-TPP</td>
<td>441</td>
</tr>
<tr>
<td>IV/PO PK profiles</td>
<td>441</td>
</tr>
<tr>
<td>Triple quadrupole mass spectrometer</td>
<td>69</td>
</tr>
<tr>
<td>Triple quadrupole MS (MALDI-3Q)</td>
<td>276</td>
</tr>
<tr>
<td>tris(2-carboxyethyl)phosphine (TCEP)</td>
<td>289</td>
</tr>
<tr>
<td>Trypsin-immobilized magnetic nanoparticles (TIMNs)</td>
<td>220</td>
</tr>
<tr>
<td>applications</td>
<td></td>
</tr>
<tr>
<td>Tandem mass spectrometry (MS/MS)</td>
<td>289</td>
</tr>
<tr>
<td>Two-dimensional polyacrylamide gel electrophoresis (2D PAGE)</td>
<td>108–109</td>
</tr>
<tr>
<td>drawbacks</td>
<td>108</td>
</tr>
<tr>
<td>workflow for</td>
<td></td>
</tr>
<tr>
<td>Type 1 diabetes mellitus (T1DM)</td>
<td>382, 383</td>
</tr>
<tr>
<td>Ultra performance liquid chromatography (UPLC) mass spectrometry</td>
<td>192</td>
</tr>
<tr>
<td>advantage</td>
<td>193</td>
</tr>
<tr>
<td>utility</td>
<td>193</td>
</tr>
<tr>
<td>Ultraviolet-laser desorption (UVLD)</td>
<td>5</td>
</tr>
<tr>
<td>Ultraviolet-laser matrix-assisted laser desorption ionization (UVMALDI)</td>
<td>5</td>
</tr>
<tr>
<td>UniProt databases</td>
<td>238</td>
</tr>
<tr>
<td>UniProtKB databases</td>
<td>238</td>
</tr>
<tr>
<td>UV absorber semiconductor</td>
<td>11</td>
</tr>
<tr>
<td>UV detectors</td>
<td>260, 264</td>
</tr>
<tr>
<td>UV-MALDI</td>
<td>269</td>
</tr>
<tr>
<td>UVPD spectrum</td>
<td>53</td>
</tr>
<tr>
<td>Vacuum ultraviolet (VUV)</td>
<td>51</td>
</tr>
<tr>
<td>Vasopressin</td>
<td>394</td>
</tr>
<tr>
<td>4-Vinylpyridine</td>
<td>289</td>
</tr>
<tr>
<td>Worldwide Protein Databank (wwPDB) project</td>
<td>151</td>
</tr>
<tr>
<td>X-ray crystallography</td>
<td>139, 158, 175, 205, 270</td>
</tr>
<tr>
<td>X-ray crystal structure</td>
<td>182</td>
</tr>
<tr>
<td>X-ray exposure time</td>
<td>196</td>
</tr>
<tr>
<td>YGGFLR, ESI-MS/MS spectra of</td>
<td>52</td>
</tr>
<tr>
<td>Zinc fingers</td>
<td>203</td>
</tr>
<tr>
<td>Z-Val-Ala-Asp-TPP</td>
<td></td>
</tr>
<tr>
<td>metabolic pathway</td>
<td>444</td>
</tr>
<tr>
<td>radiochromatogram</td>
<td>444</td>
</tr>
<tr>
<td>Z-Val-ASP-DPP dipeptides</td>
<td>440</td>
</tr>
<tr>
<td>Z-Val-Asp-TPP dipeptides</td>
<td>440</td>
</tr>
</tbody>
</table>