

Index

a

- accuri cytometers 63
- acquired immunodeficiency syndrome (AIDS) 58, 62, 212
- antibiotic resistance 177–178
- antibiotic susceptibility testing (AST)
 - conventional methods 178
 - integrated microfluidic based approach 181
 - advantages 179, 180
 - bead rotation biosensor 179
 - detecting devices 180
 - electrochemical sensors 179
 - limitations 182
 - multiplexing capabilities 179
 - pH sensor 179
 - surface-plasmon resonance-based biosensor platforms 179
 - limitations, current method 178
 - PD modeling
 - advantages of microfluidic based approaches for 185
 - bacterial killing rate constant 187
 - Hill modeling 186
 - MIC and Hill coefficient determination, monomicrobial culture 191
 - MIC and Hill coefficient determination, polymicrobial culture 191, 192
 - monomicrobial cultures, *E.coli* against amikacin 188
 - polymicrobial, *E.coli* against amikacin 189
 - significance 184, 185
 - PK modeling
 - advantages of microfluidic based approaches for 185
 - amikacin, blood 192
 - for monomicrobial cultures 193
 - parameters in 192, 193
 - PD modeling comparison 192
 - significance 184, 185
 - tobramycin, blood 192, 194
 - translation of microfluidic based approach
 - blood samples 183
 - infrastructure requirements 183
 - minimum inhibitory concentration (MIC) 183
 - PK/PD modeling 183
 - sample preparation 183
 - sensitivity 182
 - susceptibility testing 182
- atherosclerosis 213, 214

b

- benchtop analytic cytometers 63
- bioelectronic interfaces
 - coupling regimes 131
 - equivalent circuit model 130
 - extra-cellular coupling
 - advantages 133
 - disadvantages 133
 - field effect transistors (FETs) 132
 - multielectrode arrays (MEAs) 132
 - extra-cellular nanoscale interface
 - advantages 133
 - flexible silicon electronics 134
 - free-floating electrodes 132, 134
 - future of 138, 139
 - goal 130
 - in-cell coupling 137, 138
 - intra-cellular coupling 134
 - intra-cellular nanoscale interfaces
 - advantage 136
 - intra-cellular coupling configuration 135
 - nanofabricated electrodes 136, 137
 - nanostraws 135

- biofilms 119
- BioFlux system 119, 120
- blood 8, 9
- bone marrow 9, 10
- bone outgrowth endothelial cells (BOECs) 216
- bovine pulmonary artery endothelial cells (BPAEC) 94
- Boyden chamber 105
- Braille display microfluidics 119, 121
- c**
- Caenorhabditis elegans*
 - future applications 256
 - multi trap microfluidics
 - – parallel processing 262–264
 - – serial processing 264–266
 - – single layer 262
 - roundworm 245
 - single trap microfluidics 259
 - – axonal regrowth, microfluidic chip 260
 - – double layers device 259
 - – immobilization methods 258
 - – laser axotomy chip for imaging 259
 - – laser nanoaxotomy platform 261
 - – “one-by-one” approach 258
 - – single-layer device 258
 - versatile animal model
 - – COPAS Biosort system 250
 - – culturing techniques 247
 - – drug screening model 249
 - – flatbed scanners 251
 - – high-throughput optical sorting systems 249
 - – neurological disease 247–249
 - – novel automation and image techniques 251
- Campanot chamber 221
- cancer
 - cerebrospinal fluid 10–11
 - CTCs 15–16
 - drug delivery and pharmacokinetics 236–237
 - in vitro models 231
 - liver 225, 226
 - metastasis 232–236
 - microfluidics 120
 - microscale tumor spheroid models 231–232
 - mortality 230
 - mouse models 231
 - single-cell genomics 30
 - solid clinical sample 4–8
 - surface treatment 19
- cell enrichment
 - acoustophoresis 21
 - – acoustic wave 21, 22
 - – interdigital transducers (IDT) 22
 - CellSearch system 15, 16
 - density gradient centrifugation 13
 - electrophoresis
 - – dielectric properties 20
 - – dielectrophoresis (DEP) 20, 21
 - – direct current (DC)/alternating current (AC) 20
 - – electrical field 20
 - – head and neck squamous cell carcinoma (HNSCC) 20
 - – LMP agarose hydrogel 20
 - filtration
 - – antibodies 17
 - – micro-pillars as sieve 16, 17
 - – polydimethylsiloxane (PDMS) 17
 - fluorescence activated cell sorting (FACS) 13, 14
 - hydrodynamics
 - – antibodies 18
 - – dean flow fractionation 18
 - – deterministic lateral displacement (DLD) 17, 18
 - – inertial focusing 17, 18
 - laser capture microdissection (LCM) 12
 - magnetic activated cell sorting (MACS) 14, 15
 - magnetophoresis 19
 - microfabrication techniques 16
 - nanoscale techniques 16
 - optical tweezers/traps 21, 22
 - surface treatments 19
- cell penetrating peptides (CPPs) 147
- cell reprogramming 143, 162, 164–166, 169
- CellSearch system
 - cytokeratin 16
 - epithelial mesenchymal transition (EMT) 16
 - isolation of CTCs 15
- CellSqueeze technology 165–167
- cellular immunophenotyping
 - functional phenotyping, *see* functional phenotyping
 - immune status
 - – clinical studies 59
 - – evaluation of 59
 - – external factors 57
 - – surface markers 58
 - surface marker phenotyping, *see* surface marker phenotyping

cerebrospinal fluid 10
 chimeric antigen receptor (CAR) 80
 circulating tumor cells (CTCs) 9
 citrate phosphate dextrose adenine (CPDA) 9
 clinical samples
 – liquid samples, *see* liquid clinical samples
 – solid samples, *see* solid clinical samples
 commercial flow cytometers 62, 63
 CompuCyte iGeneration® 64
 COPAS Biosort system 250, 257, 264, 265

d

dean flow fractionation 18
 density gradient centrifugation 13
 dielectrophoresis (p-DEP) microwell array
 – advantages 89
 – immune-cell cytotoxicity 88, 89
 – tumor-cell endothelial cell interaction
 – – HUVECs 87, 88
 – – vascular endothelial growth factor (VEGF) 87
 digital MDA 35
 direct RNA sequencing (DRS) 39

e

electro-cortical encephalography (ECoG)
 132, 134
 electroporation 144, 145, 147, 165, 168, 171
 ELISpot technologies 66
 endosome escape 144
 endothelial cell activation 107
 epifluorescence-based imaging cytometry 64
 epithelial mesenchymal transition (EMT) 16
 EuroFlow Consortium 64

f

FACS, *see* fluorescence activated cell sorting (FACS)
 Fahraeus effect 107
 Fahraeus–Lindqvist effect 107
 Fahraeus–Lindqvist effect 205
 field effect transistors (FETs) 132
 flow cytometry 60
 – commercial flow cytometers 62, 63
 – fluorescence-based flow cytometric analysis 62
 – future developments 64
 – high-content imaging cytometry 63
 – limitations
 – – antibody, choice of 64, 65
 – – lack of standardization 64
 – – optical spillover 64
 – – time and investment 65
 – multicolor flow cytometry 60–62

fluorescence activated cell sorting (FACS)
 13–15, 62
 fluorescence imaging technology 46
 fluorescence in situ hybridization (FISH) 30
 fluorescence-based flow cytometric analysis 62
 FLUOROSpot™ 66
 free-floating electrodes 132, 134
 functional phenotyping
 – ELISpot technologies 66–67
 – emerging single cell technologies 68–70
 – – multiplexed immunoassays 67–68
 fused deposition modeling (FDM) 111

h

hematopoiesis 9
 hemolytic uremic syndrome (HUS) 117
 high-content imaging cytometry 63
 human immunodeficiency virus (HIV) 119
 human leukocyte differentiation antigens (HLDA) 60
 human umbilical vein endothelial cells (HUVECs) 216
 Huntington's disease 247, 248
 hydroxyurea 118
 hyperbranched rolling circle amplification (HRCAs) 32

i

immune phenotypes 57, 59
 immunophenotyping, *see* cellular immunophenotyping
 in-cell coupling 137, 138
 induced pluripotent stem cells (iPSCs) 164
 intercellular communication
 – *in vivo* and *in vitro* studies 76
 – biofilms 76
 – transplantation 75
 – tumors, treatment of 76
 – vaccines 75
 intra-cellular coupling 134
 intracellular delivery, macromolecules
 – delivery efficiency, defining 171
 – *in vitro* and *in vivo* applications 145
 – applicability across cell types 158, 161
 – – murine embryonic stem cells (mESCs) 159
 – autofluorescence in immune cells 171, 173
 – cell penetrating peptides (CPPs) 143
 – cell types 144, 145, 161, 162
 – cytosolic delivery diffusion 151
 – – bidirectional transport 153
 – – dextran delivery 153, 155
 – – efficiency 153, 154

- intracellular delivery, macromolecules (*contd.*)
 - endocytotic method 151
 - kinetics 153
 - modeling diffusion 153, 155, 156
 - SEM imaging, membrane disruptions 157, 158
 - TEM imaging, membrane disruptions 158, 159
 - cytosolic delivery diffusion 152
 - delivery concept
 - cell speed 150
 - constriction dimensions 150
 - design 148, 149
 - holes 148
 - multiple delivery cycles 151
 - number of constrictions 150
 - delivery efficiency 172
 - design parameters 169, 170
 - device design guidelines 169 170
 - device nomenclature 170
 - device recovery 171
 - electroporation 144
 - advantages 144
 - electrical fields 144
 - endocytotic delivery 143
 - in vitro and in vivo applications 147
 - membrane poration 143
 - microfluidic platform 143
 - microinjection 144
 - nanomaterial and antibody delivery 162, 164
 - reagent use 171
 - research and clinical applications
 - cell reprogramming 164, 166
 - immune cell function 166
 - quantum dot delivery 166, 167
 - scrape loading method 145
 - shear-based method 145
 - sonoporation 144
 - target materials 146
 - therapeutic and research applications 143
 - viral vectors 144
 - iPSCs, *see* induced pluripotent stem cells (iPSCs)
- k**
- Klebsiella infections 177
- l**
- lab-on-a-chip, *see* micro total analysis systems (mTAS)
 - laminar flow (FLO) 110, 214, 229, 253, 254, 257
 - laser capture microdissection (LCM) 12
 - laser scanning imaging-based high-content imaging cytometry 64
 - laser-guided cell micropatterning (LGCM) 91
 - light emitting diodes (LEDs) 134
 - liquid clinical samples
 - blood 9
 - eosinophils and basophils 9
 - lymphocytes 9
 - neutrophils and monocytes 8
 - platelets 8
 - red blood cell (RBC) 8
 - white blood cells (WBCs) 8
 - bone marrow
 - red marrow 9
 - yellow marrow 9
 - cerebrospinal fluid 10
 - placental or umbilical cord blood 10
 - processing 12
 - saliva 11
 - urine 10
- m**
- magnetic activated cell sorting (MACS) 14, 15
 - malaria 212
 - MALBAC, *see* multiple annealing and looping-based amplification cycles (MALBAC)
 - MDA, *see* multiple displacement amplification (MDA)
 - MEF, *see* mouse embryonic fibroblast (MEF)
 - mESCs, *see* mouse embryonic stem cell (mESCs)
 - MIC, *see* minimum inhibitory concentration (MIC)
 - micro total analysis systems (mTAS) 105
 - micro-angiopathy 106
 - micro-stereolithography (μ SL) 111
 - microengraving 81
 - microfluidic hydrodynamic trapping
 - advantages 91
 - cell-cell fusion 90
 - cell-cell fusion 90
 - intercellular communication via gap junctions 89, 90
 - sequential hydrodynamic trapping device 89
 - microfluidics
 - advantages 120
 - design and applications
 - *ex vivo* autoperfusion chamber 112
 - differential properties, analyzing 112

- geographic information system (GIS) 113
 - hamster cremaster microvascular network 113
 - parallel channels 112
 - platelet adhesion 112, 113
 - vascularization 112
 - device fabrication
 - microfluidic chips 252
 - PDMS 252
 - reactive ion etching (RIE) tools 251
 - soft-lithography 252
 - disadvantages 122
 - disease specific applications 115
 - antiplatelet therapies 115
 - flowing sickle cell blood 118
 - hemolytic uremic syndrome (HUS) 117
 - high-throughput viability screening 119
 - hydroxyurea 118
 - PDMS based device 117
 - sickling of red blood cells (RBCs) 118
 - TNF- α 117
 - transthrombus pressure gradient 117
 - fabrication
 - 3D printing methods 111
 - AutoCAD software 110
 - bilayer assembly 110
 - biomaterials 110
 - bioprinting 110
 - laminar flow (FLO) 110
 - photolithographic photoresist 110, 111
 - photoresist SU8 110
 - rounded master molds 111
 - sacrificial molding 110
 - flow control and valve multiplexing 255–257
 - fluid dynamics modeling
 - circular tubing connections 253
 - COMSOL or Fluent software 254
 - fluidic circuit 252, 253
 - laminar flow 254
 - rectangular cross-sections 253
 - Reynolds number 254
 - multiwell plates, interfacing with 255, 256
 - microinjection 144, 147
 - microraft array (MRA) 84
 - microsystem models, of pathophysiology
 - cancer, *see* cancer
 - organ-specific pathologies, *see* organ-specific pathologies
 - vascular and hematologic pathologies, *see* vascular and hematologic pathologies
 - microvascular disease
 - blood flow
 - blood rheological factors 107
 - cellular factors 107
 - vascular factors 107
 - endothelial cell activation 107
 - macro-modeling
 - *in vitro* models 108
 - *in vivo* data 108
 - endothelial wall and erythrocytes interactions 107
 - limitations 108
 - parallel plate-flow chambers (PPFCs) 108, 109
 - tissue engineering 108
 - micro-modeling, *see* micro-fluidics
 - microvasculature 106
 - microvasculature dysfunction 106
 - microwell arrays
 - advantages 87
 - limitations 87
 - microengraving 81
 - NK-cell cytotoxicity 83, 84
 - RNA-seq, microfluidics 85
 - single-cell barcode chip (SCBC) 85
 - EGF Receptor VIII cells 85
 - glioblastoma (GBM) cells 86
 - U87PTEN cells 86
 - stem cell co-culture array 84
 - T-cell cytotoxicity 82–84
 - T-cell proliferation 82
 - minimum inhibitory concentration (MIC) 203
 - mouse embryonic fibroblast (MEF) 89
 - mouse embryonic stem cell (mESCs) 89
 - MRA, *see* microraft array (MRA)
 - mTAS, *see* micro total analysis systems (mTAS)
 - multicolor flow cytometry 60–62
 - multielectrode arrays (MEAs) 132
 - multiple annealing and looping-based amplification cycles (MALBAC) 34
 - multiple displacement amplification (MDA) 31, 34
 - multiplexed immunoassays 67–68
- n**
- nanofabricated electrodes 136, 137
 - nanoparticle vectors 144
 - nanostraws 135
 - Navier–Stokes equations 253
 - neural dust, *see* free-floating electrodes
 - neurons 29
 - next-generation sequencers 48
 - non-steroid anti-inflammatory drugs (NSAIDs) 222

o

- optical tweezers 91
- organ specific pathologies
 - challenges
 - chemical microenvironment and signaling 228, 229
 - scaling 227, 228
 - opportunities
 - patient specific chips 230
 - regenerative medicine 230
- organ-specific pathologies
 - brain
 - brain-on-a-chip model 220
 - Campenot chamber 221
 - scaling of 220
 - stroke 221
 - challenges
 - chemical microenvironment and signaling 228, 229
 - scaling 227, 228
 - kidney 222, 223
 - liver
 - hepatitis 225
 - liver fibrosis 224
 - liver on a chip microsystem 225
 - liver transplantation 225
 - MEMS-based assay 224
 - sol-gel thin film assay 224
 - lung 218, 219
 - opportunities
 - patient specific chips 230
 - regenerative medicine 230

p

- parallel plate-flow chambers (PPFCs) 108, 109
- placental or umbilical cord blood 10
- planar patch technology 135
- plate-flow chambers (PPFCs) 108
- polydimethylsiloxane (PDMS) 81, 134
- polyfunctionality 67
- polymethyl methacrylate (PMMA) 81
- population delivery chip 265
- primer extension pre-amplification (PEP) 31

q

- quantum dots 143, 144, 146, 166–169, 173

r

- reverse transcription quantitative PCR (RT-qPCR) 39
- Reynolds number 110, 254
- RNA-Seq 40
- rolling circle amplification (RCA) 32

s

- saliva 11
- SCBC, *see* single-cell barcode chip (SCBC)
- self-assembled monolayers (SAMs) 110
- sickle cell disease 208
- single cell analysis
 - acoustic methods 96
 - advantages 97
 - tilted-angle standing surface acoustic waves (taSSAW) 96
 - ultrasonic method, in microwell arrays 96
 - ultrasonic standing waves (USW) 95
 - advantages
 - cancer treatments 80
 - cellular heterogeneity 80
 - circulating tumor cells (CTCs) 30
 - DEP arrays, *see* dielectrophoresis (p-DEP) microwell arrays
 - future
 - clinical applications of microfluids 48
 - hurdles 47
 - microfluidics expansion 46
 - scalability, using microfluidics 45
 - human microbiome 29
 - magnetic methods 95
 - drawback 94
 - magnetic microflaps 94
 - magnetic pattern arrays 94
 - microwell arrays, *see* microwell arrays
 - optical methods
 - laser-guided cell micropatterning (LGCM) 91, 92
 - limitations 93
 - optical tweezers 93
 - optoelectronic tweezers 92, 93
 - sperm 30
 - stochastic gene expression 29
- single cell genomics
 - approaches
 - hyperbranched rolling circle (HRCA) 32
 - multiple annealing and looping-based amplification cycles (MALBAC) 34
 - multiple displacement amplification (MDA) 31, 34
 - polymerase chain reaction (PCR) 31
 - RNA-FISH 42
 - super resolution barcoding 42
 - Taq DNA polymerase 31
 - microfluidics 34
 - digital MDA 35
 - microliter chambers 35
 - nanoliter chambers 35
 - technical challenges

- – contamination 31
- – fluorescence activated cell sorting (FACS) 31
- – fluorescence in situ hybridization (FISH) 30
- – laser capture microdissection (LCM) 31
- – limiting dilution 31
- – microfluidic capture 31
- – micropipetting 31
- – mouth-pipetting 31
- – multiplexing problem 30
- – optical tweezers 31
- – whole genome amplification (WGA) 30
- single cell tagged reverse transcriptase (STRT) 41
- single cell transcriptome
 - approaches
 - cDNA microarrays 39, 40
 - cell expression by linear amplification and sequencing (CEL-Seq) 41
 - reverse transcription quantitative PCR (RT-qPCR) 39, 40
 - RNA-Seq 41
 - Smart-Seq 41
 - SOLiD NGS system 40
 - switch mechanism at 5'-end of RNA template (SMART) 40
 - template switching 40
- microfluidics
 - 96 cell-capture sites 44
 - BioMark™ system 44
 - cell digital PCR (dPCR) 44
 - droplet systems 44
 - magnetic oligo(dT) beads 43
 - microwell, cell trapping 43
 - microwell, cell trapping 43
 - RT-qPCR device 44
- technical challenges
 - amplification-based methods 38
 - contamination 38
 - direct RNA sequencing (DRS) 39
 - FACS 38
 - LCM 38
 - single cell isolation 38
- single worm trapping 258, 259
- single-cell barcode chip (SCBC) 85, 86
- soft-lithography 252
- solid clinical samples
 - animals, tissue samples 5
 - biopsies 4
 - cellular subtypes
 - antigen presenting cells (APCs) 7
 - blood vessels 7
 - epithelial cells 5–7
 - fibroblasts 7
 - processing 11, 12
 - xenograft transplant of human cancer cells 5
- spectral overlap 42, 62, 64
- spikes, 129, *see* action potentials
- STRT, *see* single cell tagged reverse transcriptase (STRT)
- surface marker phenotyping, *see* flow cytometry
- swine influenza virus 119
- switch mechanism at 5'-end of RNA template (SMART) 40
- t**
- 3D inkjet printing 111
- thrombosis 205
- transmission electron microscopy (TEM) 135
- transwell assay 105
- 2D diffusion model 153
- two-photon polymerization (TPP) 111
- u**
- urine 10
- v**
- vascular and hematologic pathologies
 - arterial tree 205
 - atherosclerosis 213, 214
 - future opportunities 216, 217
 - limitations 214, 216
 - malaria 212
 - sickle cell disease
 - adherence to vascular endothelium 211
 - beta globin gene, mutation 208
 - blood rheology 210
 - blood rheology 210
 - microfluidic models of, vaso-occlusion 209
 - sickle hemoglobin or HbS 208
 - treatments 211
 - thrombosis
 - coagulation 205, 206
 - microfluidic models of 206, 207
 - vascular endothelium 207
 - vascular tree 205
- von Willebrand Factor (vWF) 107, 207
- w**
- Weibel–Palade bodies 112
- whole-genome amplification (WGA) 30, 33
- z**
- Zigmond chamber 105

