

Contents

1. Clinical Utility/Relevance of Cell Biology Techniques

What Is Clinical Utility/Relevance	1
Signal Transduction	1
Cell Division	1
Cell Differentiation	1
Apoptosis	1
Cell and Tissue Morphogenesis	2
Cell Migration	2
What Are the Informatics Challenges in Quantitative Cell Biology Imaging?	3
Why Are Open Source Approaches Essential?	4
Open Source Tools for Data Acquisition, Visualization, Analysis, and Dissemination	6
Supporting Open Source Software	6
Partnering Commercial and Open Source Efforts	8
Summary	9
Introduction to Controlled Drug Delivery Systems	9
Advantages of Controlled Delivery Systems	9
History of Controlled Drug Delivery	10
Sustained Release Drug Delivery Systems	10
Advantages of Sustained Release Systems	11
Sustained Release Mechanisms	11
Liposomes in Drug Delivery	11
What Are Liposomes?	11
Liposomes in Drug Targeting	12
Types of Liposome Targeting	12
Nanoparticles in Drug Delivery	13
Advantages and Disadvantages of Nanoparticles	13
Drug Loading Procedures	14
Applications of Nanoparticles	14
Nanospheres	14
What Is Molecular Nanotechnology?	15
Background and Definitions	15
Evolution of the Biopolymer	18
Synthetic Absorbable Polyesters	18
Poly(Ortho Esters)	20
Poly(Ortho Ester) III	21
Poly(Ortho Ester) IV	21

Polyanhydrides as Carriers of Drugs	21
Bioabsorbable Poly(Ester-Amides)	23
Amino Acid-Derived Polymers	24
Applications Comments	25
Polyphosphazenes as New Biomaterials	26
Bacterial Polyesters: Structural Variability in Microbial Synthesis	27
Biosynthetic Polysaccharides	29
Chitosan	29
Pullulan	30
Elsinan	30
Chemical Modifications of Proteins and Polysaccharides and Its Effect on Enzyme-Catalyzed Degradation	30
Red Blood Cells as Drug Carriers	31
Introduction	31
Drug Loading	32
Red Blood Cells as Drug Carriers against Retroviruses	32
Polymerization and Characterization of Biopolymers	32
Polymerization	32
Characterization	34
Mathematical Models for Controlled Release Mechanism	35
Mixing/Diffusion Process: Flory's Model	35
Rubber Elasticity: Simple Mechanical Model	36
Dynamic Model of Electrolyte Gel	38
Chemical Capacitance Model	39
Electric Potential Capacitance Model	39
Kinetic Model	41
Dextran Sulfate: Pharmaceutical Uses	42
References	44

Target Drug Delivery and the Blood-Brain Barrier

Introduction	46
History	46
Structure and Function	46
Transport	47
Glucose Transport	48
Amino Acid Transport	48
Peptide Transport	49
Disorders of the Blood-Brain Barrier	49
Getting Past the Barrier	51
Routes and Methods of Administration	51
Nonpharmaceutical Methods	52
Tailored and Carrier Drugs	52
Mechanical Disruption	53
Artificial Cells	54
Introduction	54
Methods of Preparation	55
Microencapsulation of Bioactive Sorbents	57

Microencapsulation of Cells or Microorganisms	57
Microencapsulation of Genetically Engineered Cells	60
Microencapsulation of Enzymes and Multienzyme Systems	61
Red Blood Cell Substitutes	62
Biodegradable Artificial Cells	62
General Discussions	62
General Discussion	63
Bibliography	72

Appendices

Appendix A: Glossary of Technical Terms	73
Appendix B: Chronological History of Nanotechnology	79
Chronology of Significant Events in Nanotechnology Research	79
Appendix C: List of Symbols	98
History and Facts on the Evolution of Nanotechnology	100
MITRE Corporation's List of Nanotechnology Research Sites	103
DoD Task Force Forecasts for 1998–2020	104
References	105
Bibliography	114

2 Applications of 3D Printing in Cell Biology

Computer Aided Design Model Used for 3D Printing	121
Model of a Turbine Showing the Benefits of 3D Printing	
in Industry	122
3D Modeling	123
Printing	123
Finishing	124
Current Uses	125
3D Printing, a Key Technology for Making Biobots	125
Synthetic Organs	125
Projected Uses in NASA Space Program	126
Science Objectives for Everyone	127
Space Applications	128
Earth Applications	128
Operational Requirements	129
Operational Protocols	129
How the 3D Printer Will Be Useful in the Future	129
Fabrication of Tissue-Engineered Constructs	132
Bioprinting	133
Bioprinting Technologies	134
Alginate and Chitosan as Biomaterial	135
Fabrication Technologies for Vasculature Network	138
Fabrication of Vascular Conduits	140
Materials and Methods	140
Fabrication Process	142
Coaxial Nozzle	142

Results	143
Discussion and Conclusion	145
Dispensing through the Coaxial Nozzle	148
Cell Viability Distribution over the Cross Section	149
Discussion and Conclusion	150
Results	152
Evaluation of Media Perfusion Capabilities	153
Materials and Methods	154
Media Perfusion System	155
Embedding a Vasculature System into Bulk Hydrogel	156
Perfusion and Diffusional Characterization	157
Quantitative Measurement of Small Molecular Diffusivity	157
Reference	162
 3. Transforming Bench Work Cell Biology with Cancer Informatics: From Silos to Systems	
Cancer Researchers and Data Mining	163
Definition of Data Mining	163
Data Mining General Models	164
General Application of Data Mining	164
Application of Data Mining in Cancer Studies	166
Guiding Principles for an Integrated Data Warehouse	167
Introduction	167
Data Warehouse Architecture	168
Building Cancer Data Warehouse	169
References	169
 4. Overview of the Cancer Informatics Landscape	
Telemedicine	172
E-health	173
Health Systems	173
Hospital Information Systems	174
Health Information Systems	174
Cloud-Based Informatics Platforms	176
Application of Cloud Computing in Health Care	179
Excel Macros for Data Analysis	189
References	247
 5. Current Trends for Global Coalition of all STEM Stakeholders via Cancer Informatics	
Challenges to Integrating Genomics	250
Health Information Technology Infrastructure	251
Putting Thoughts into Action	251
EHRs as a Research Tool	253
The 100,000 Genomes Project	254

Advancing Research and Patient Care	256
Other Genetic Research Resources	257
Opportunities	258
Translation of Genomics for Patient Care and Research	259
Engaging Patients	259
The Platform for Engaging Everyone Responsibly	260
Patient Trust, Consent, and Opting In	261
Platform-Supported, Complete Learning Cycles	262
Simultaneous Learning Cycles	264
Health-Care Disparities	265
Improving Health with a Knowledge-Based System	265
Innovation within Health Systems	266
Managing Priorities in a Health System	267
Promoting Health Services Research	268
Using Genomic Data in the Clinic	269
Leveraging EHRs for Genomics	272
Creating a Supportive Infrastructure	273
Clinical Decision Support	276
Managing Big Data	277
Insurance and Regulatory Issues	278
Data Sharing	279
Standards and Scale	280
Use Cases	280
Potential Next Steps and Considerations	282
Possible Next Steps	283
EHR Interoperability	285
Clinical Decision Support	286
Understanding Consumer Value and Preferences	287
References	289

6. Conclusion and Discussion

Future Trends in Cancer Cell Biology and Informatics	291
Introduction	291
Objective	293
Scope	293
Non-Scope	293
Responsibility	293
Specimens	293
Specimen Type	293
Validation Specimen Collection, Storage, and Preparation	293
Instrumentation	295
Reagents	295
Validation Summary	296
Veridex CellTracks AutoPrep Procedure	297
Specimen Preparation	297
Setup of CellTracks AutoPrep System Run	298
Loading AutoPrep	298

Unloading Specimens from AutoPrep	299
Control Specimen Analysis and QC	300
CellTracks Analyzer II [®] Image Acquisition	300
Identification of Control CTCs	301
Control Specimen QC	302
Clinical Specimen Analysis	302
Generate Specimen Reports	303
Acceptance/Rejection Criteria for Identification of CTCs	303
Rubicon PicoPlex WGA of CTCs	303
Initial Preparation of CTCs	303
WGA Protocol	306
Analyzing Amplification Efficiency Results	307
Purifying and Quantifying PicoPlex Products	308
The DNA Clean & Concentrator [™] -5 Protocol	308
DNA Purification Procedure	309
LightMix [®] Kit HER2/neu Oncogene Detection Protocol	309
Interpretation of HER2/neu qPCR Results	310
CTC Recovery (Total for Each 10 mL Tube of Human Whole Blood)	311
Sensitivity and Reproducibility of Veridex CellSearch System	312
Sensitivity and Reproducibility of HER2/neu Oncogene Amplification and Detection	314
Method Comparison of CTC Enumeration	315
Necessary Preparations before Starting the Enrichment Procedure	315
Preparation of Washing Buffer	315
Enrichment Procedure	316
Deviations	320
Conclusions	320
References	321
Appendix	321
Friedman Test	321
Descriptive Statistics	322
Correlation Coefficient	322
Passing and Bablok Regression	323
Repeated Measures ANOVA	323
Repeated Measures ANOVA on Log-Transformed Data	324