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Chapter 4 The Mechanisms Underlying Cardiac Arrhythmias
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Arrhythmia Mechanisms and Novel Antiarrhythmic Approaches Identified Using the Hypokalemic Mouse Model Summary; References;
Chapter 5 The Mechanisms Underlying Drug-Induced Arrhythmias; Introduction; The Classical Model of Drug-Induced QT Prolongation and Proarrhythmia: HERG Blockade; Additional Mechanisms Contributing to Drug-Induced Arrhythmias; Drug-Induction Activation of Depolarizing Ion Channels; Drug-Induced Changes in Ion Channel Expression; Drug-Induced Sodium Channel Dysfunction; Summary; References;
Chapter 6 Assessing Cardiac Safety in Drug Development; Introduction
Preclinical Evaluation of Cardiac Drug Safety The ICH S7B Guidelines; Single Cell Safety Studies; The Purkinje Fiber Model; The Ventricular Wedge Model; Isolated Heart Models; In Vivo Models; The Impact of Species-Related Differences in Cardiac Electrophysiology on Preclinical Drug Safety Assessment; Methods to Provoke Arrhythmias in Preclinical Studies; Programmed electrical stimulation; Reductions in the extracellular K⁺ concentration; Clinical Evaluation of Cardiac Safety; The Thorough QT study; Thorough QT study design; Additional Biomarkers to Detect Drug-Induced Proarrhythmia
Variability of repolarization

Sommario/riassunto

Ensuring the safety of new medical products remains a major challenge for the pharmaceutical industry. Cardiac safety, particularly drug-induced heart rhythm abnormalities, remains an important cause of pipeline attrition and has resulted in countless major product recalls or label changes. The risk of encountering this major adverse event continues to shape the drug development and regulatory landscape. Extensive research over the past decade has shed light on the root causes of arrhythmias that are triggered by medications and has helped drive, and optimize, drug safety testing. However,

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Nota di contenuto	Cover -- Title Page -- Copyright -- Contents -- List of Contributors -- Acknowledgments -- Part I Introduction and Background -- Chapter 1 Introduction to Modeling Terminology and Concepts -- 1.1 Mapping or Modeling - Which Is Correct? -- 1.1.1 Definition of the Term "Model" -- 1.1.2 Evolution of the Geological Model Concept -- 1.2 Why Use "Multidimensional"? -- 1.3 Evolution of Digital Geological Modeling -- 1.4 Overview of the Book -- 1.4.1 Intended Audience -- 1.4.2 Part I: Introduction and Background -- 1.4.3 Part II: Building and Managing Models -- 1.4.3.1 Technical Considerations - Chapters 5-8 -- 1.4.3.2 Alternative Model Building Approaches - Chapters 9-12 -- 1.4.3.3 Model Application and Evaluation - Chapters 13-15 -- 1.4.4 Part III: Using and Disseminating Models -- 1.4.5 Part IV: Case Studies -- 1.4.6 Part V: Future Possibilities and Challenges -- References -- Chapter 2 Geological Survey Data and the Move from 2-D to 4-D -- 2.1 Introduction -- 2.2 The Role of Geological Survey Organizations -- 2.2.1 Establishment of Geological Surveys -- 2.2.2 Systematic versus Strategic Mapping Approaches -- 2.2.3 Geological Mapping by

Geological Surveys -- 2.2.4 Difficulty in Maintaining Adequate Financial Support -- 2.3 Challenges Facing Geological Survey Organizations -- 2.4 A Geological Map is Not a Piece of Paper -- 2.4.1 Early Geological Maps -- 2.4.2 Early Digital Mapping and Modeling -- 2.4.3 Advantages of Digital Mapping -- 2.5 The Importance of Effective Data Management -- 2.6 The Challenges of Parameterization - Putting Numbers on the Geology -- 2.6.1 Parameterization of Geological Models -- 2.6.2 Model Scale -- 2.6.3 Parameter Heterogeneity -- 2.6.4 Model Uncertainty -- 2.7 Use of 3D Geological Models with Process Models -- 2.8 The Evolving Mission of the Geological Survey of the Netherlands.

2.9 Experience With a Multiagency and Multijurisdictional Approach to 3D Mapping in the Great Lakes Region -- 2.10 Conclusions -- References -- Chapter 3 Legislation, Regulation, and Management -- 3.1 Introduction -- 3.2 Layers of the Subsurface -- 3.3 Legal Systems -- 3.4 Land Ownership -- 3.5 Regulation and Management -- 3.5.1 Ground Investigation -- 3.5.2 Spatial Planning -- 3.5.3 Natural Resources -- 3.5.4 Environmental and Cultural Issues -- 3.6 Approaches to Subsurface Development -- 3.6.1 Existing Spaces -- 3.6.2 New Developments -- 3.7 Involving Stakeholders -- 3.8 Delivery of Information -- 3.9 The Role of 3D Subsurface Models -- 3.10 Conclusions -- References -- Chapter 4 The Economic Case for Establishing Subsurface Ground Conditions and the Use of Geological Models -- 4.1 Introduction -- 4.2 The Nature of Geotechnical Investigations -- 4.2.1 Geotechnical Investigations for Management of Geotechnical Risk -- 4.2.2 How Geological Models Sit Within the Geotechnical Investigation Process -- 4.2.3 Potential Impact of Geotechnical Risks -- 4.3 Benefits of Using 3D Models and Establishing Subsurface Ground Conditions -- 4.3.1 Cost of Geotechnical Investigations -- 4.3.2 Geotechnical Baseline Report -- 4.4 Processes, Codes, and Guidelines for Establishing Subsurface Conditions and Managing Risk -- 4.4.1 Risk Reduction Strategies to Manage Deficient Ground Information -- 4.4.2 Investments to Mitigate Against Deficient Ground Information -- 4.4.3 Code Requirements -- 4.5 Examples of the Use of 3D Geological Models for Infrastructure Projects -- 4.5.1 Investigating ThreeDimensional Geological Modeling as a Tool for Consultancy -- 4.5.2 ThreeDimensional Geological Modeling for a Nuclear Power Facility in Anglesey, Wales, UK, to Enhance Ground Investigation Quality and Optimize Value. 4.5.3 Integrating 3D Models Within Project Workflow to Control Geotechnical Risk -- 4.5.4 The Economic Value of Digital Ground Models for Linear Rail Infrastructure Assets in the United Kingdom -- 4.5.5 Employing an Integrated 3D Geological Model for the Reference Design of the Silvertown Tunnel, East London -- 4.5.6 A New Dutch Law on Subsurface Information to Enable Better Spatial Planning -- Acknowledgments -- References -- Part II Building and Managing Models -- Chapter 5 Overview and History of 3D Modeling Approaches -- 5.1 Introduction -- 5.2 Historical Development of 3D Modeling -- 5.2.1 Representation of the Third Dimension -- 5.2.2 Electrical Analog Models -- 5.2.3 The Adoption of Digital Mapping Technologies -- 5.2.4 Evolution of 3D Mapping and Modeling Collaborative Forums -- 5.3 The Mahomet Aquifer: An Example of Evolving Subsurface Modeling -- 5.3.1 Early Modeling Efforts -- 5.3.2 Initial 3D Geological and Hydrogeological Evaluations -- 5.3.3 Recent Geological and Hydrogeological Models -- 5.4 Digital 3D Geological Modeling Approaches Discussed in This Book -- 5.4.1 StackedSurface Approach to Model Creation -- 5.4.2 Modeling Based on CrossSections and Boreholes -- 5.4.3 ThreeDimensional Gridded Voxel Models -- 5.4.4

Integrated RuleBased (Implicit) Geological Models -- References --
Chapter 6 Effective and Efficient Workflows -- 6.1 Introduction -- 6.1.1
Understanding the Geologic Modeling Process -- 6.1.2 Developing
Custom Workflows -- 6.2 Operational Considerations -- 6.2.1 User
Requirements -- 6.2.2 Defining Mapping Objectives -- 6.2.2.1
Delineation of Model Domain -- 6.2.2.2 Definition of the General
Geologic Framework Model -- 6.2.2.3 Determination and
Representation of the Desired Model Accuracy -- 6.2.2.4 Consideration
of Formats for Final Deliverables -- 6.2.3 Geologic Setting and Natural
Complexity.
6.2.4 Existing Data Availability and Management -- 6.2.5 Collection of
New Data -- 6.2.6 Staff Availability and Expertise -- 6.3 Selection of
Modeling Methods and Software -- 6.4 Products and Distribution --
6.5 Model Maintenance and Upgrades -- 6.6 Illinois State Geological
Survey 3D Modeling Workflows -- 6.6.1 Project Objectives -- 6.6.2
Project Schedule -- 6.6.3 Project Staffing Considerations -- 6.6.4
Software Selection -- 6.6.5 Data Assessment -- 6.6.6 Project
Deliverables -- 6.6.7 PostProject Model Management -- 6.7 Modeling
Workflow Solutions by Other Organizations -- 6.7.1 University of
Waterloo, Department of Earth and Environmental Sciences -- 6.7.2
Delaware Geological Survey -- 6.7.3 Ontario Geological Survey -- 6.7.4
Geological Survey of Denmark and Greenland -- 6.8 Creating a Custom
Workflow -- Acknowledgments -- References -- Chapter 7 Data
Sources for Building Geological Models -- 7.1 Introduction -- 7.2
Defining and Classifying Data -- 7.2.1 Data Versus Information --
7.2.2 Classifying Data -- 7.2.2.1 Spatial Location and Extent Using
Points, Lines, and Polygons -- 7.2.2.2 Framework Versus Property Data
-- 7.2.2.3 Elevation, Surficial, and Subsurface Data -- 7.3 Legacy Data
-- 7.4 Elevation Data -- 7.5 Surficial and Subsurface Geological Data --
7.5.1 Geological Survey Data -- 7.5.1.1 Map Data -- 7.5.1.2 Boreholes
-- 7.5.1.3 Analytical Databases -- 7.5.1.4 Reports and Academic
Contributions -- 7.5.1.5 3D Models -- 7.5.1.6 Accessibility -- 7.5.2
Soil Data -- 7.5.3 Geotechnical Data -- 7.5.4 Water Well Data -- 7.5.5
Petroleum Data -- 7.6 Geophysical Data -- 7.6.1 Seismic Survey
Method -- 7.6.1.1 Seismic Refraction Surveys -- 7.6.1.2 Seismic
Reflection Surveys -- 7.6.1.3 Surface Wave Surveys -- 7.6.2 Resistivity
Survey Method -- 7.6.3 Electromagnetic Survey Method -- 7.6.3.1 Time
Domain Electromagnetic Surveys (TDEM).
7.6.3.2 Frequency Domain Electromagnetic Surveys -- 7.6.3.3 Airborne
Electromagnetic Surveys -- 7.6.4 Gravity Surveys -- 7.6.4.1 Ground
based Gravity Surveys -- 7.6.4.2 Airborne Gravity Surveys -- 7.6.5
Ground Penetrating Radar -- 7.6.6 Borehole Geophysics -- 7.6.6.1
Borehole Geophysical Logging -- 7.6.6.2 Inhole Seismic Geophysical
Logging -- Acknowledgments -- References -- Chapter 8 Data
Management Considerations -- 8.1 Introduction -- 8.2 Data
Management Methods -- 8.2.1 Standards and Best Practice -- 8.2.2
The Database System -- 8.2.3 Data Modeling -- 8.2.4 Relational
Databases -- 8.2.5 EntityRelationship Diagrams -- 8.2.6
Normalization Process -- 8.2.7 Denormalization Process -- 8.2.8
Extract, Transform, Load (ETL) Processes -- 8.2.9 Data Warehousing --
8.2.10 The Important Role of Metadata -- 8.3 Managing Source Data
for Modeling -- 8.3.1 Data from Multiple Data Sources -- 8.3.2
Managing the Connectivity among Data Sources -- 8.3.3 Facilitating
Sharing of Database Designs -- 8.4 Managing Geological Framework
Models -- 8.4.1 BGS Model Database Design Principles -- 8.4.2
Versioning Existing Models -- 8.4.3 Creating New Models Based on
Existing Models - "Model Interoperability" -- 8.5 Managing Geological
Properties Data and Property Models -- 8.5.1 Characteristics of

Property Data Sources and Models -- 8.5.2 Applications within the British Geological Survey -- 8.6 Managing Process Models -- 8.7 Integrated Data Management in the Danish National Groundwater Mapping Program -- 8.8 Transboundary Modeling -- 8.8.1 The H3O Program: Toward Consistency of 3D Hydrogeological Models Across the DutchBelgian and DutchGerman Borders -- 8.8.2 The Polish-German TransGeoTherm Project -- 8.8.3 The GeoMol Project -- Acknowledgments -- References -- Chapter 9 Model Creation Using Stacked Surfaces -- 9.1 Introduction -- 9.2 Rationale for Using Stacked Surfaces.
9.3 Software Functionality to Support StackedSurface Modeling.
