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Nota di contenuto	Biophysical Methods for Biotherapeutics; Contents; Preface; About the Editor; List of Contributors; Section 1 Early Discovery Stages and Biotherapeutic Candidate Selection; 1 Biophysical Methods Applied in Early Discovery of a Biotherapeutic: Case Study of an Egfr-Igf1r Bispecific Adnectin; 1.1 Introduction; 1.2 Target Identification; 1.3 Target Generation; 1.3.1 Multiple Constructs Strategy; 1.4 Hit Evaluation; 1.4.1 Qualitative and Rapid Self-Association Check; 1.4.2 Qualitative and Rapid Thermal Stability Check; 1.4.3 Confirmation of Binding; 1.5 Lead Selection; 1.5.1 Self-Association; 1.5.2 Thermal Stability; 1.5.3 Binding Affinity, Kinetics, and Epitope; 1.6 Lead Optimization; 1.7 Lead Formatting; 1.7.1 Solubility; 1.7.2 Thermal Unfolding Behavior; 1.8 Final Development Candidate Selection; 1.9 Concluding Remarks; Acknowledgment; References; 2 X-ray Crystallography for Biotherapeutics; 2.1 Introduction to X-ray Crystallography; 2.1.1 Early X-Ray Crystallography for Biologics; 2.2 Modern X-ray Crystallography; 2.2.1 Construct Design and Protein Production; 2.2.2 Macromolecular Crystallization; 2.3 X-ray Data Collection; 2.3.1 Crystal Mounting; 2.3.2 Collecting a Data Set; 2.3.3 Data Reduction; 2.4 Solving the Structure of the Crystal; 2.4.1 Molecular Replacement; 2.4.2 Heavy Atom Techniques; 2.4.3 Confirming the Validity of a Solution; 2.4.4 Building and Refining the Structure; 2.5 Understanding the Target Through Structure; 2.5.1 The

Model; 2.5.2 The Protein Databank and Related Resources; 2.5.3 Information Provided by X-Ray Crystallography; 2.6 Applications of X-ray Crystallography to Biotherapeutics; 2.6.1 Antibody-Based Biotherapeutics; 2.6.2 Antibody Design; 2.6.3 Protein Receptor Interactions  
2.7 Future Applications of Crystal Structures in Biotherapeutics  
2.7.1 Protein Engineering; 2.8 Conclusion; Acknowledgments; References; 3 Solubility and Early Assessment of Stability for Protein Therapeutics; 3.1 Introduction; 3.2 Measuring Protein Solubility; 3.2.1 Direct Measurement of Solubility: Concentration to Precipitation; 3.2.2 Indirect Assessment of Solubility: The Second Virial Coefficient (B<sub>22</sub>) and Self-Interaction Chromatography; 3.3 Assessment of Protein Stability; 3.3.1 Thermal Stability; 3.3.2 Aggregation; 3.3.3 Chemical Modifications; 3.4 Computational Predictions  
3.4.1 Identifying Aggregation Promoting Regions  
3.4.2 Interaction Hot Spots; 3.5 Enhance the Solubility of Biotherapeutics; 3.5.1 Site-Directed Mutagenesis; 3.5.2 Pegylation; 3.5.3 Glycosylation; 3.5.4 Formulation Optimization; 3.6 Development of Rapid Methods to Identify Soluble and Stable Biotherapeutics; 3.7 Concluding Remarks; References; Section 2 First-in-Human and Up To Proof-of-Concept Clinical Trials; 4 Biophysical and Structural Characterization Needed Prior to Proof of Concept; 4.1 Introduction  
4.2 Biophysical Methods for Elucidation of Protein Structure and Physiochemical Properties

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#### Sommario/riassunto

With a focus on practical applications of biophysical techniques, Biophysical Methods for Biotherapeutics helps formulation and analytical scientists in pharma and biotech better understand and use biophysical methods. Author Tapan K. Das links fundamental biophysics to the process of biopharmaceutical development using a chapter organization according to the steps of the drug development process. The text provides information to help organizations develop short- and long-term strategies for resource investment in biophysical research.

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