Table of contents

PART I: SCAFFOLDS: IDENTIFICATION, REPRESENTATION DIVERSITY AND NAVIGATION

Identifying and Representing Scaffolds

Markush Structures and Chemical Patents

Scaffold Diversity in Medicinal Chemistry Space

Scaffold Mining of Publicly Available Compound Data

Exploring Virtual Scaffold Spaces

PART II: SCAFFOLD HOPPING METHODS

Similarity-Based Scaffold Hopping Using 2D Fingerprints

CATS for Scaffold-Hopping in Medicinal Chemistry

Reduced Graphs

Feature Trees

Feature Point Pharmacophores (FEPOPS)

Three-Dimensional Scaffold Replacement Methods

Spherical Harmonic Molecular Surfaces (ParaSurf and ParaFit)

The XED Forcefield and Spark

Molecular Interaction Fingerprints

SkelGen

PART III: CASE STUDIES

Case Study 1: Scaffold Hopping for T-Type Calcium Channel and Glycine Transporter Type 1 Inhibitors

Case Study 2: Bioisosteric Replacements for the Neurokinin 1 Receptor (NK1R)

Case Study 3: Fragment Hopping to Design Highly Potent and Selective Neuronal Nitric Oxide Synthase Inhibitors