Schrödinger

Workshop #3 for Educator's Week 2026

Searching for the "Chemical Core": Ligand-Based Virtual Screening with Phase

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Workshop Learning Objectives

1. Molecular Feature Identification and Abstraction

- *Model 3D Pharmacophores:* Use Phase to move beyond 2D structures, helping students visualize how proteins "read" a ligand's spatial map
- *Identify Essential Features:* Teach students to categorize chemical groups as essential or auxiliary to understand their specific roles in protein-ligand binding

2. Exploring Chemical Diversity

- *Virtual Bioisostere Screening:* Design challenges where students use virtual screening to identify chemically diverse molecules that fulfill the same biological role.
- *Analyze Phase Fitness:* Use Fitness Scores to demonstrate how different scaffolds can overcome drug resistance or patent hurdles by satisfying identical spatial requirements

3. Evaluating "In Silico" Success: Validation and Enrichment

- Implement inquiry-based labs where students validate their own search models by screening "blinded" libraries and using ranking metrics to distinguish active compounds from decoys

Hands-on Demo

Classroom Exercise Suggestions

1. **Exercise 1: The "Essential Pharmacophore Feature" Filter**
   - Does every part of a drug matter? Finding the "Minimum Viable Pharmacophore"
   - ***Task:*** Students start with a 5 or 6-feature model (donors, acceptors, rings). They must delete one feature at a time and re-run the search
   - ***Data to collect:*** Watch how the "Hit List" grows as the model becomes less picky
   - ***Main takeaway:*** Identify which feature is the "deal-breaker"—the one that, when removed, lets in too many "garbage" molecules

2. **Exercise 2: The "Scaffold Hop" Challenge**
   - Can two molecules that look completely different on paper behave the same way in the body?
   - ***Task:*** Use a pharmacophore based on a common drug (e.g., Ibuprofen) to search a database of structurally diverse compounds
   - ***Data to collect:*** Find the top-ranked molecule that has a completely different central ring system than the original drug
   - ***Main takeaway:*** Explain how different chemical "skeletons" can still hold functional groups in the exact same 3D positions

Alignment to Student Learning Outcomes from the American Chemical Society (ACS) Guidelines

1. Chemical Information & Database Literacy (Section 5.3)

- **ACS Requirement:** Students must be able to "retrieve, organize, and visualize chemical information from databases"
- **Workshop Alignment:** By using Phase to screen libraries, students learn how to query vast chemical spaces using a 3D spatial hypothesis rather than a simple text-based name or 2D string
- **Student Learning Outcome:** Students will demonstrate the ability to execute a virtual screen and filter large datasets to identify lead compounds based on geometric and electronic criteria

2. Foundational Concepts: Macromolecules & Supramolecular Chemistry (Section 5.1)

- **ACS Requirement:** Students should understand "the structure and function of biological macromolecules and the principles of molecular recognition"
- **Workshop Alignment:** The workshop focuses on the Pharmacophore, which is the physical embodiment of "Molecular Recognition." Students define the intermolecular forces (H-bonds, pi-stacking, etc.) required for a ligand to communicate with its biological target
- **Student Outcome:** Students will be able to abstract a complex 3D molecule into its essential pharmacophoric features and explain how these features facilitate specific non-covalent interactions with a receptor

Thank you for attending!

Please join us for the rest of the events today:

- **Faculty Perspectives on Using Teaching with Schrödinger**: Thurs. April 30th from 11:30am–12pm ET
- Launching your Industry Career with a Computational Degree: Panel #3
  - Recommended for graduate students and post-docs looking to enter industry after graduation

We will email today's workshop materials so you can walk through the same steps on your own.

For any questions, please reach out to teaching@schrodinger.com