Schrödinger

Workshop #1 for Educator's Week 2026

Teaching Protein-Ligand Complementarity using Schrödinger's Ligand Designer

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Workshop Learning Objectives

1. Visualize and Quantify Molecular Complementarity

- Utilize Interaction Maps and Real-time Scoring within the Ligand Designer interface to visually identify "hot spots" for H-bonding and hydrophobic interactions
- Translate a 2D chemical structure into a 3D "fit" within a binding pocket

2. Execute Iterative Lead Optimization Workflows

- Learn to add or substitute functional groups on a core scaffold to improve a ligand's Pose Score
- Interpret visual "Clash" indicators and "Growth Space" visualizations to explain why specific chemical modifications enhance or disrupt binding affinity

3. Integrate Computational "Inquiry-Based" Labs into Existing Curricula

- Gain ideas on how to design classroom activities that replaces static textbook models of a protein-ligand "Lock and Key" theory with dynamic modeling with Ligand Designer

Hands-on Demo

Classroom Exercise Suggestions

1. **The Steric Clash:** Have students add a bulky t-butyl group into a tight pocket
   - *Observation:* The "Clash" icons (red disks) appear
   - *Lesson:* VSEPR theory and Van der Waals radii in 3D space

2. **The H-Bond Matchmaker:** Find a lone Carbonyl (C=O) on the protein backbone. Have students add an Amine (NH_2) to the ligand
   - *Observation:* A dashed yellow line appears
   - *Lesson:* Dipole-dipole interactions and directional bonding

3. **The Solvation Challenge:** Look at "Unfilled Enclosure"
   - *Observation:* Adding a hydrophobic group to a greasy pocket improves the score.
   - *Lesson:* The Hydrophobic Effect and Entropy (ΔS)

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

1. Macromolecules & Biological Chemistry (Section 5.1)

- **ACS Requirement:** Students should understand the structure and function of biological macromolecules
- **Workshop Alignment:** By using **Ligand Designer**, students move beyond static 2D images to explore 3D protein-ligand complementarity. They learn how specific amino acid residues (the "Lock") dictate the necessary chemical features of the "Key"
- **Student Outcome:** Students can explain the role of non-covalent interactions (H-bonding, van der Waals, and the hydrophobic effect) in stabilizing biological complexes

2. Critical Thinking & Problem-Solving (Section 6.1)

- **ACS Requirement:** Students must develop the ability to "design an experiment, collect and analyze data, and communicate their results"
- **Workshop Alignment:** The **"Modify and Measure"** activity is a micro-experiment. Students hypothesize a modification, execute the build, and analyze the resulting Pose Score
- **Student Outcome:** Students can write a "Design Justification" report, using quantitative computational data to defend their qualitative chemical intuition

Alignment to Student Learning Outcomes from the American Society for Biochemistry and Molecular Biology (ASBMB) Guidelines

1. Macromolecular Structure, Function, and Regulation

- **ASBMB Standard:** Students should understand that "Structure is determined by environmental factors and the cumulative effects of weak interactions”
- **Workshop Alignment:** Using Ligand Designer, students observe how the protein environment (pH, hydrophobicity, and sterics) dictates whether a ligand binds or "clashes"
- **Student Outcome:** Students can predict how specific mutations in a protein (e.g., swapping a polar Serine for a non-polar Alanine) will alter drug binding affinity

2. Energy is Required and Transformed in Biological Systems

- **ASBMB Standard:** Students must understand the thermodynamic basis of biological interactions ($\Delta G = \Delta H - T\Delta S$)
- **Workshop Alignment:** The Real-time Scoring in Maestro provides a proxy for ΔG. Students see that a "good" score isn't just about H-bonds (ΔH) but also about the displacement of ordered water molecules in a hydrophobic pocket (Desolvation/Entropy, ΔS)
- **Student Outcome:** Students can explain the "Thermodynamic Driving Force" behind a protein-ligand interaction using computational data

Thank you for attending!

Please join us for more free workshops this week:

- **Mapping the Reaction "Mountain Pass" and Visualizing Transition States with Schrödinger's AutoTS Workflow:** Wed. April 29th from 11-11:30am ET
  - Great for educators teaching physical chemistry, organic chemistry, etc.
- **Searching for the "Chemical Core" using Ligand-Based Virtual Screening with Phase**: Thurs. April 30th from 11-11:30am ET
  - Recommended for educators teaching biochemistry, medicinal chemistry

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