2015 Science Writers Symposium

New Drug, Old Drug, No Drug

Uses of

Spectral Data–Activity Relationships (SDAR)

Modeling

William B. Mattes, Ph.D., DABT

Director, Division of Systems Biology

National Center for Toxicological Research

Food and Drug Administration

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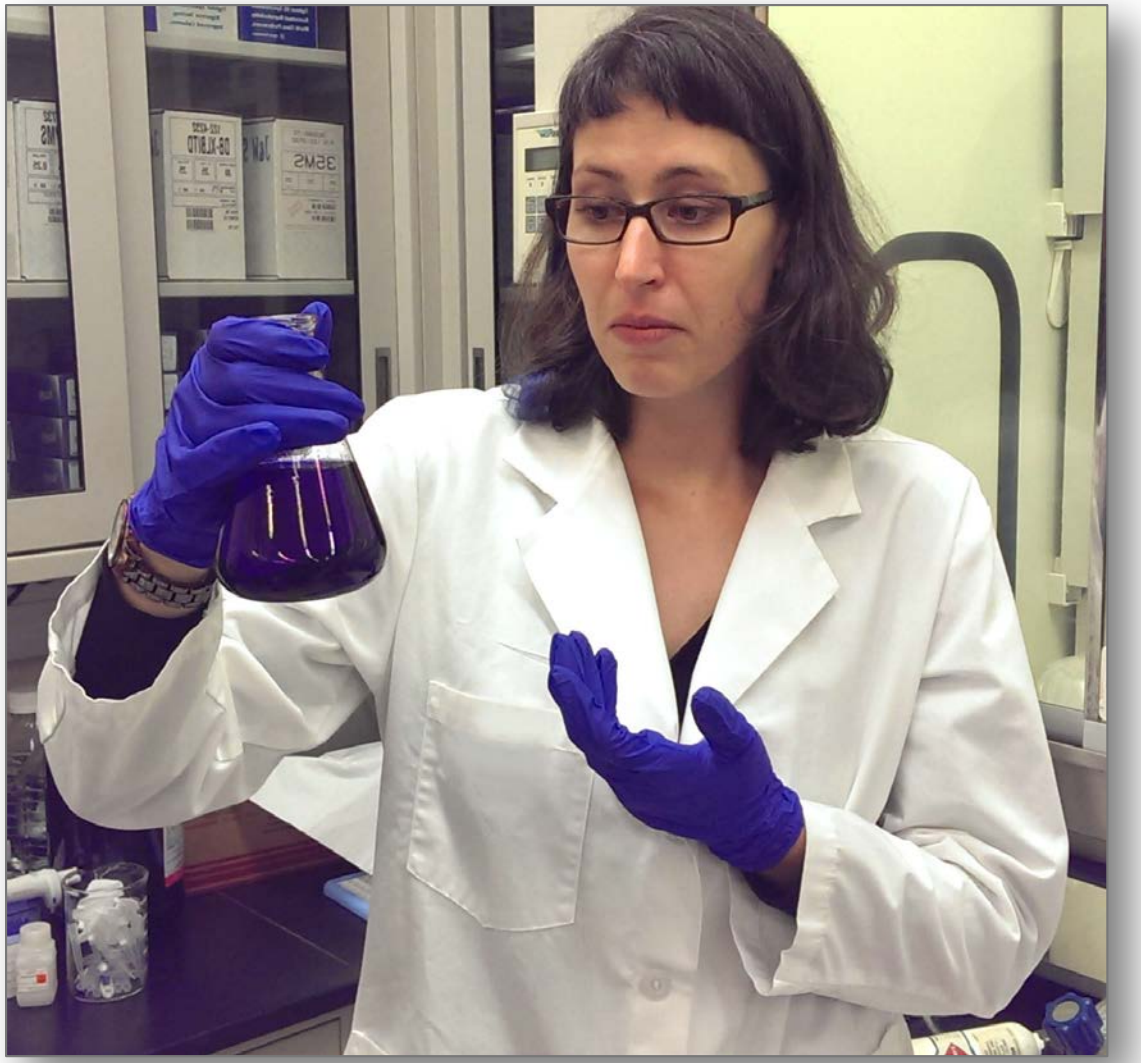
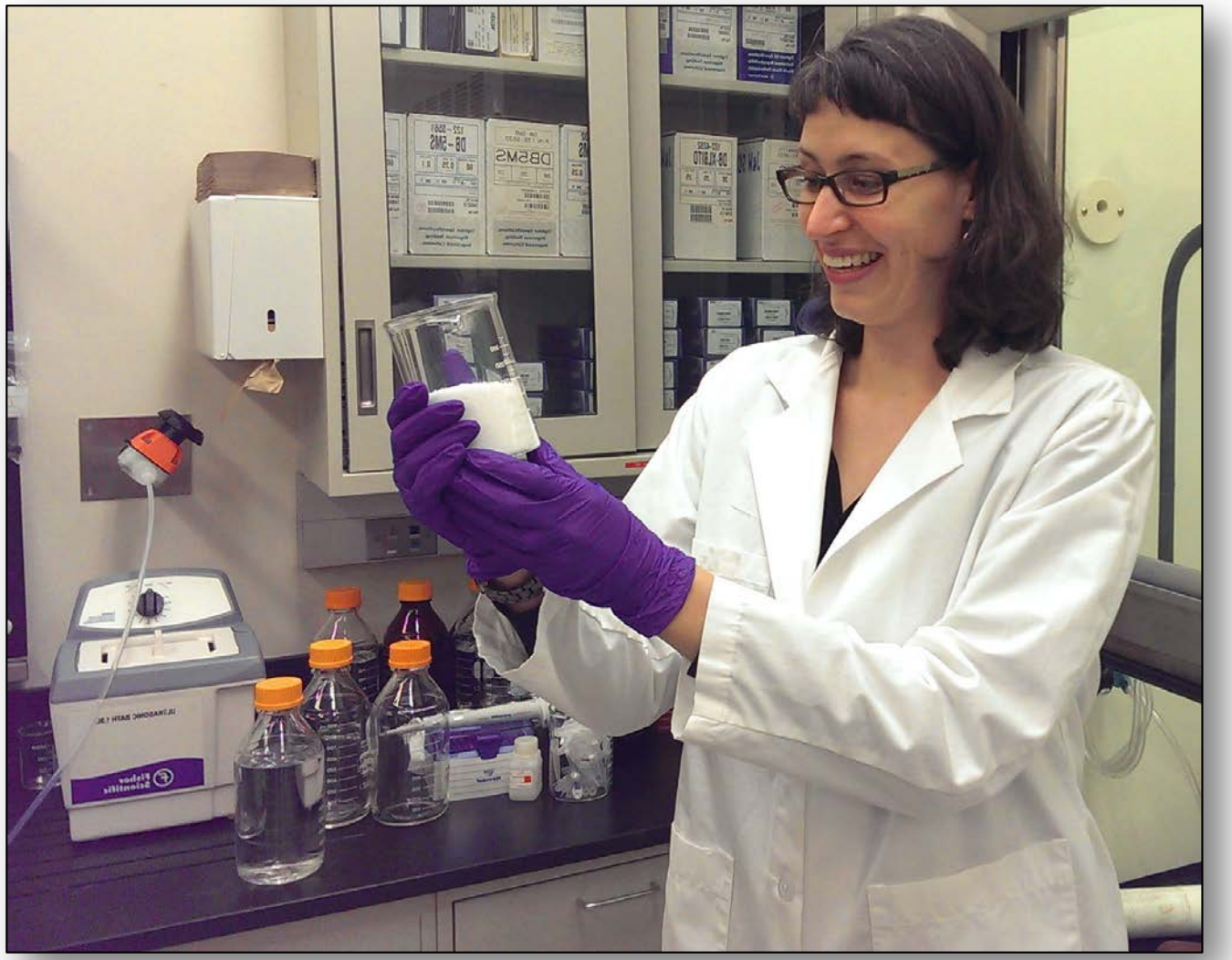
Suppose you have a new chemical that could be a drug and don't know what it can do?

- **Efficacy?**
- **Toxicity?**

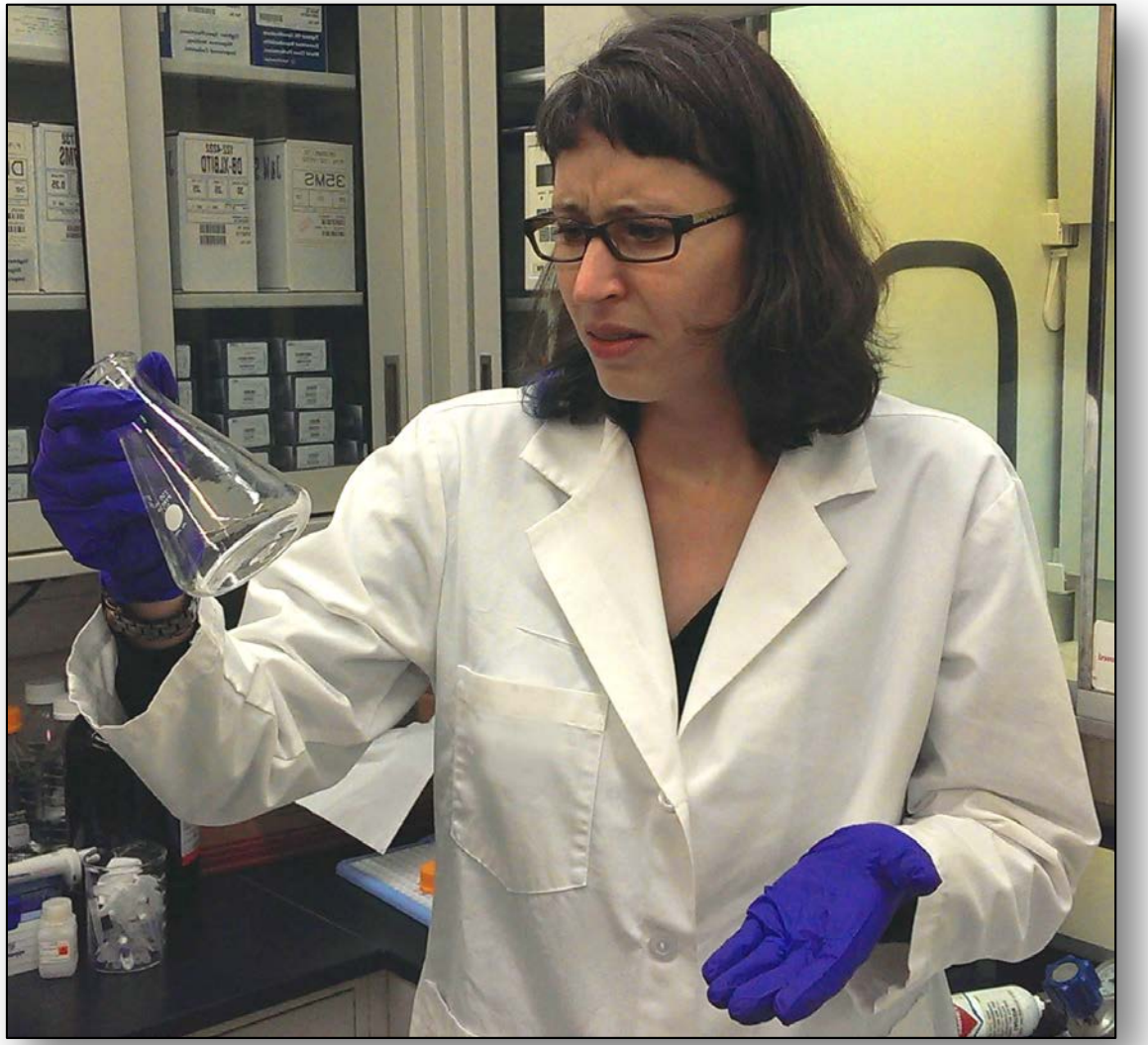


Suppose you thought you had a new drug…



Suppose you thought you had a new drug…

…but it has bad side effects.



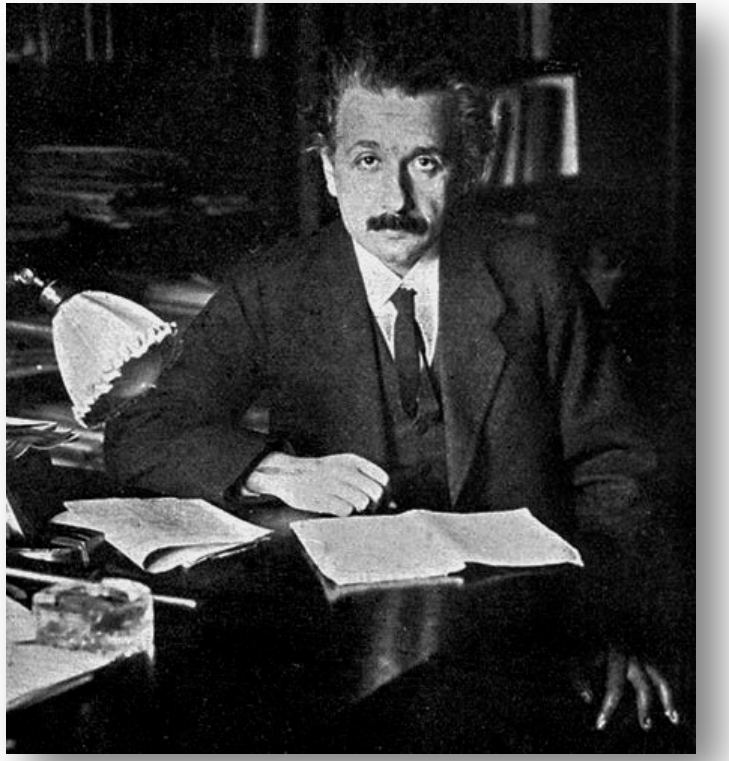
Suppose you don't have a drug …and nobody does.

- **Lou Gehrig's Disease (ALS)**
- **Parkinson's Disease**

Computational Medicinal Chemistry

- **Inexpensive**
- **Fast**
- **Accurate**

SDAR Modeling: A New Way to Test Molecules

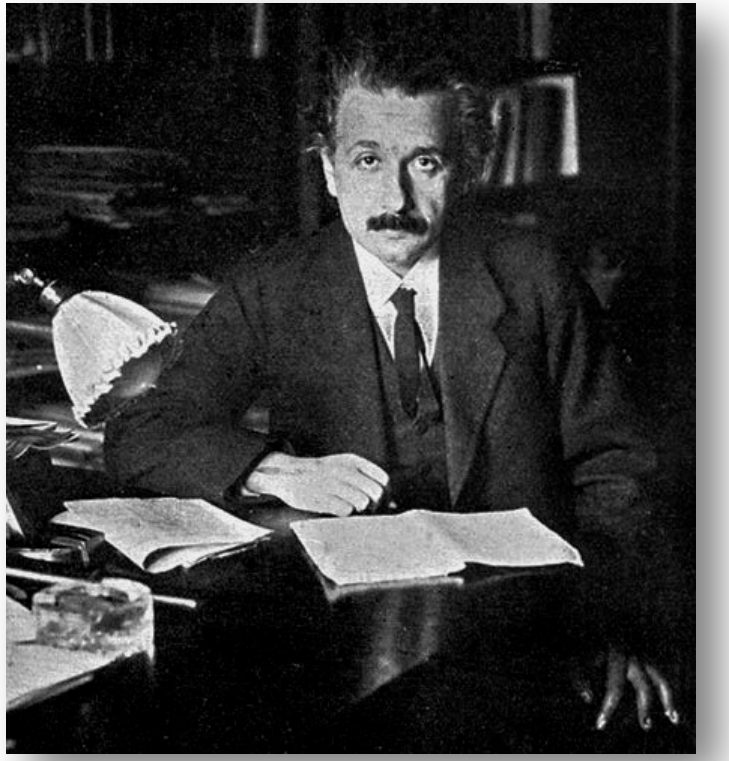


Albert Einstein

Max Plank

Spectral
Data–
Activity
Relationships

SDAR Modeling: A New Way to Test Molecules



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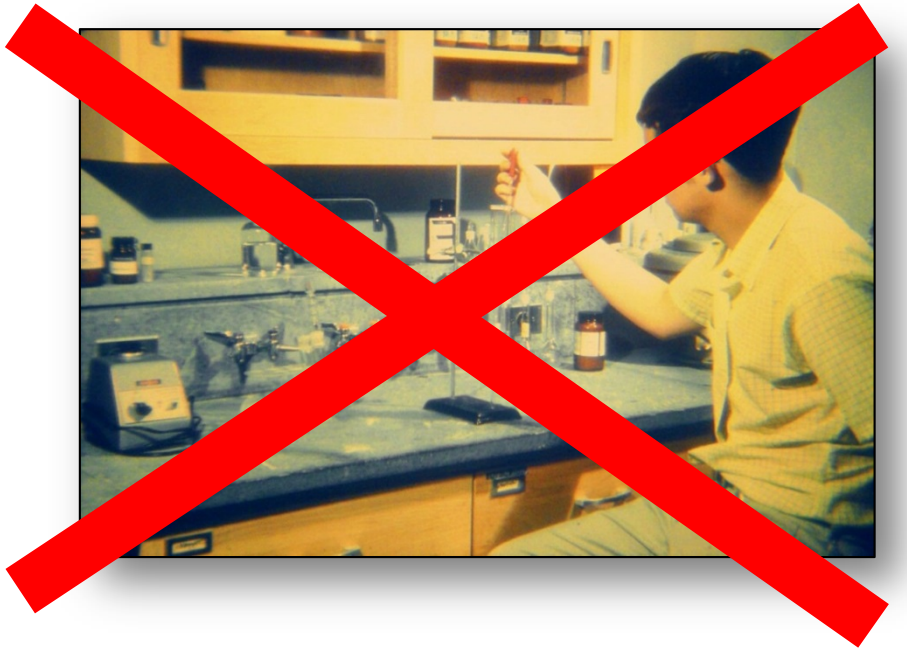
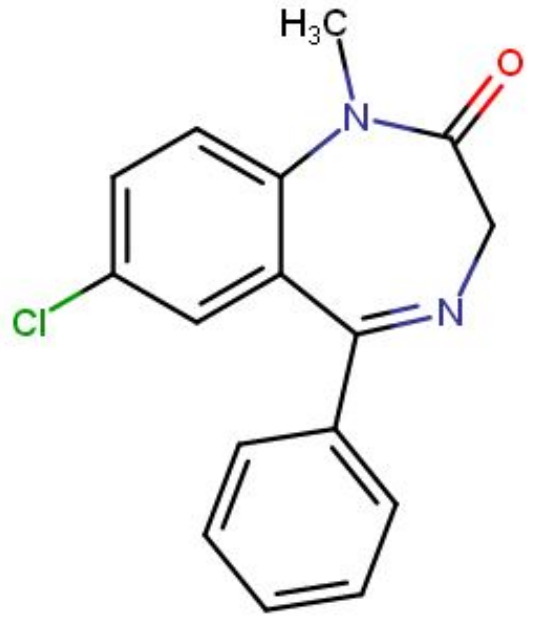


What Does a Drug Look Like?

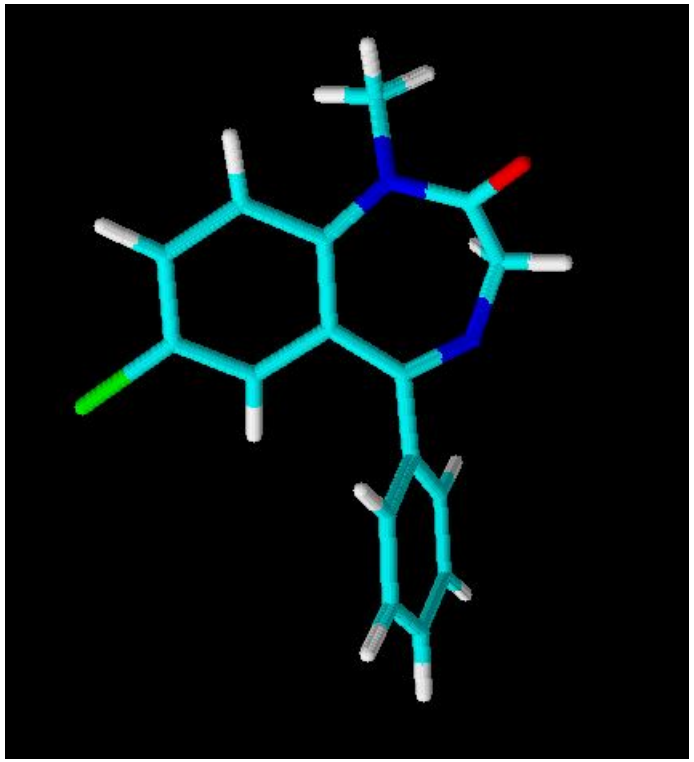
- Most are small molecules, atoms held together by chemical bonds.



Diazepam (Valium)

What Does a Drug Look Like?

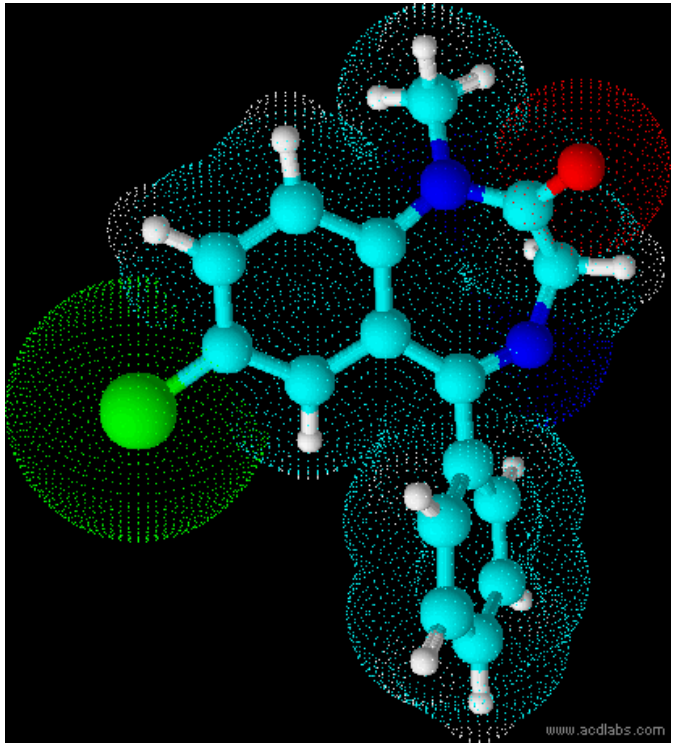
- Most are small molecules, atoms held together by chemical bonds.
- But far from flat



Diazepam (Valium)

What Does a Drug Look Like?

- Most are small molecules, atoms held together by chemical bonds.
- The electrons of each atom determine the biochemical reactions that the molecule will have when used.

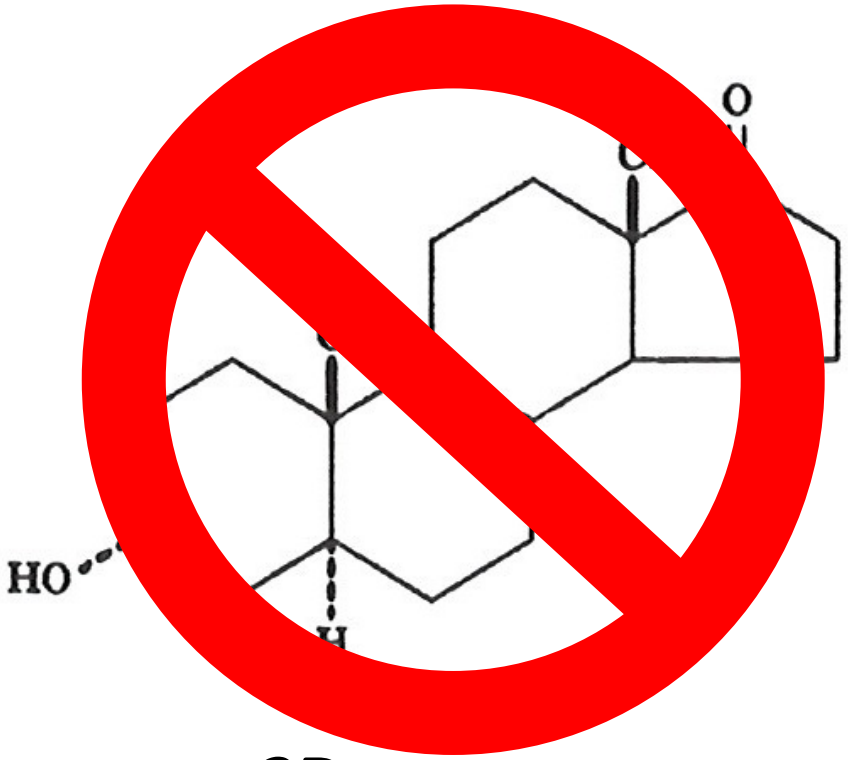


Diazepam (Valium)

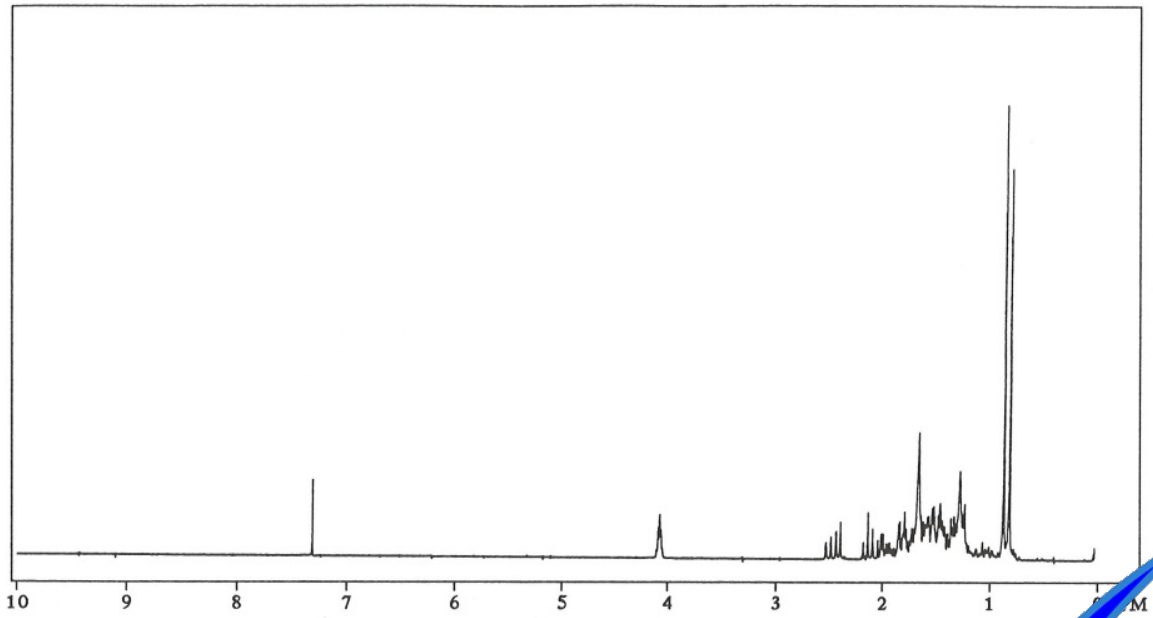
SDAR Modeling:
A New Way to Do Computational Medicinal Chemistry

Uses signals from an NMR machine, similar to an MRI, which gives spectra instead of images.

SDAR Modeling: A New Way to Do Computational Medicinal Chemistry



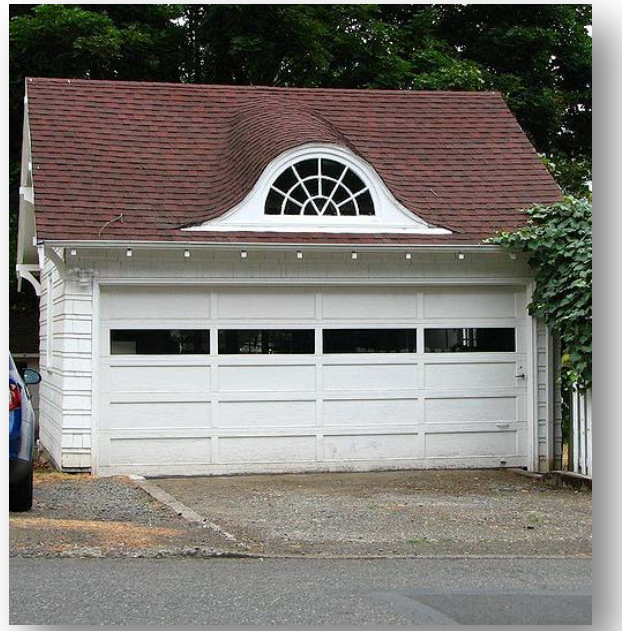
2D structure
(Androsterone)



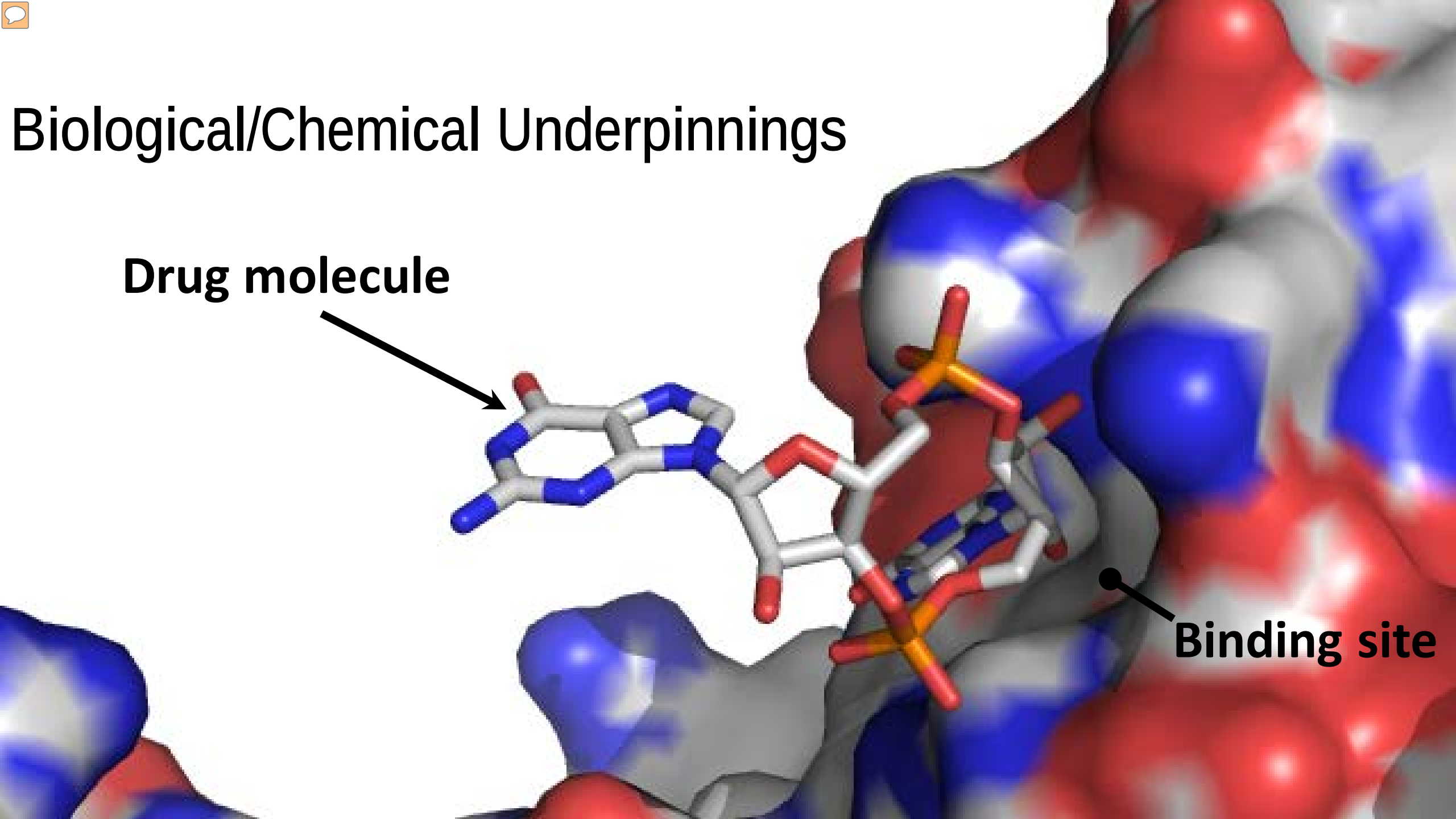
NMR spectrum
(chemical shifts)

SDAR Modeling: What Are We Trying to Do?

?

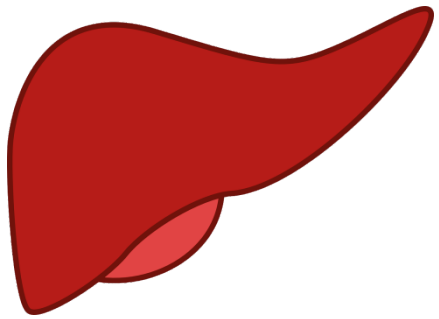


Biological/Chemical Underpinnings

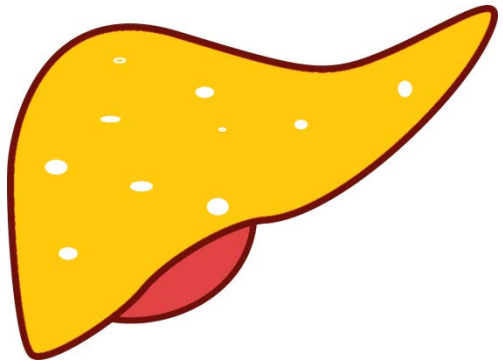


Example: Phospholipidosis (PLD)

Normal



Fatty

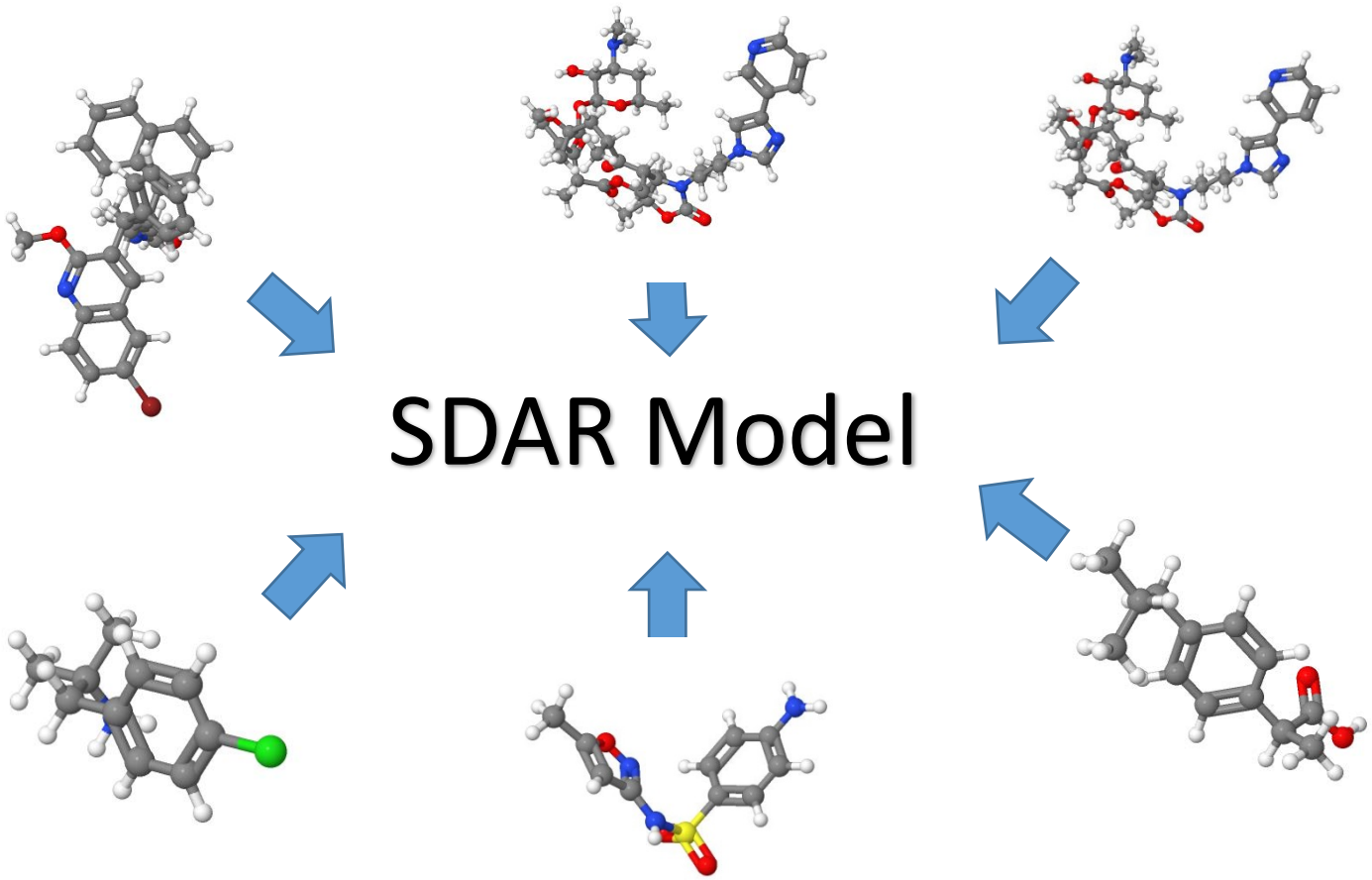


Jaundice

SDAR Modeling Phospholipidosis (PLD)

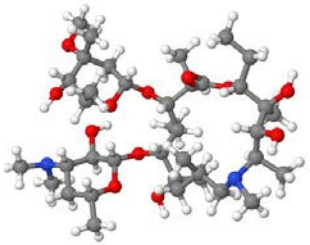
Known compounds

Some cause PLD.
Some don't.



SDAR Modeling Phospholipidosis (PLD)

New compound



SDAR Model

Prediction: PLD, Y/N?

SDAR Uses

- Predict activity of new compound.
  - If “activity” is toxicity, avoid it.
  - If “activity” is therapeutic (e.g., antibiotic), enhance important features via a new candidate.
- Design effective new drugs that avoid typical toxicities.

Drug Efficacy Bottom Line

That's how you…

- Test new drugs
- Repurpose old drugs
- Address orphan diseases

Drug Safety Bottom Line

That's how you…

- Test for side effects and toxicity.

  An FDA reviewer of a new drug application could use the SDAR model to detect whether PLD was a likely effect.

The SDAR Team

- Richard Beger, Ph.D.
- Daniel Buzatu, Ph.D.
- Steven Harris, M.S.
- Jon Wilkes, Ph.D.
- Svetoslav Slavov, Ph.D.
- Steven Harris, M.S.
- Naomi Kruhlak , Ph.D.
- James Willard, Ph.D.

Thank you!