Extending and supporting "wet' practicals

~with computer-based exercises

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Laboratory Practicals for Science Students

- Laboratory experience is desirable for Science graduates.
  - How to ask and answer questions is as important as what the answers are.
- Alternative learning environment helps to reinforce of conceptual grasp.
- Enforced time for reflection and interaction.

Laboratory Practicals for Science Students

Delivery can be constrained by:

- Space and timetable.
- Expense and staff time.
- Use of animals.

Outcomes can be constrained by:

- Quality of data.
- Slowness of responses.
- Number of experiments that can be completed.

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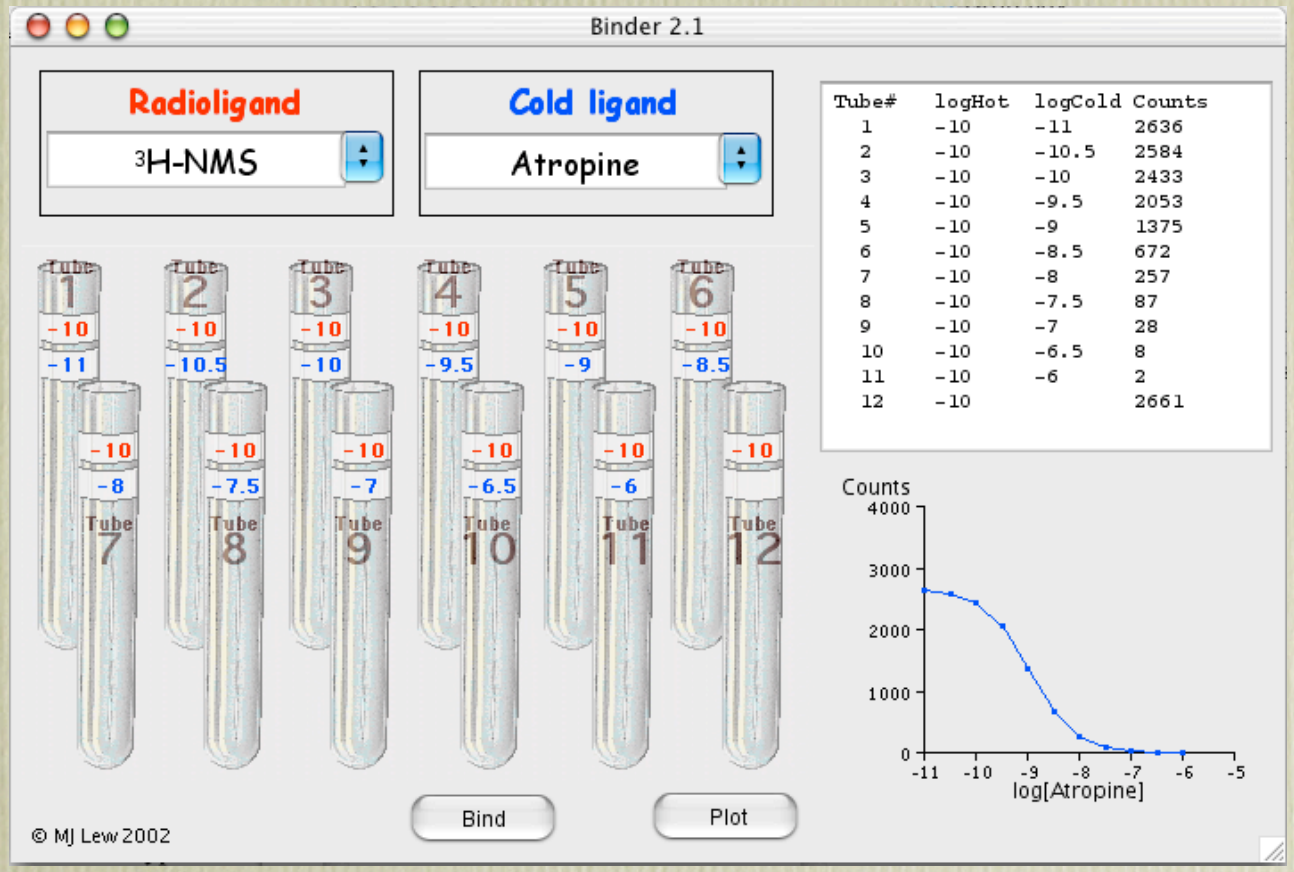
Use computers instead?

A Dry Practical



Learning objectives

- Saturation binding
  to characterise a radioligand
- Competition binding
  to characterise cold ligands
- Analysis
  to obtain drug and receptor parameters
- Reinforcement of drug-receptor interaction concepts.

Learning Study Questions

- Do practical notes designed to encourage student-directed exploration lead to superior learning outcomes?
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Conventional Notes

1a. Perform a saturation binding experiment using ^{3}H-NMS as the radioligand without any cold ligand. You may need to experiment with radioligand concentrations to determine the best concentration range to show the concentration-binding curve for the radioligand.

The theoretical relationship between ligand concentration and receptor binding is expressed in the equation:

$$[LR]/[R]t = [L]/([L] + KL)$$

where [LR] is the concentration of bound receptors, [R]t is the total concentration of receptors, [L] is the concentration of radioligand and KL is the equilibrium dissociation constant of the radioligand. It should be clear that when the concentration of radioligand is equal to its KL half of the total receptors will be bound.

Explorer's notes

Introduction

At equilibrium, the fraction of receptors bound by a ligand increases in a non-linear manner with increasing ligand concentrations, up to a point where all of the receptors become bound. You should be able to exploit that information in designing a simple experiment to determine the affinity of a radioligand for its receptors.

Learning objectives:

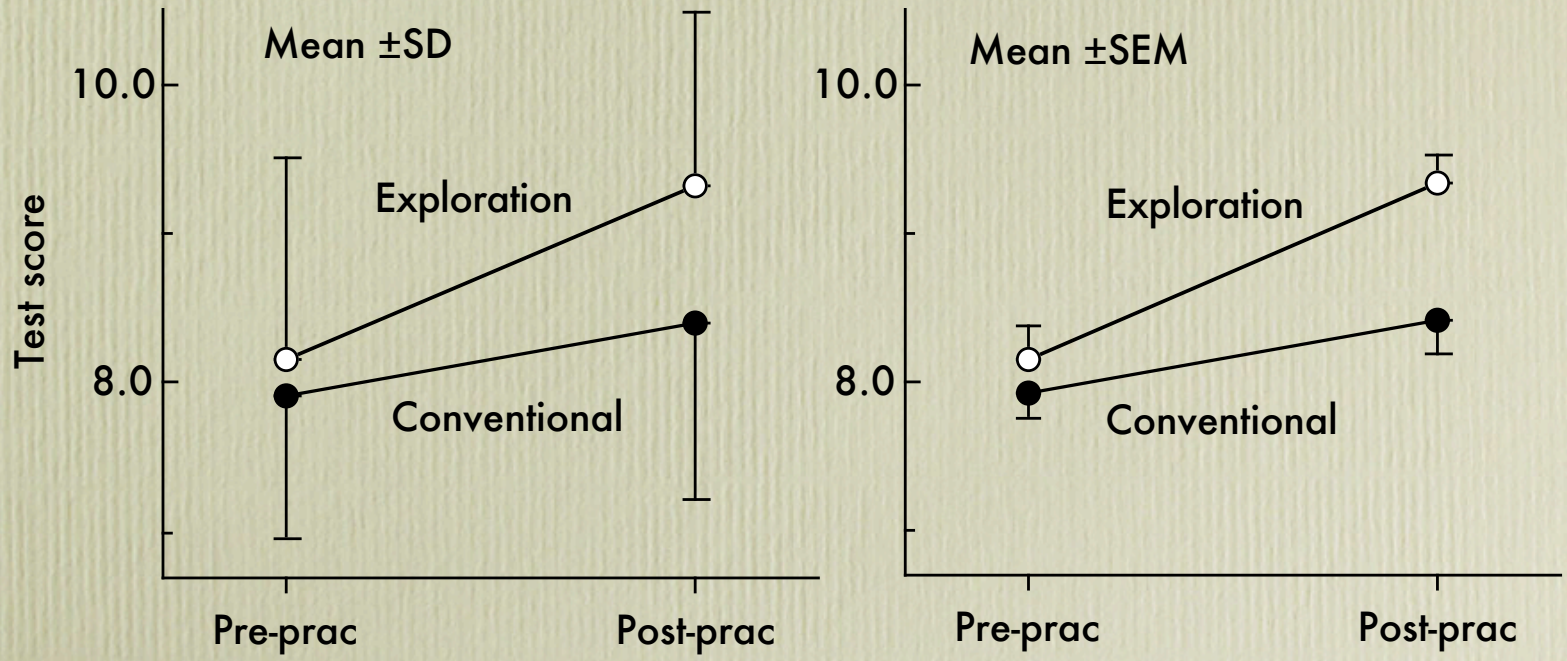
To understand simple ligand binding.

Tasks:

Design and implement an experiment to determine the affinity of ^{3}H-NMS for the receptors.

Results

(Scores out of 12)



Study Limitations

Relevant lecture material was immediately prior to practical session

- Inflation of pre-prac test scores would minimise differences in test performance

Too many tasks for students

- Learning and post-prac test performance compromised by fatigue

Study Results

- Students appeared to learn better from less prescriptive notes.
  - They did explore: audit trail data showed more experiments at each stage.

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Letting students design their own experiments is beneficial

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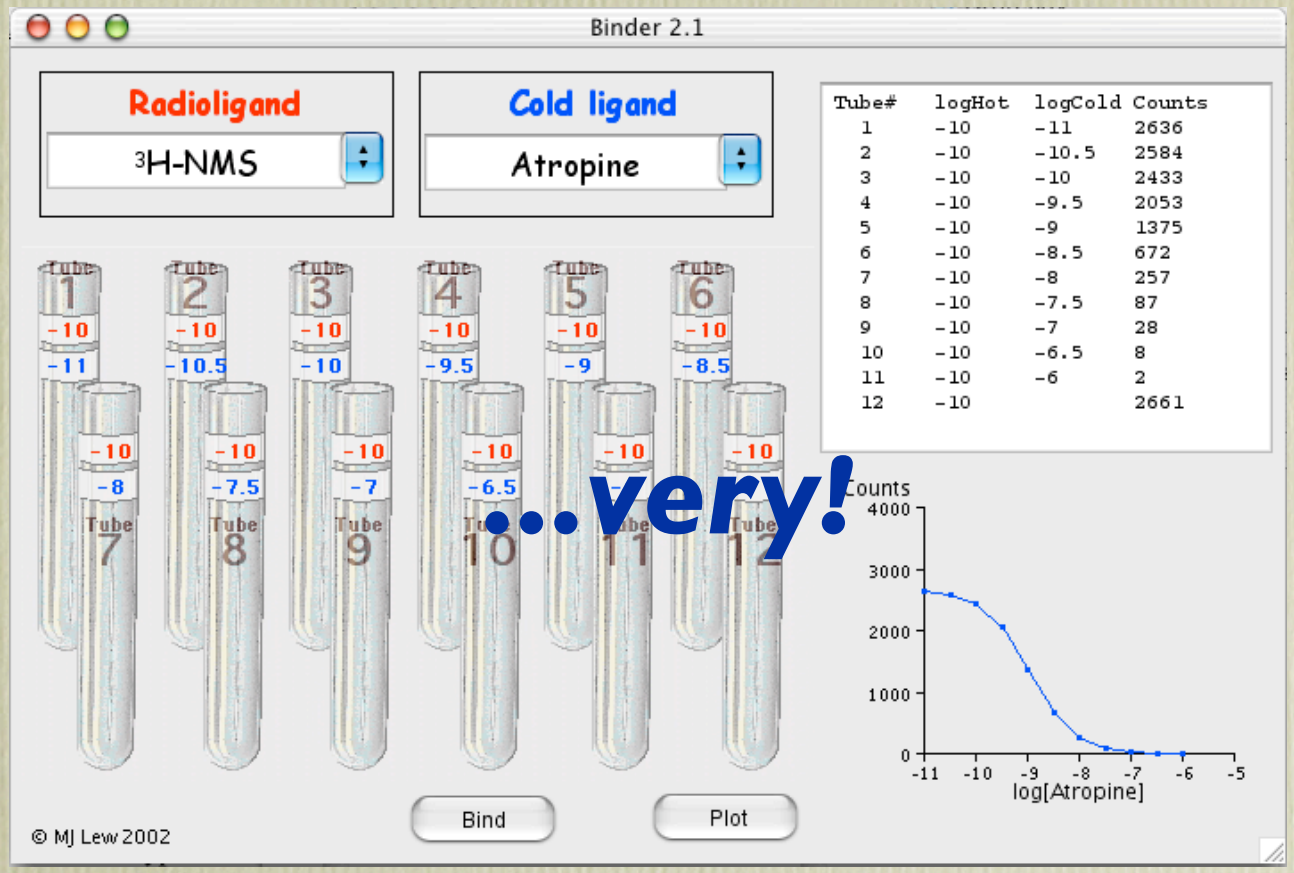

Leavening Dry with Wet
Enhancing Wet with Dry

Wet and Dry Characteristics

	Wet	Dry
Engaging	✓	x
Laboratory skills	✓	x
Biological variation	✓✓	x✓
Analytical skills	x	✓
Experimental design	x	✓

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Complementary!

A Wet and Dry Practical

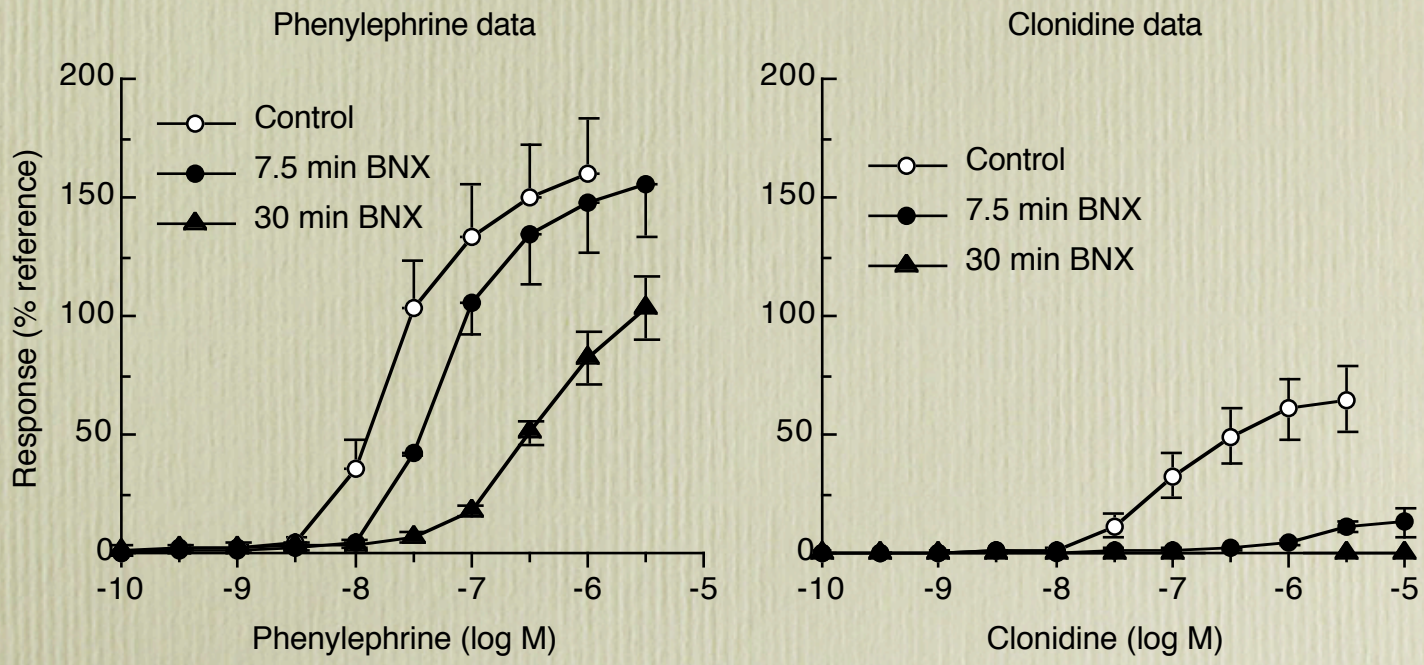
- Rat aortic rings
  - α_1-Adrenoceptors
  - Easy setup, many per rat
  - Reproducible responses, but slow
- Drugs
  - Phenylephrine: full agonist
  - Clonidine: partial agonist
  - Benextramine: irreversible antagonist
- CRC Boss software
  - Reproducible responses, quickly
  - Direct control of efficacy and receptor density

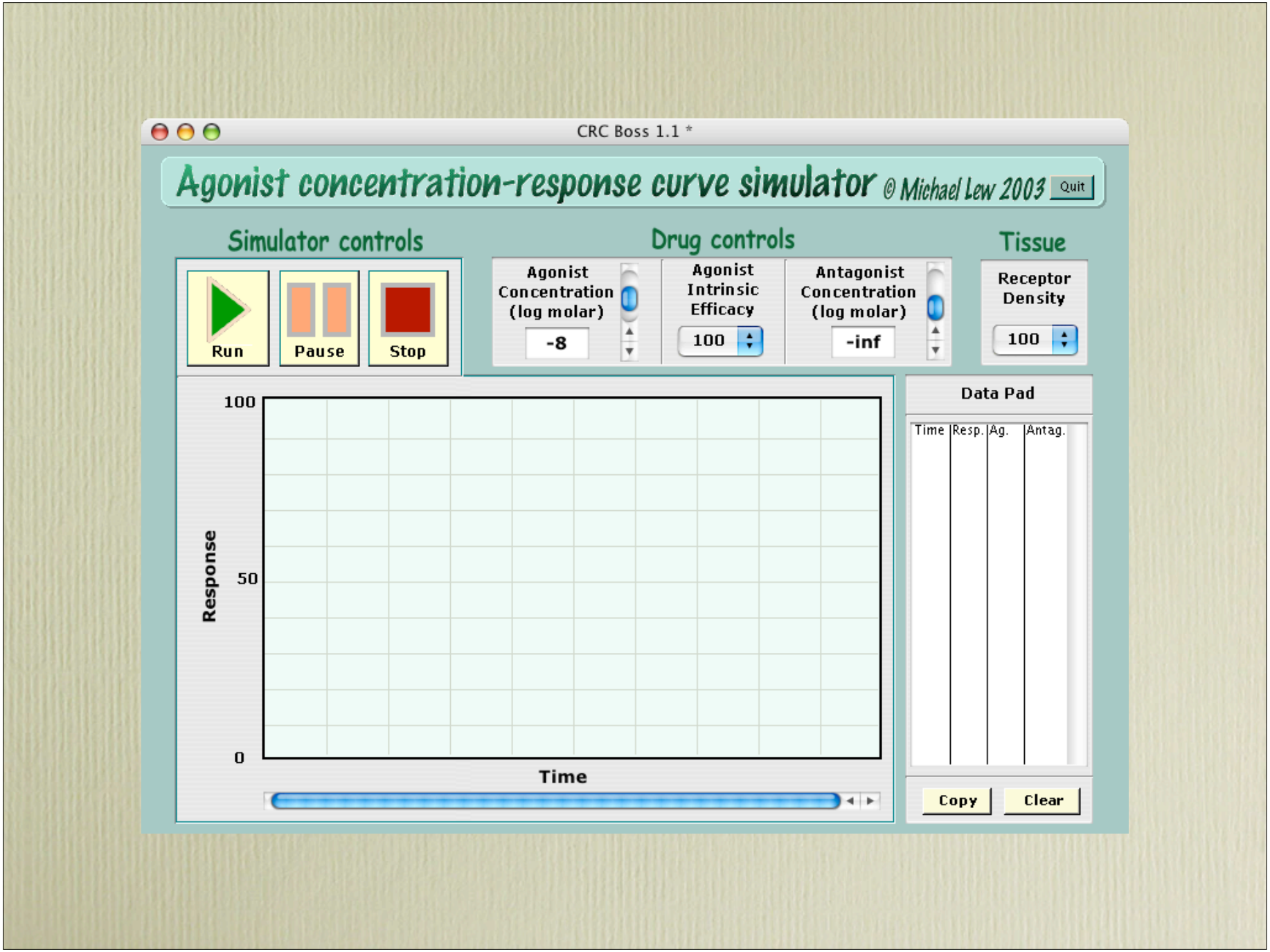
Learning objectives

- Characterisation of agonist effects
  - Full and partial agonism
  - Sensitivity to antagonists
  - Dependence on tissue properties
- Reinforcement of drug-receptor interaction concepts.

Class wet results

Two curves per group of 2 or 3 students,
ninety students in two sessions.




CRC Boss 1.1 *
Agonist concentration-response curve simulator © Michael Lew 2003
Quit
Simulator controls
Run
Pause
Stop
Drug controls
Agonist Concentration (log molar)
-8
Agonist Intrinsic Efficacy
100
Antagonist Concentration (log molar)
-inf
Tissue
Receptor Density
100
100
50
0
Response
Time
Data Pad
Time
Resp.
Ag.
Antag.
Copy
Clear

Some things tested using CRC Boss

- Interpretation of class wet results
- Relationship between efficacy and potency
- Antagonism of full and partial agonists by competitive reversible antagonists
- Tissue-dependence of agonist potency and maximum effect

Conclusions

- Computer-based exercises can engender an exploratory approach to experimental design and problem solving.
- Wet and dry exercises have complementary strengths and can synergise.