



Introduction to Drug Design

(Sex, drugs, and rock and roll . . . well,
drugs, anyway.)

Drugs

Definition: articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals, intended to affect the structure or any function of the body of man or other animals.

Biologically Active Species

Elements/Ions

Natural Products

Organic Compounds

Peptides

Proteins

Types of Drugs

Hormone Agonists

Hormone Antagonists

Enzyme Modulators

Ion Channel Inhibitors

Antibodies

Enzymes

Vaccines

Designing Drugs

1. Find a possible route for intervention

Designing Drugs

2. Find or Design a compound

a. Brute force

b. Rational drug design

Pharmacophore

SAR

QSAR

Structure-based

Designing Drugs

2. Find or Design a compound

c. Lead compound

d. Modified compounds

Testing

1. Pre-clinical

2. Phase 0

3. Phase I

4. Phase II

5. Phase III

6. Phase IV

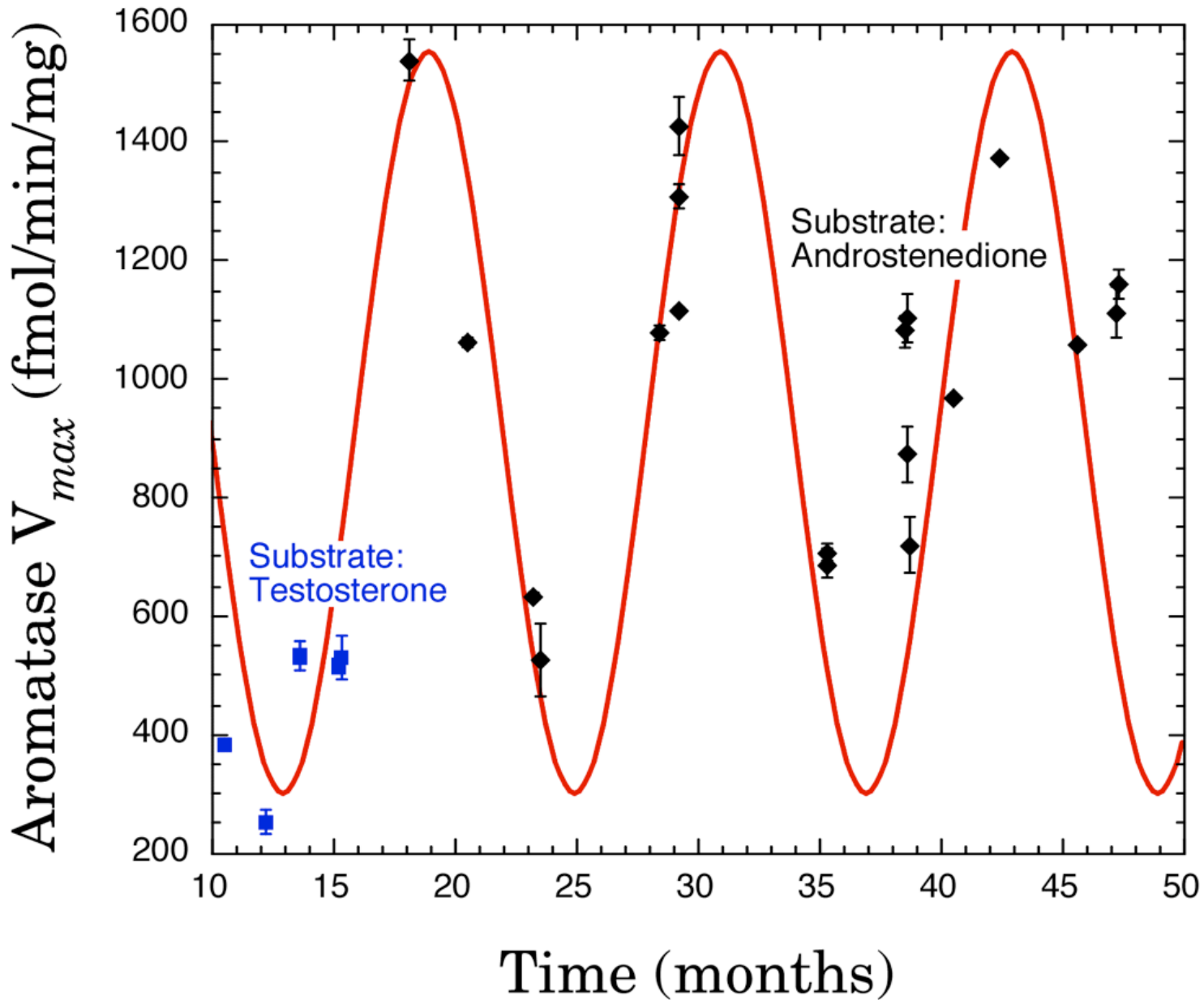
Confounding Factors

Genetic variation

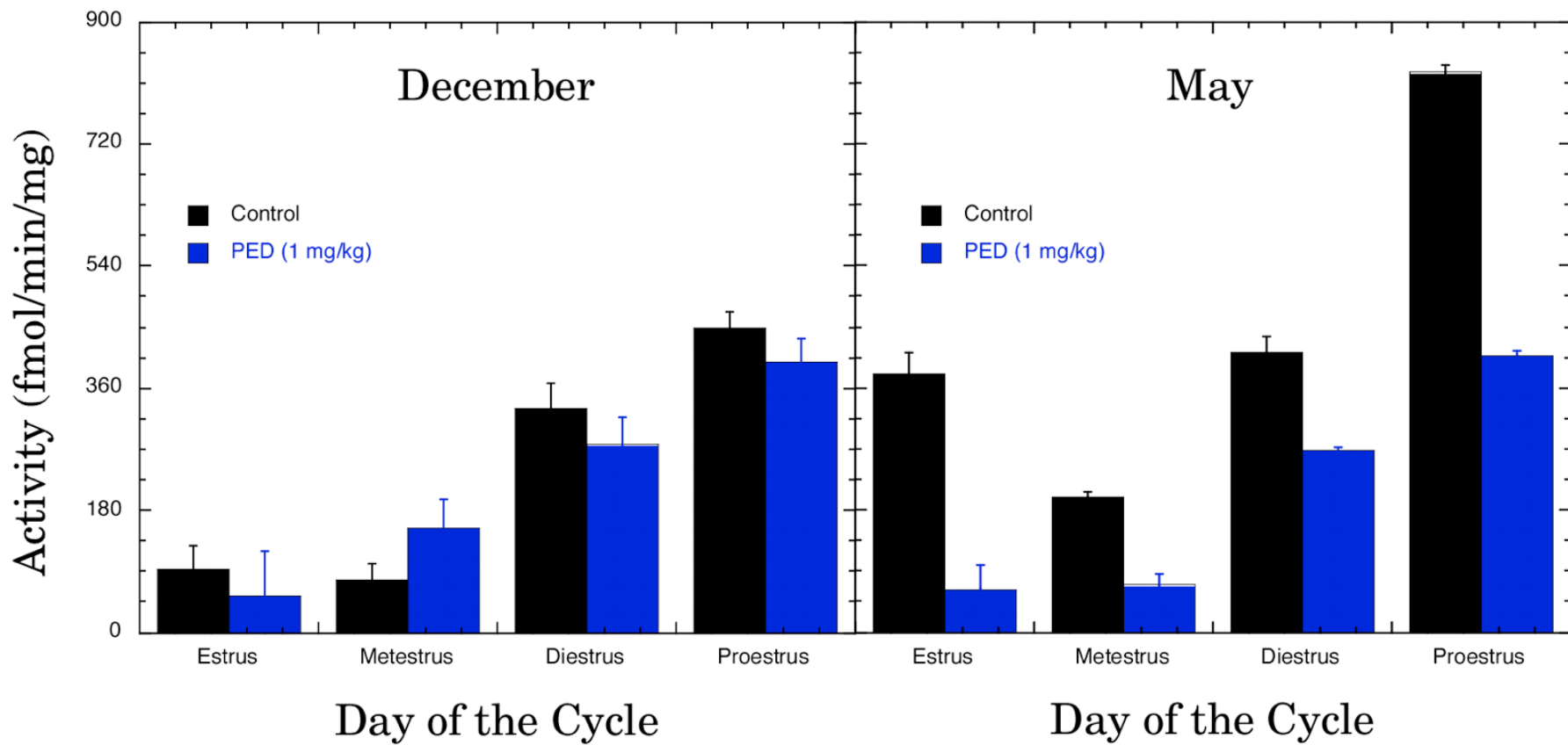
Life-style effects

Gender effects

Circannual Variation



Effect of Circannual Variations



Technical Issues

Pharmacodynamics

Technical Issues

Pharmacokinetics: ADME/Tox

Absorption

Distribution

Metabolism

Excretion

Toxicology

Technical Issues

Lipinski's Rule of Five:

$\text{Log } P \leq 5$

Hydrogen bond donor ≤ 5

Hydrogen bond acceptor ≤ 10

Molecular weight ≤ 500

Absorption

Oral

Inhaled

Injected

Intravenous

Sub-cutaneous

Intramuscular

Intraperitoneal

Transdermal

Distribution

Mechanism

Topical

Blood

Blood-brain barrier

Metabolism

How

Results

Location

Rate

Excretion

Route

Mechanism

Toxicology

Side-effects

IC_{50}

ED_{50}

TD_{50}

LD_{50}

Therapeutic index: TD_{50}/ED_{50}

Production

“Particle Physics”

Consistency of dose

Stability

Size

Elegance