

Designing a Computer Simulation Tool for PET Neuroimaging

Tom Morin

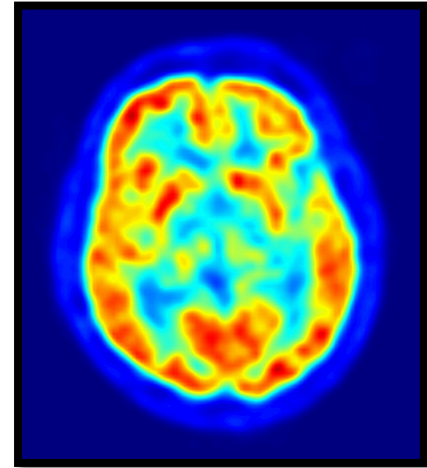
Hooker Research Group

Athinoula A. Martinos Center for Biomedical Imaging

Massachusetts General Hospital

Harvard Medical School

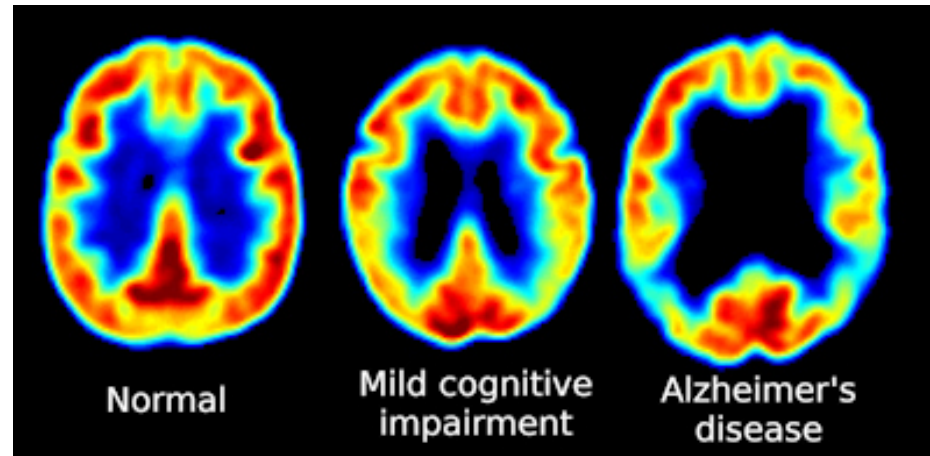
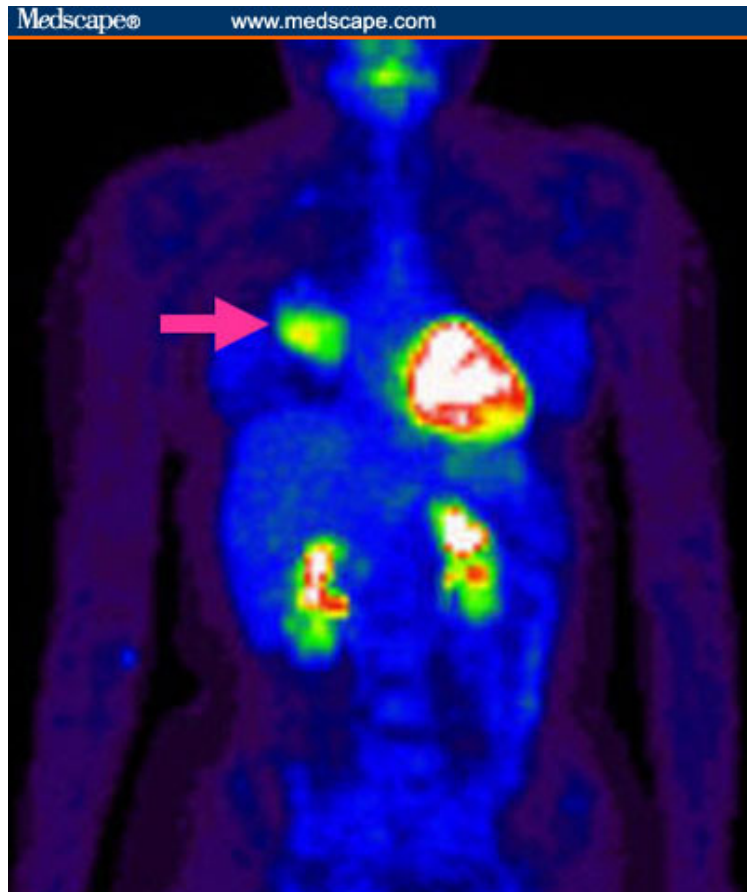
Positron Emission Tomography (PET)



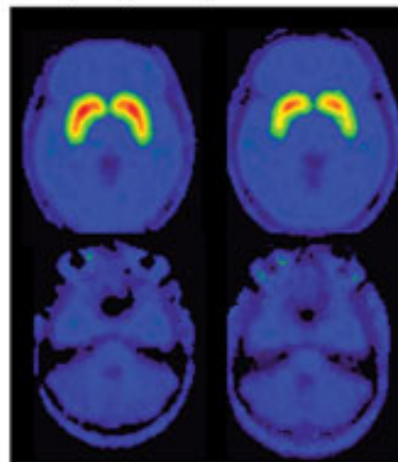
Procedure:

1. Inject a Radiotracer
2. Take the Scan
3. Get Blood Data (optional)
4. Analyze Data

Applications of PET



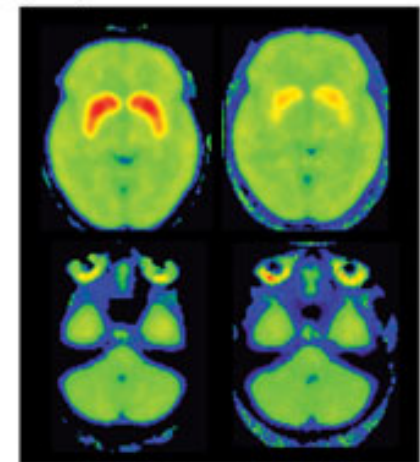
A $[^{11}\text{C}]\text{raclopride}$



Placebo

Modafinil

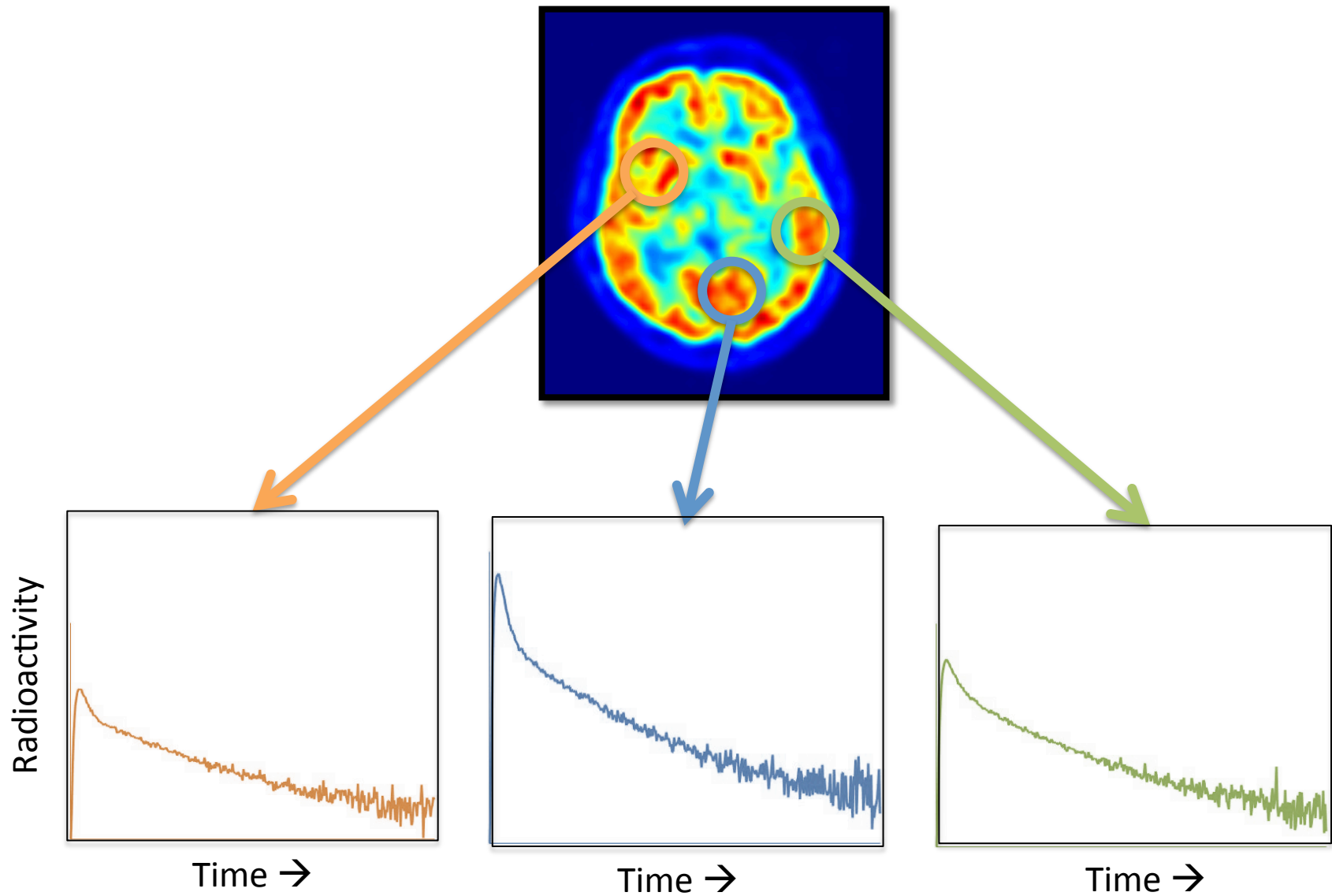
B $[^{11}\text{C}]\text{cocaine}$



Placebo

Modafinil

Time Activity Curves (TACs)



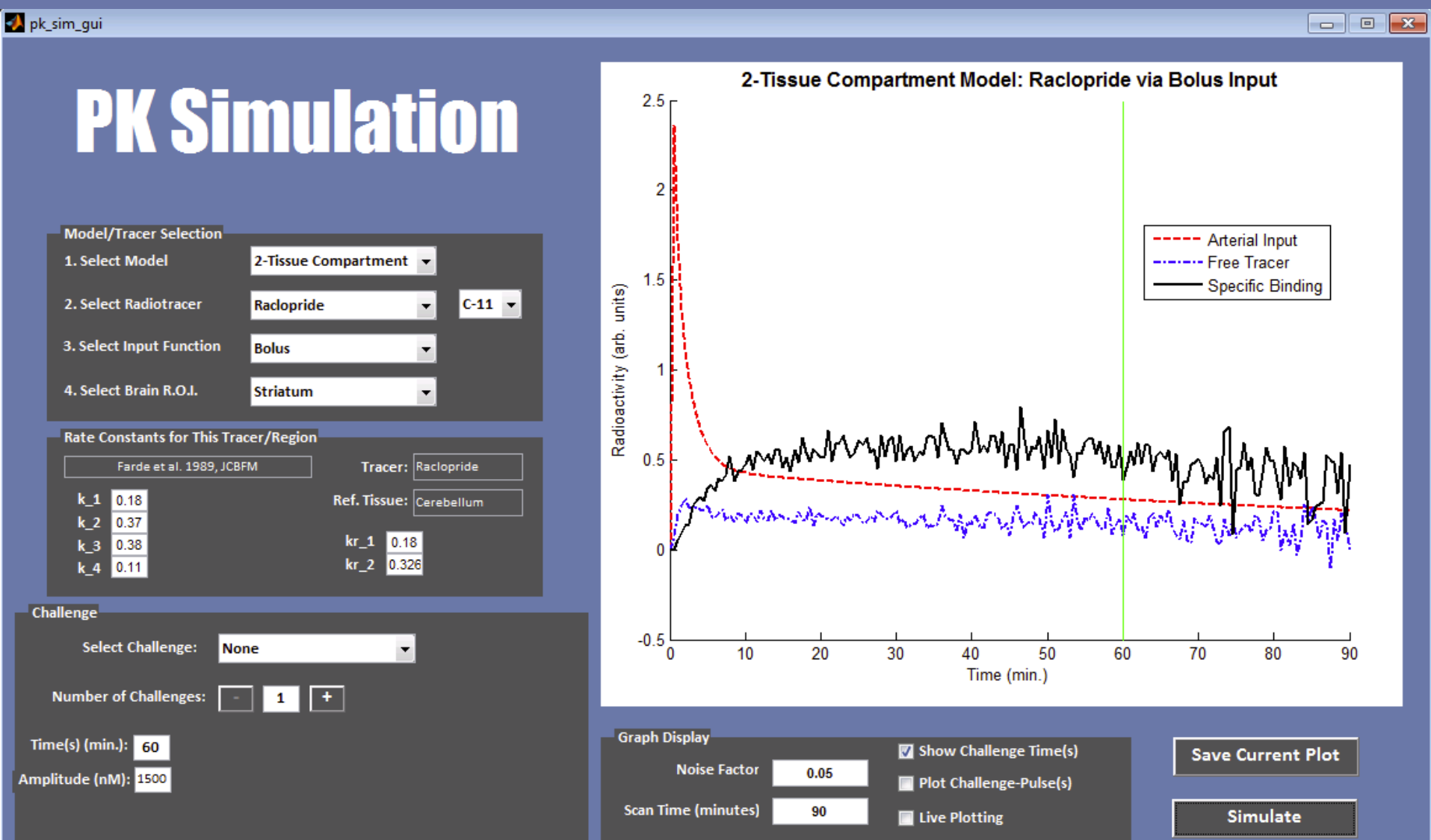
Problems With PET

- High cost machinery & staff
- Scan requires intense coordination and advanced planning
- Small procedural changes can have a big impact on results

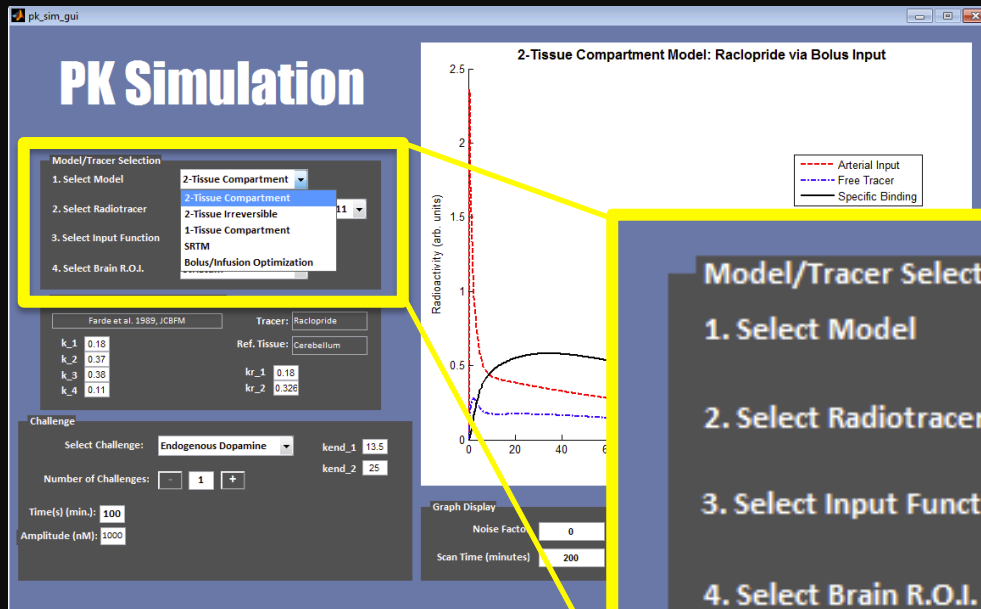
Why Use Simulation?

- Evaluate study feasibility (conserve resources)
- Strategically choose and optimize experimental design
- Facilitate new methods development

Simulation Tool Screenshot



Kinetic Models



Model/Tracer Selection

1. Select Model

2. Select Radiotracer

3. Select Input Function

4. Select Brain R.O.I.

2-Tissue Compartment

2-Tissue Compartment

2-Tissue Irreversible

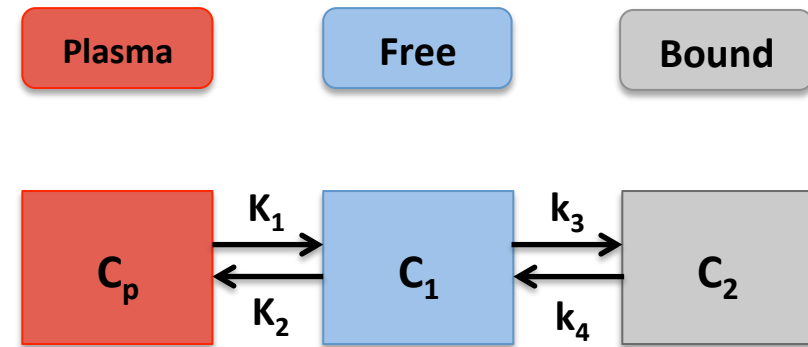
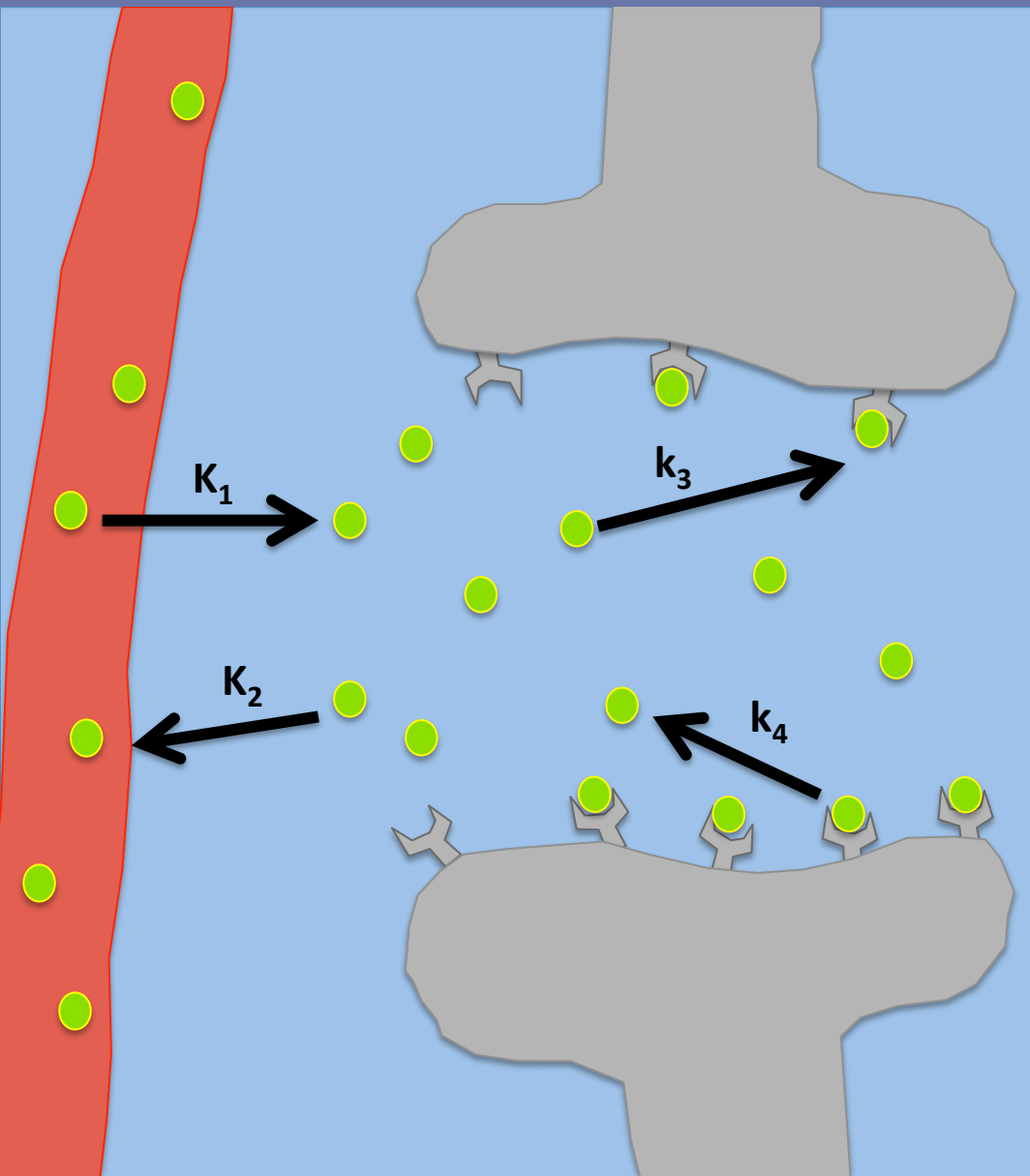
1-Tissue Compartment

SRTM

Bolus/Infusion Optimization

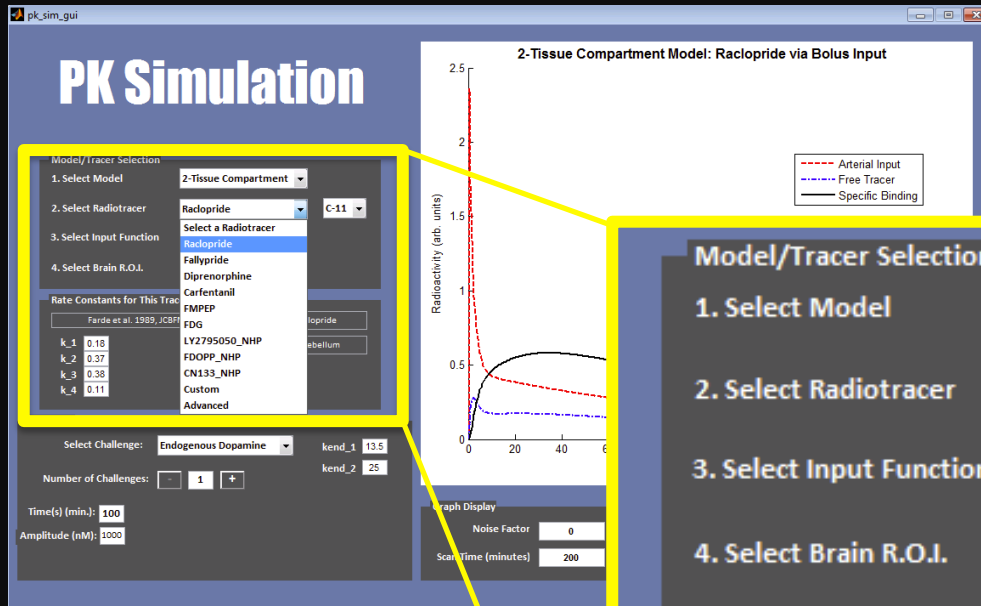
Rate Constants for This Tracer / Region

2-Tissue Compartment Model



$$\begin{aligned}\frac{dC_1(t)}{dt} &= K_1 C_p(t) - (k_2 + k_3) C_1(t) + k_4 C_2(t) \\ \frac{dC_2(t)}{dt} &= k_3 C_1(t) - k_4 C_2(t)\end{aligned}$$

Radiotracers



Model/Tracer Selection

1. Select Model: 2-Tissue Compartment

2. Select Radiotracer: Raclopride

3. Select Input Function: Select a Radiotracer

4. Select Brain R.O.I.: C-11

Rate Constants for This Tracer

Farde et al. 1989, JCBF

k ₁	0.18
k ₂	0.37
k ₃	0.38
k ₄	0.11

Select Challenge: Endogenous Dopamine

Number of Challenges: 1

Time(s) (min.): 100

Amplitude (nM): 1000

Graph Display

Noise Factor: 0

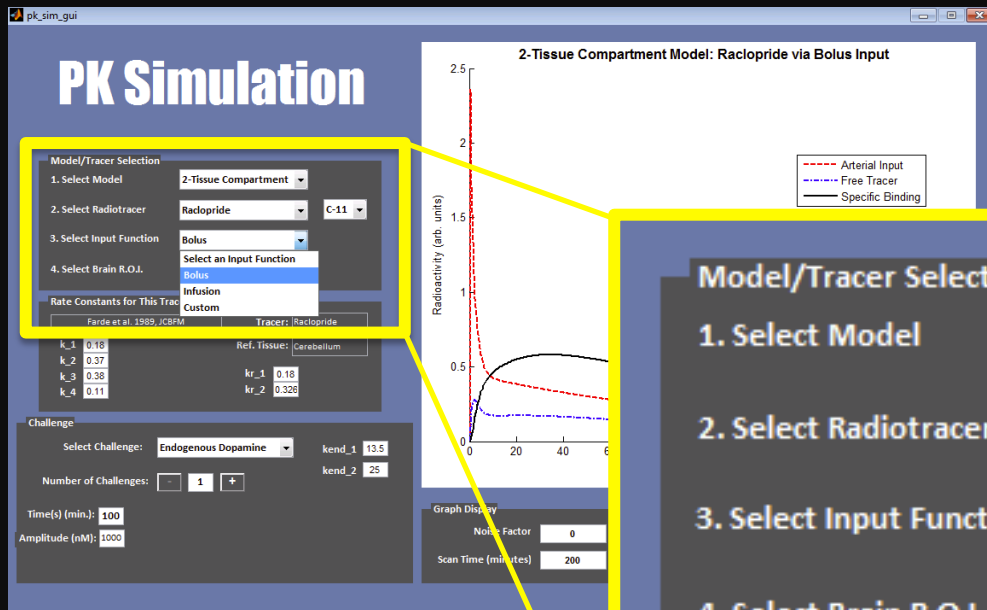
Scan Time (minutes): 200

2-Tissue Compartment Model: Raclopride via Bolus Input

Radioactivity (arb. units)

Legend: Arterial Input, Free Tracer, Specific Binding

Plasma Input Functions



Model/Tracer Selection

1. Select Model: 2-Tissue Compartment
2. Select Radiotracer: Raclopride
3. Select Input Function: Bolus
4. Select Brain R.O.I.: C-11

Rate Constants for This Tracer

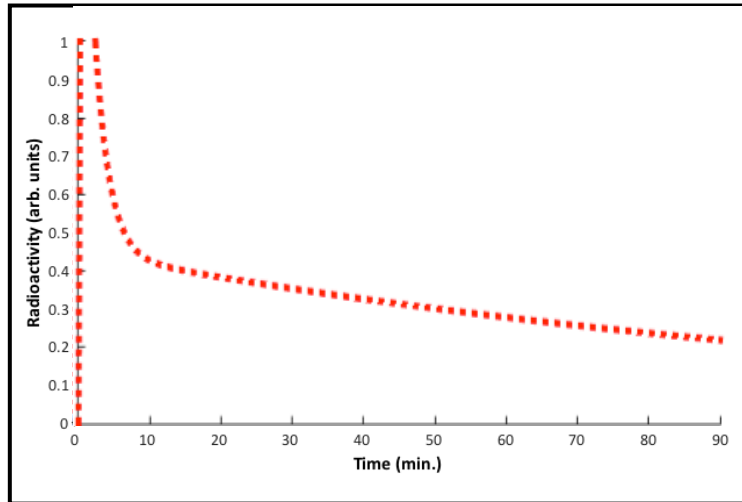
Farde et al. 1989, JCBFM

Tracer: Raclopride

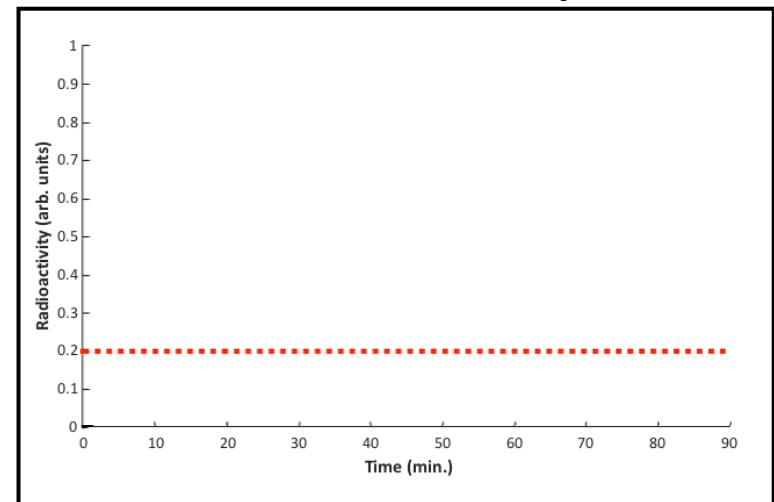
Plasma Input Functions

Example. [^{11}C]Raclopride (dopamine D2/3 selective)

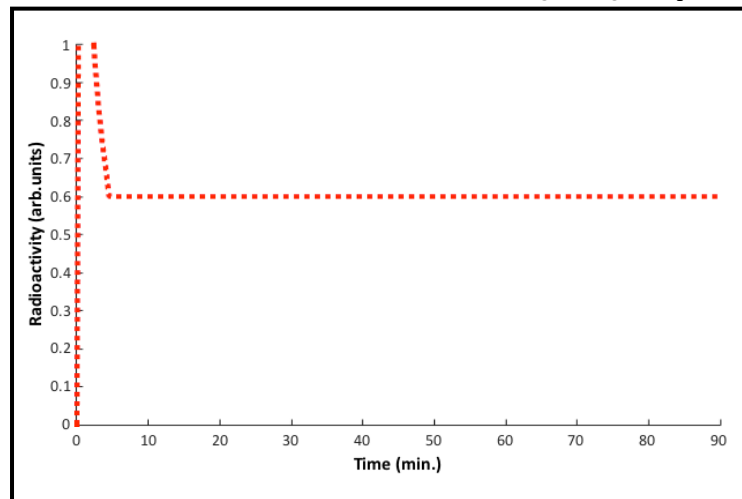
Bolus Input



Constant Infusion Input

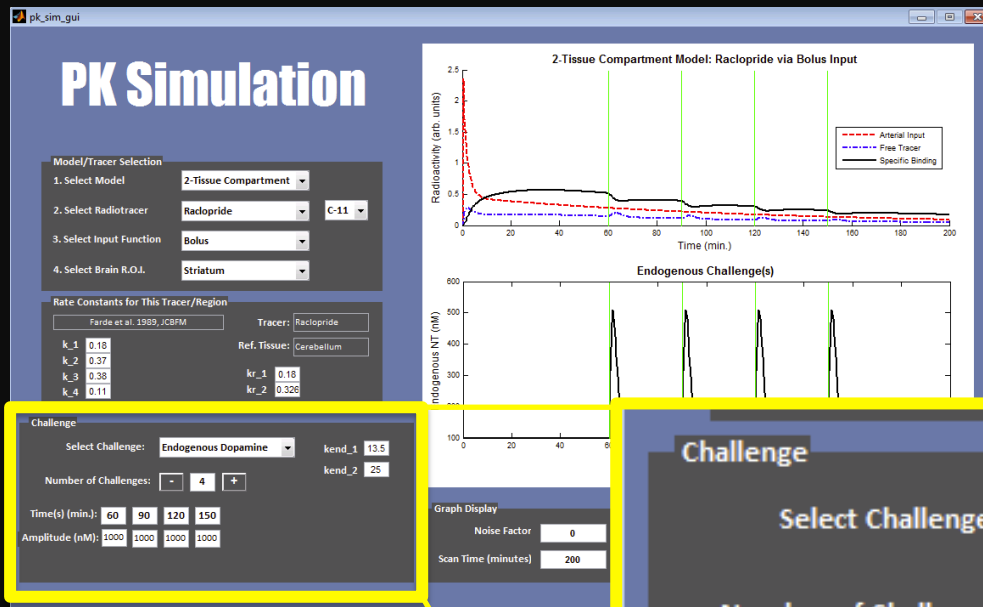


Bolus + Constant Infusion (B/I) Input



■ ■ ■ ■ Plasma Input

Competition



Challenge

Select Challenge: Endogenous Dopamine

Number of Challenges: - 4 +

Time(s) (min.): 60 90 120 150

Amplitude (nM): 1000 1000 1000 1000

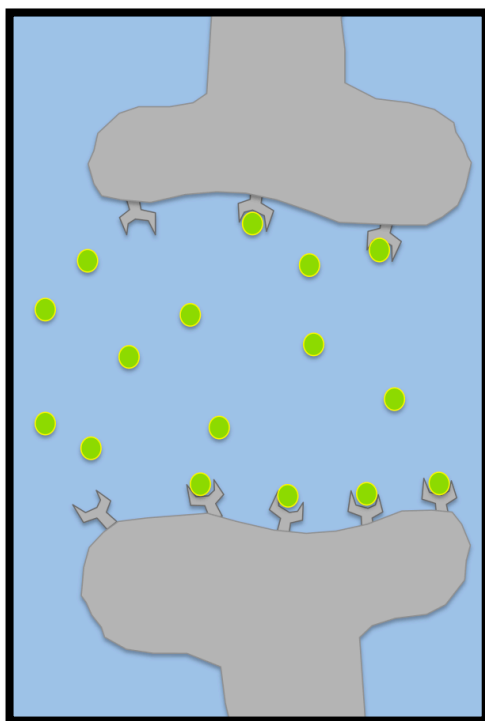
kend_1 13.5

kend_2 25

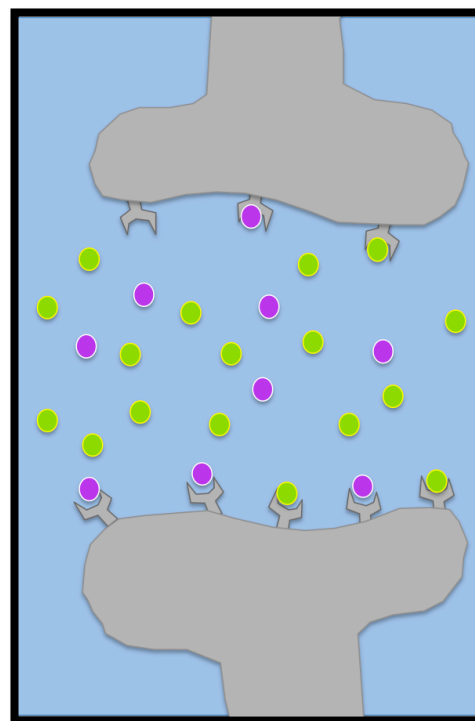
Competition

- **Endogenous**
 - ex. [^{11}C]raclopride & dopamine-releasing reward task
- **Exogenous** (pharmacological challenge)
 - ex. [^{11}C]carfentanil with morphine

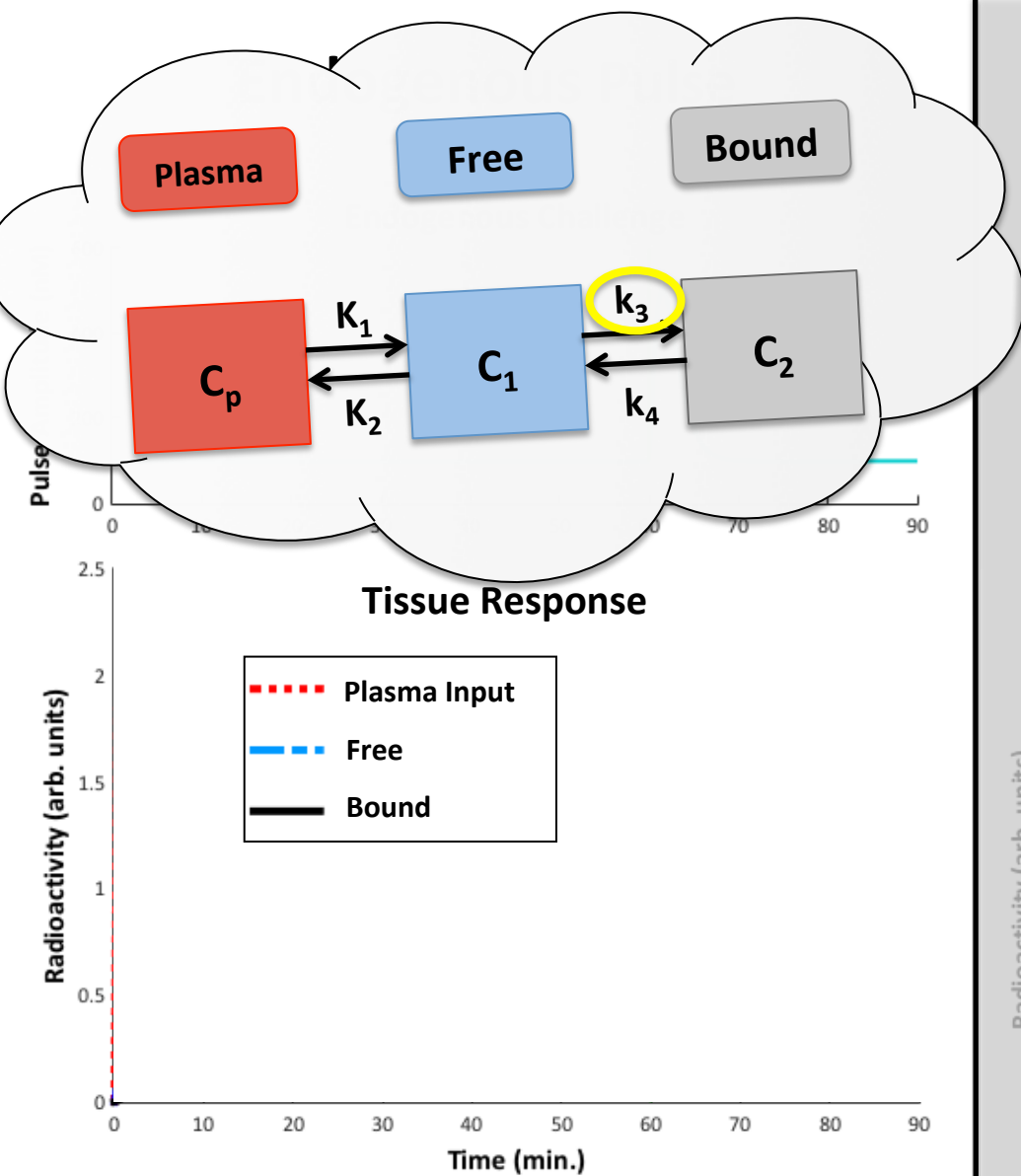
**Before
Challenge**



**After
Challenge**



Simulating Competition



Alter Rate Constants (One Method to Simulate Exogenous Challenge)

Challenge

Select Challenge:

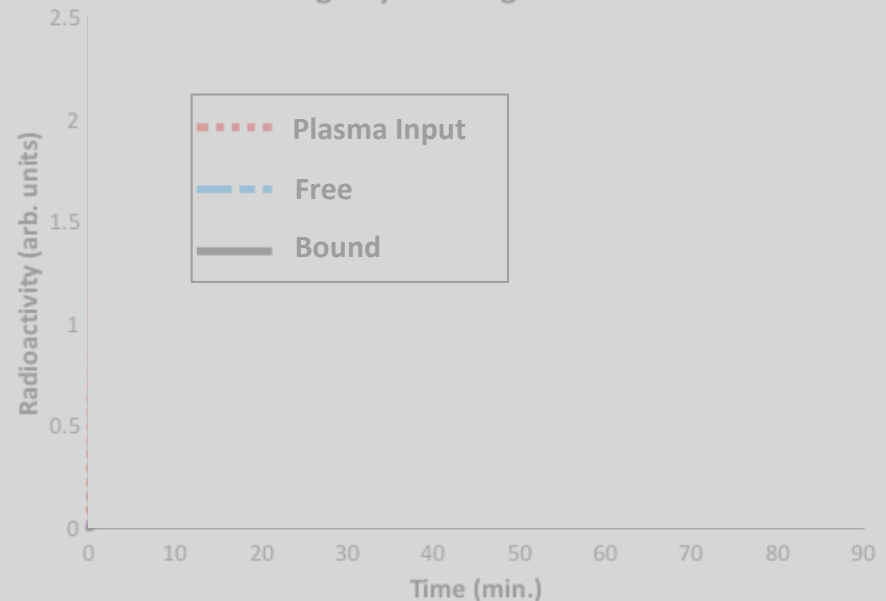
Number of Alterations:

Time(s) (min.):

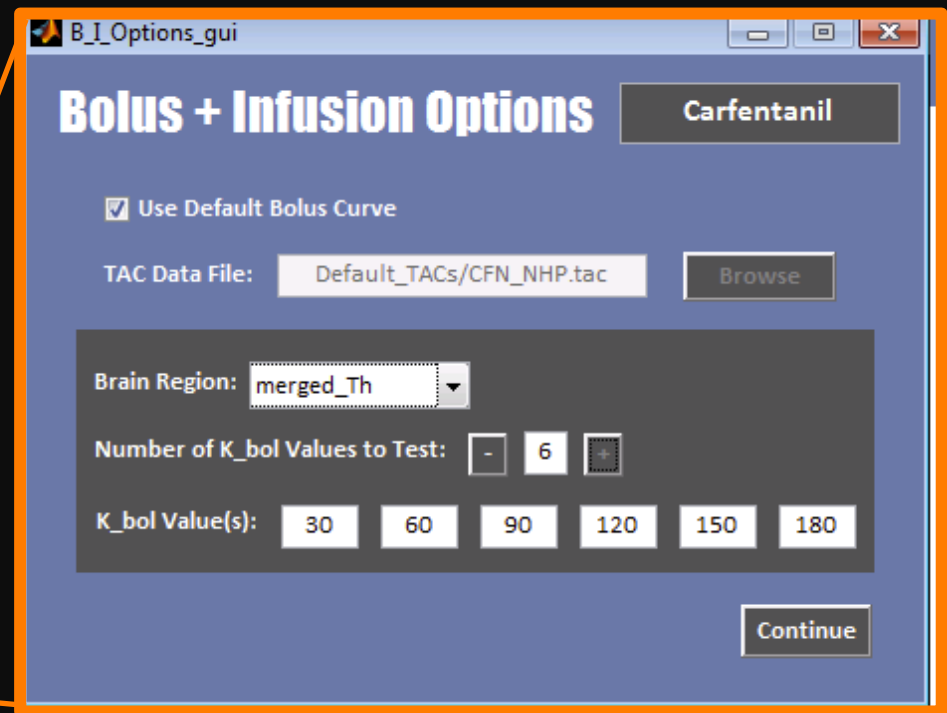
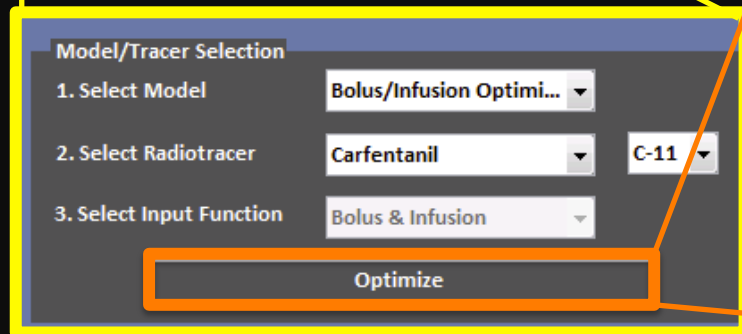
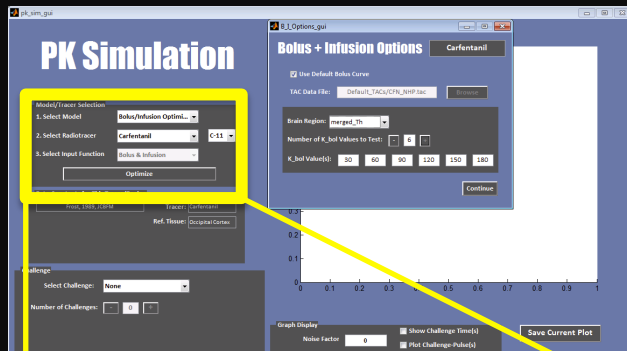
k_3 Value(s):

k_4 Value(s):

Challenge by Altering Rate Constants



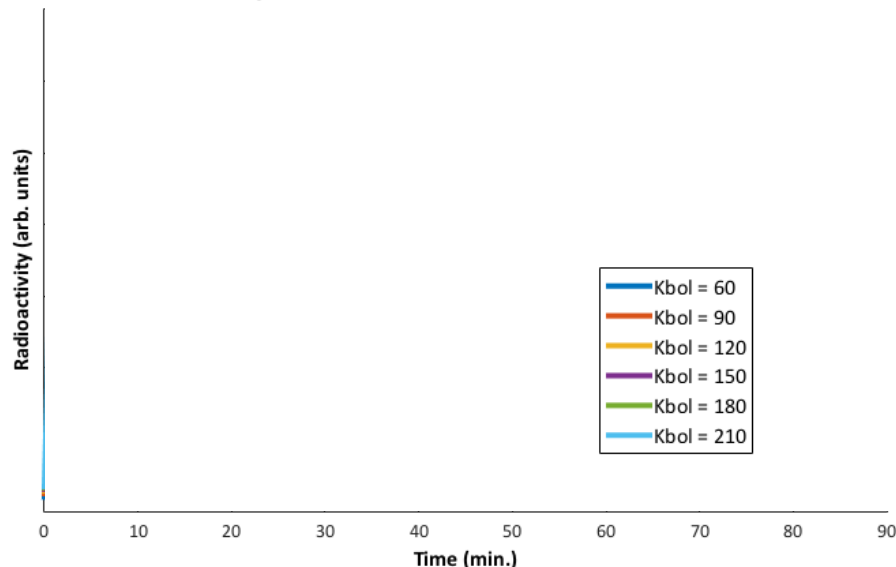
Bolus + Constant Infusion



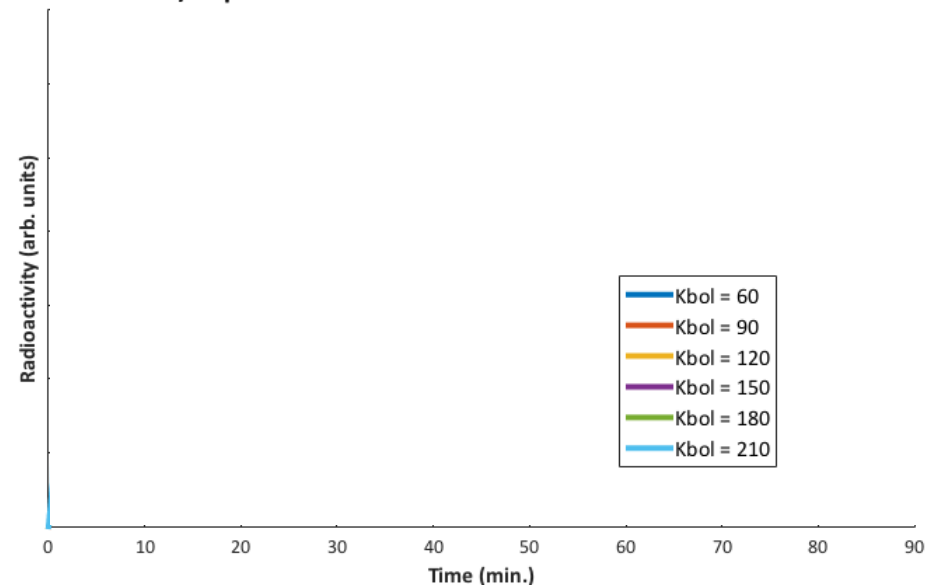
Bolus + Constant Infusion Optimization

- Regular bolus injection followed by continuous infusion
- K_{bol}
 - Bolus dose measured in minutes of infusion dose
 - Units = minutes
- Adjusting K_{bol} (adjusting how much radiotracer is initially injected), allows tracer to reach equilibrium more quickly
- Optimal K_{bol} will vary slightly between subjects and must be determined for each radiotracer

B/I Optimization for Carfentanil with REAL Data



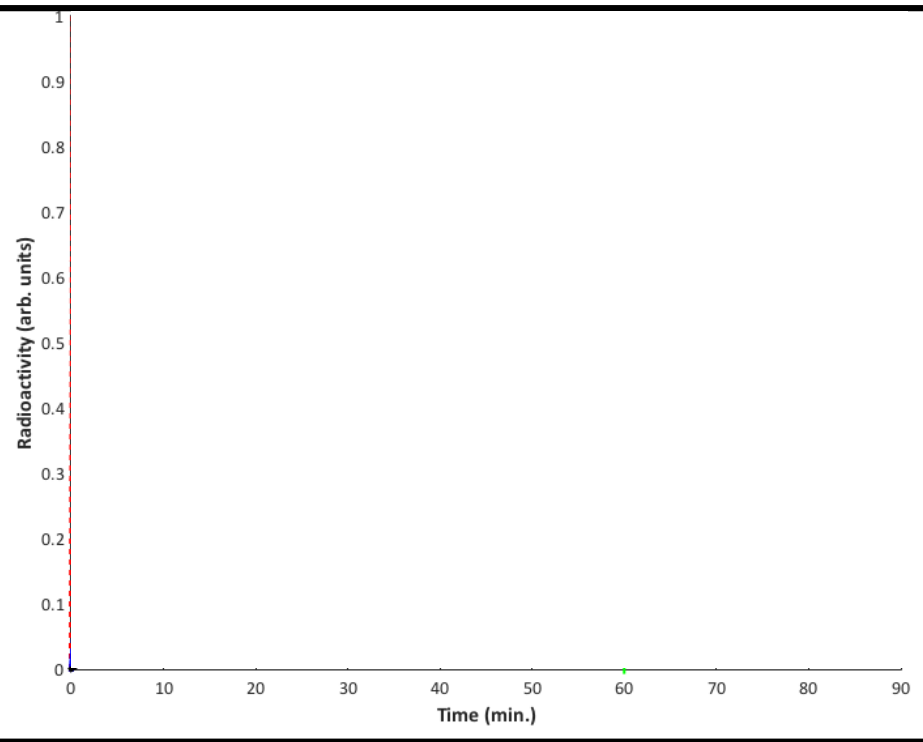
B/I Optimization for Carfentanil with SIMULATED Data



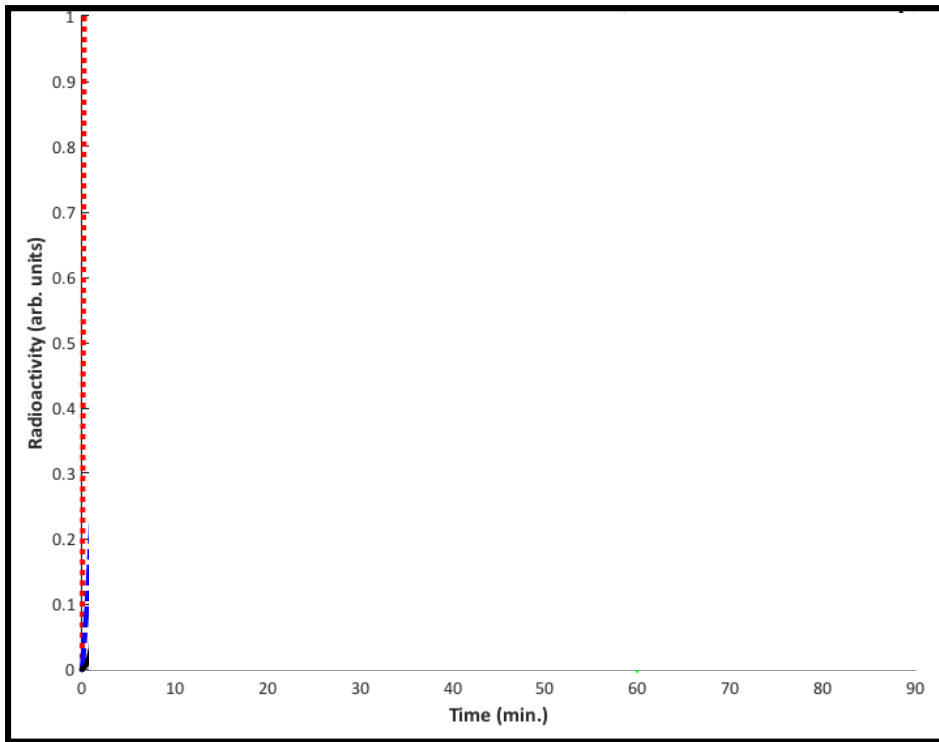
Competition with Bolus + Constant Infusion

Example: [^{11}C]Raclopride with Endogenous Dopamine Challenge at 60 min.

BOLUS Input



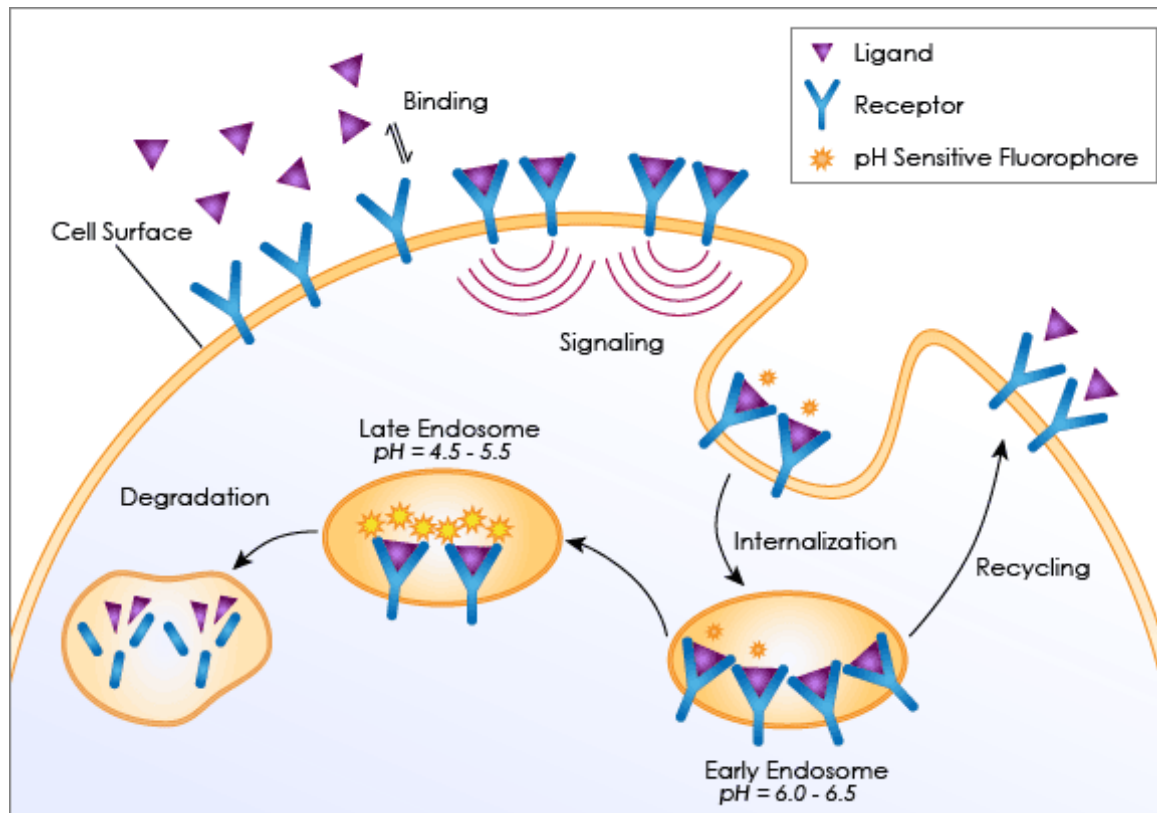
BOLUS + CONSTANT INFUSION Input



--- Plasma Input - - - Free — Bound

Future Direction

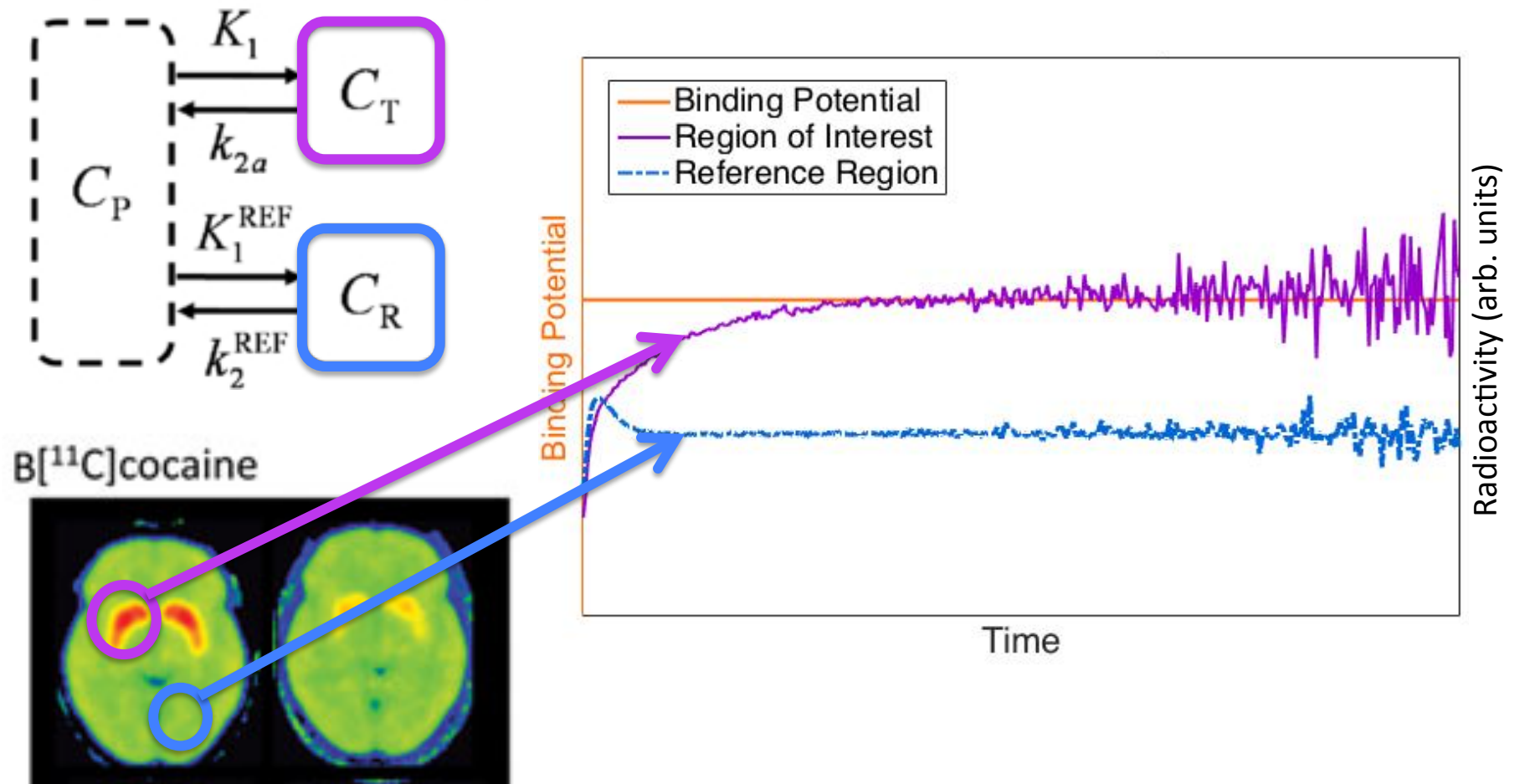
Receptor Internalization Models:



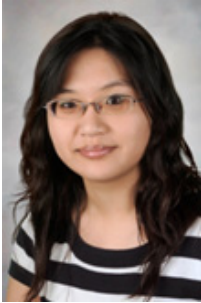
<http://www.nexcelom.com/Celigo/receptor-internalization-assay.php>

Future Direction

Reference Tissue Models:



Acknowledgements



Project Mentor:

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Principle Investigator:

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