Functional Neuroimaging with PET

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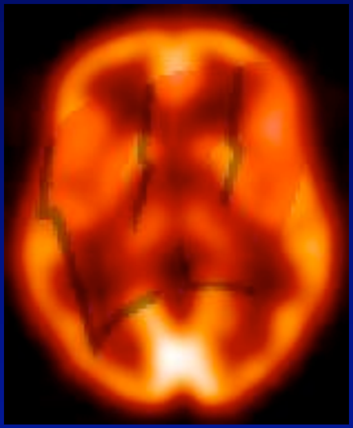
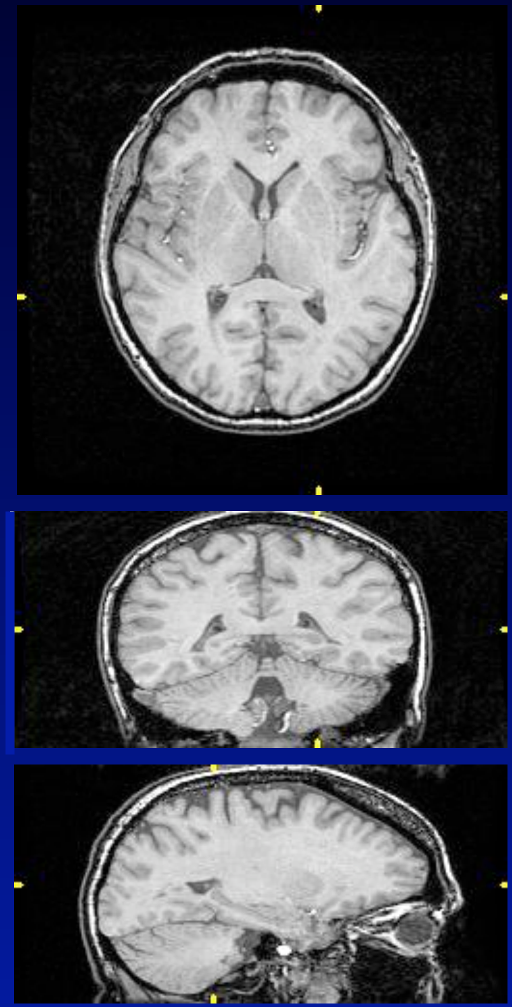


Seeing the Brain

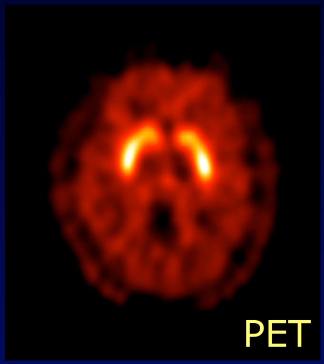
Just look at it!

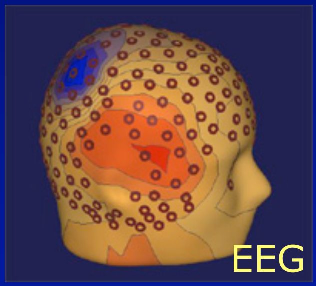
(Just try to get informed consent!)

Anatomic Images (MRI)



Functional Images





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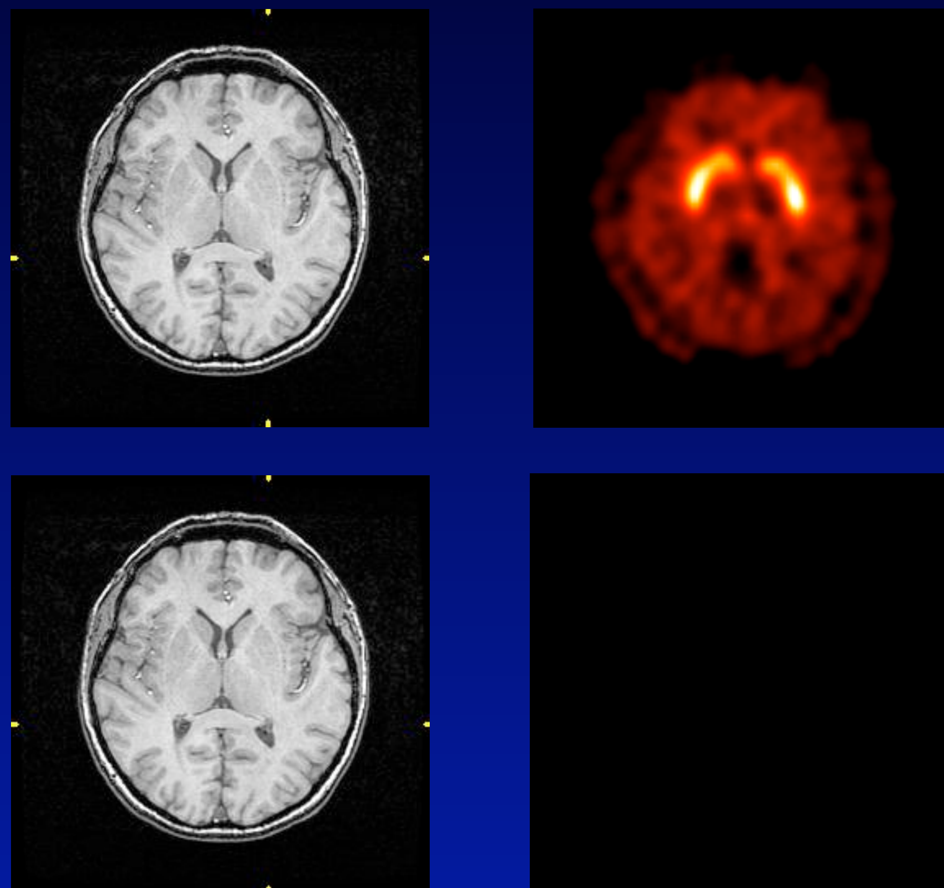
What is a Functional Image?

Anatomic Image | Functional Image

Live volunteer

Dead volunteer



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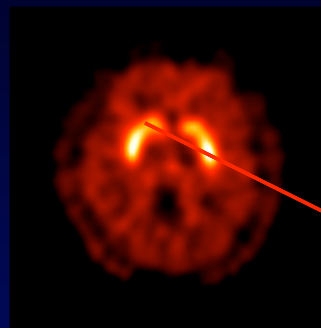
Parametric Images

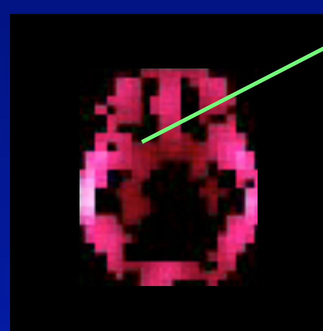
Associating a parameter of interest with locations (voxels) throughout the brain.

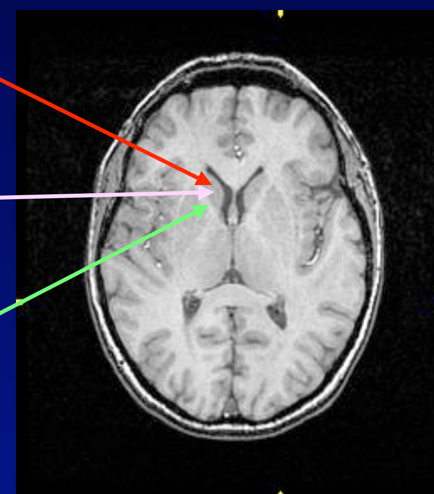
PET: concentration of radioactivity (mCi/cc brain tissue)



fMRI: paramagnetic signal from deoxygenated hemoglobin (~volts)

EEG: electrical signal strength (volts)





MRI: T1-weighted paramagnetic spin realignment (~volts)

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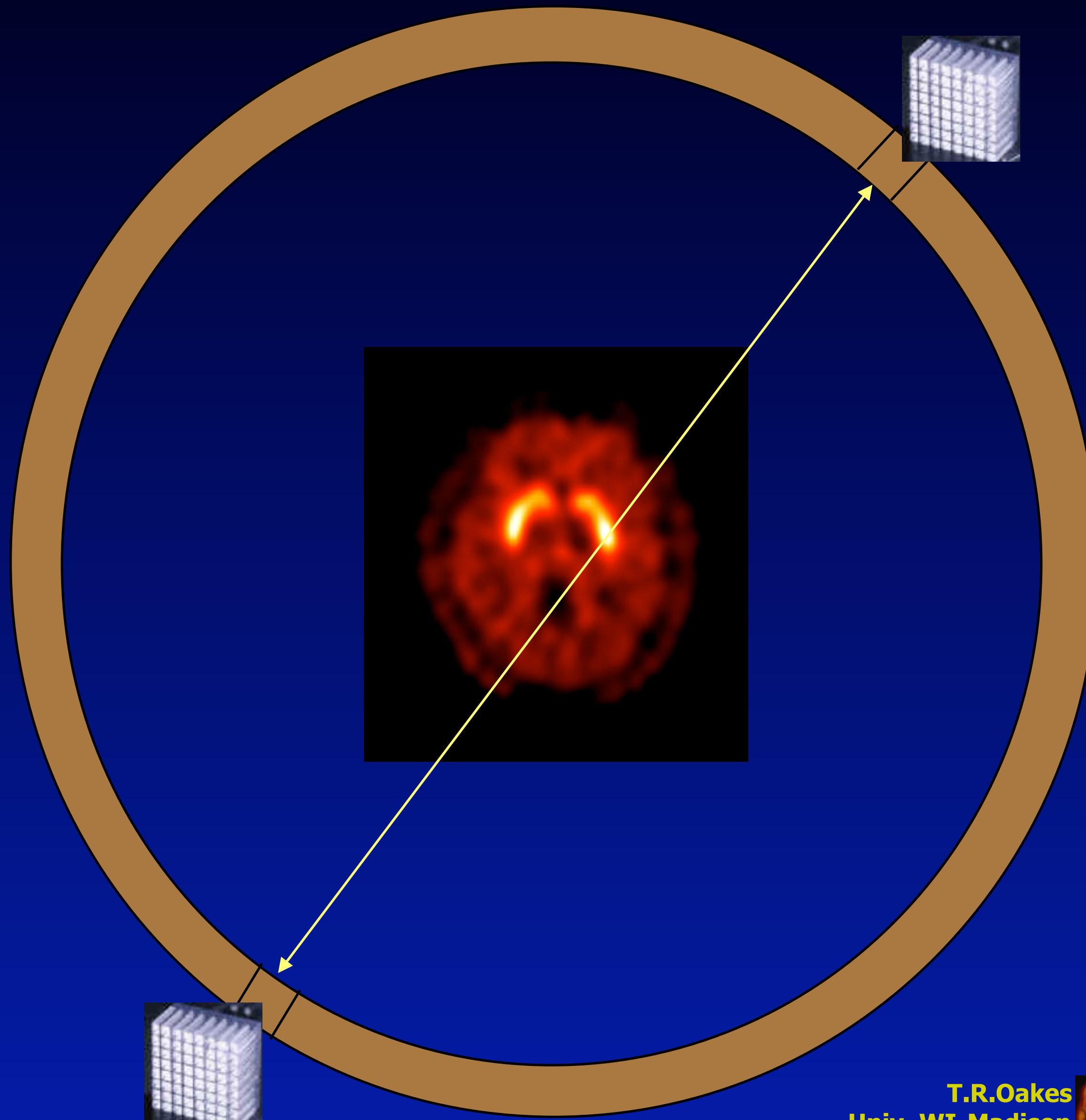
A Functional Image starts with a Measurement



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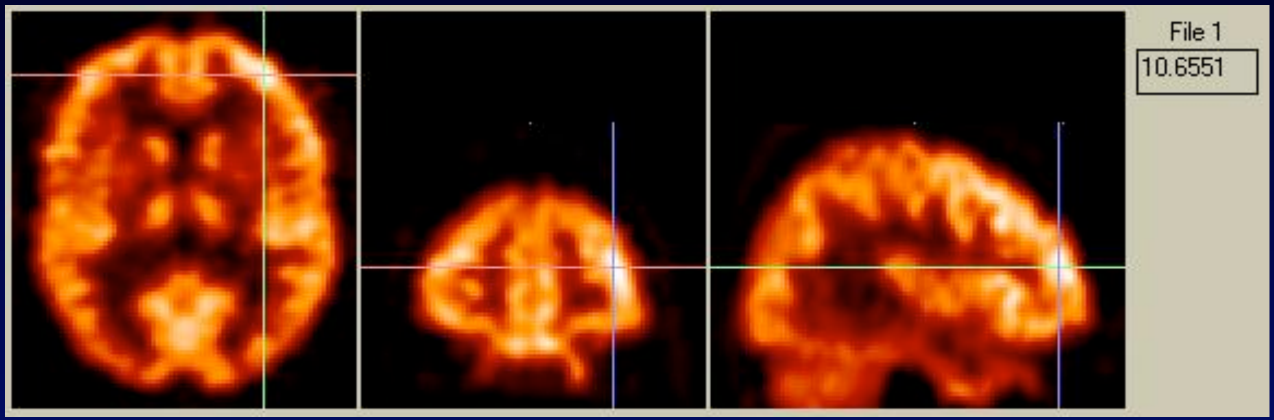
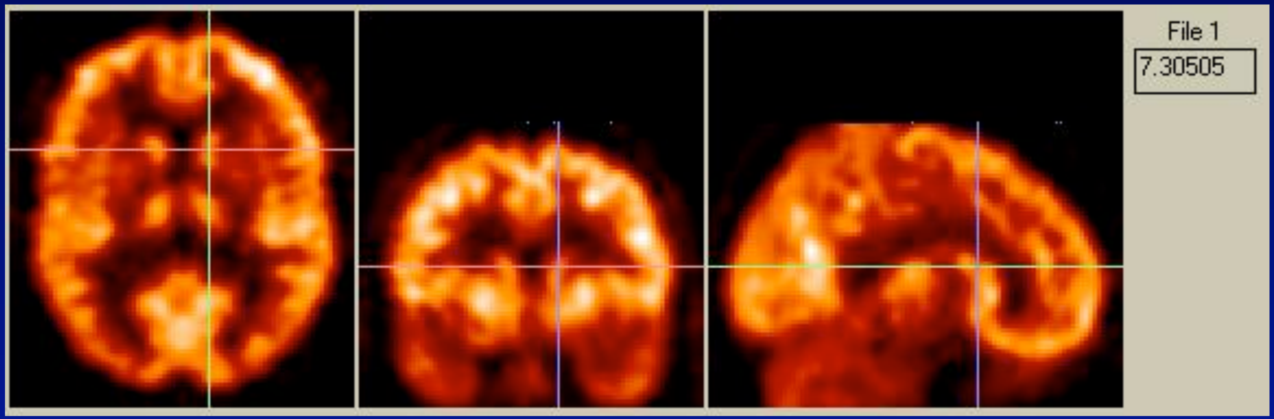
Extracting Data from Images





Examine values at specific locations (voxels) throughout the image volume.

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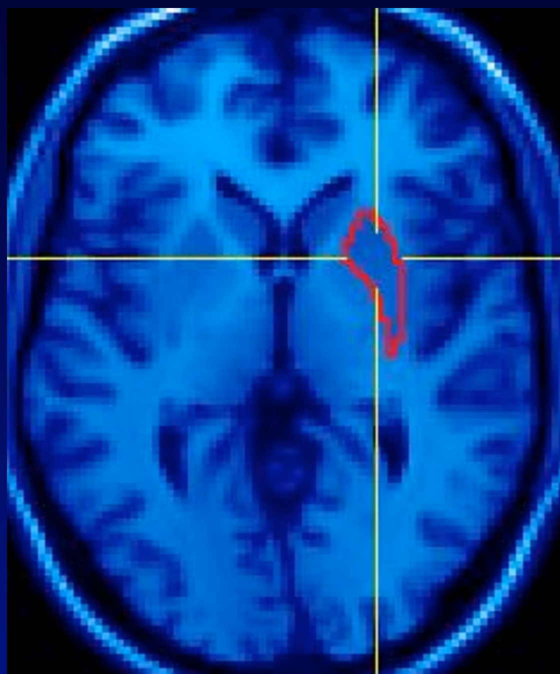
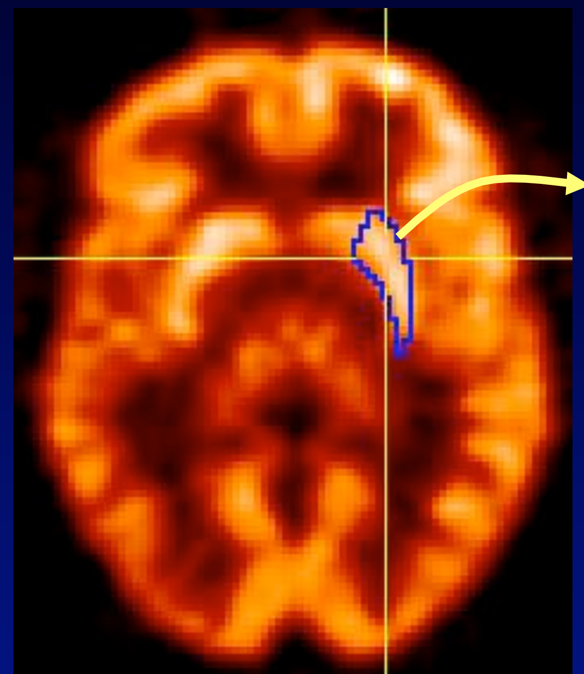
Extracting Data from Images

ROI Analysis: Extracting the average value for all voxels within a Region-of-Interest.



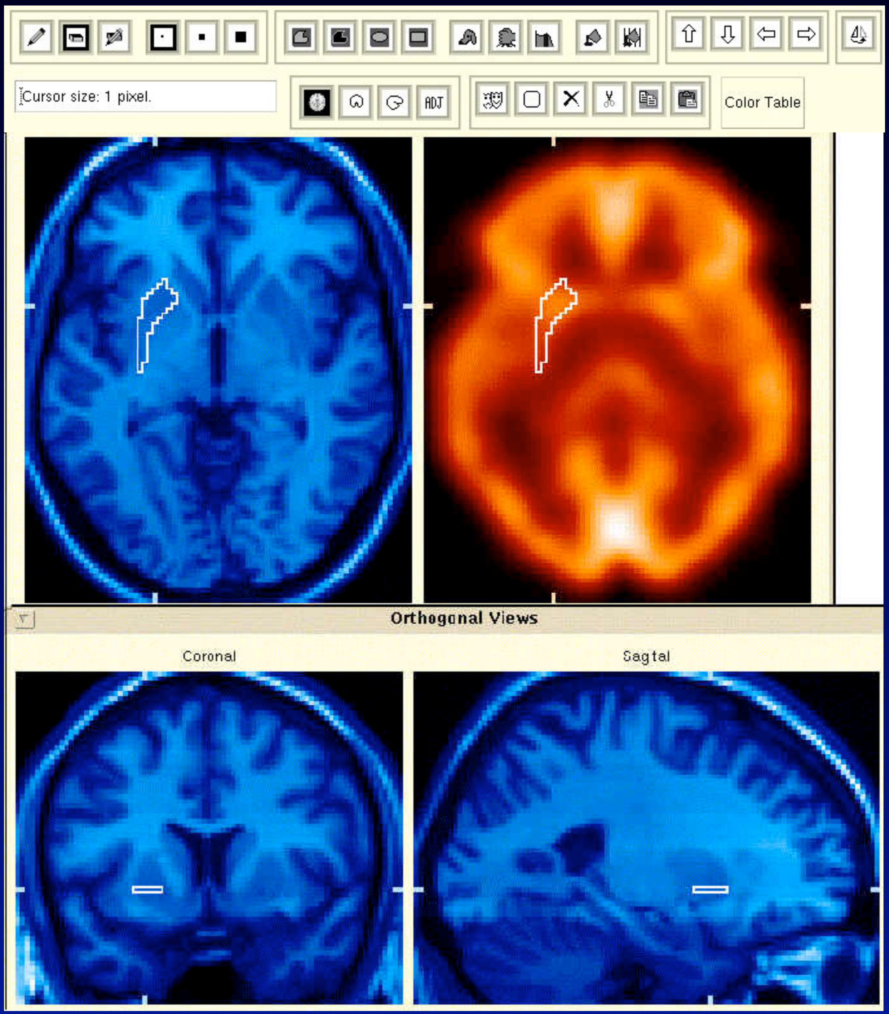
ROI is drawn on MRI image.

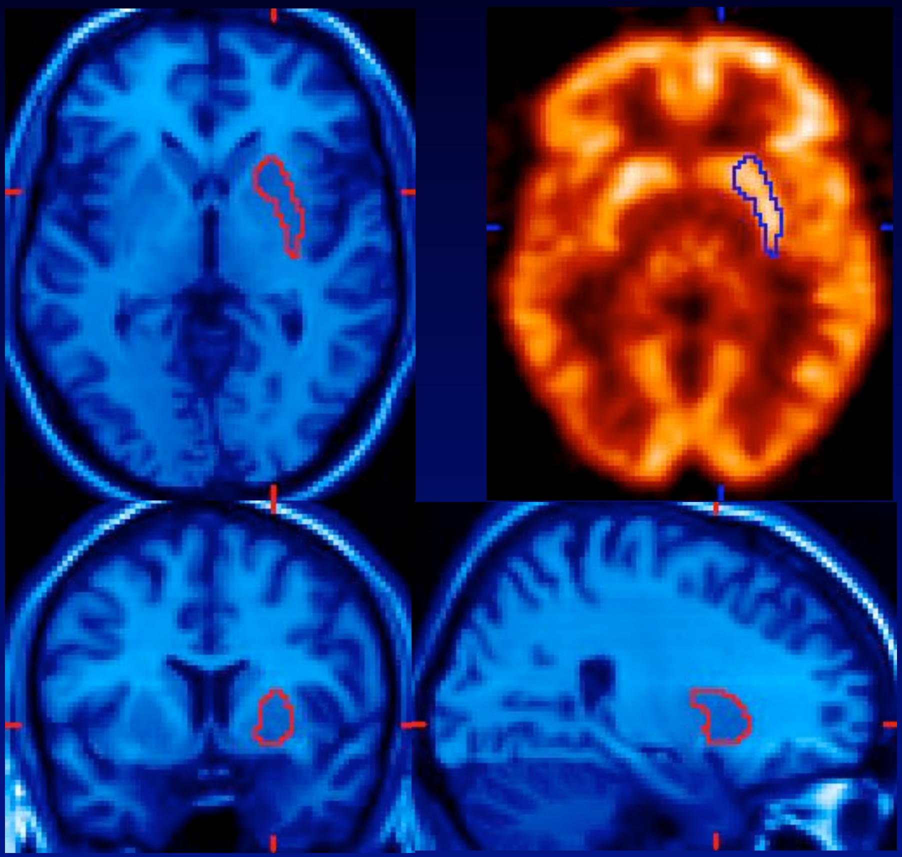


Average value of voxels inside ROI is 6.7 microCi/cc

ROI value is extracted from functional image.

ROI Analysis





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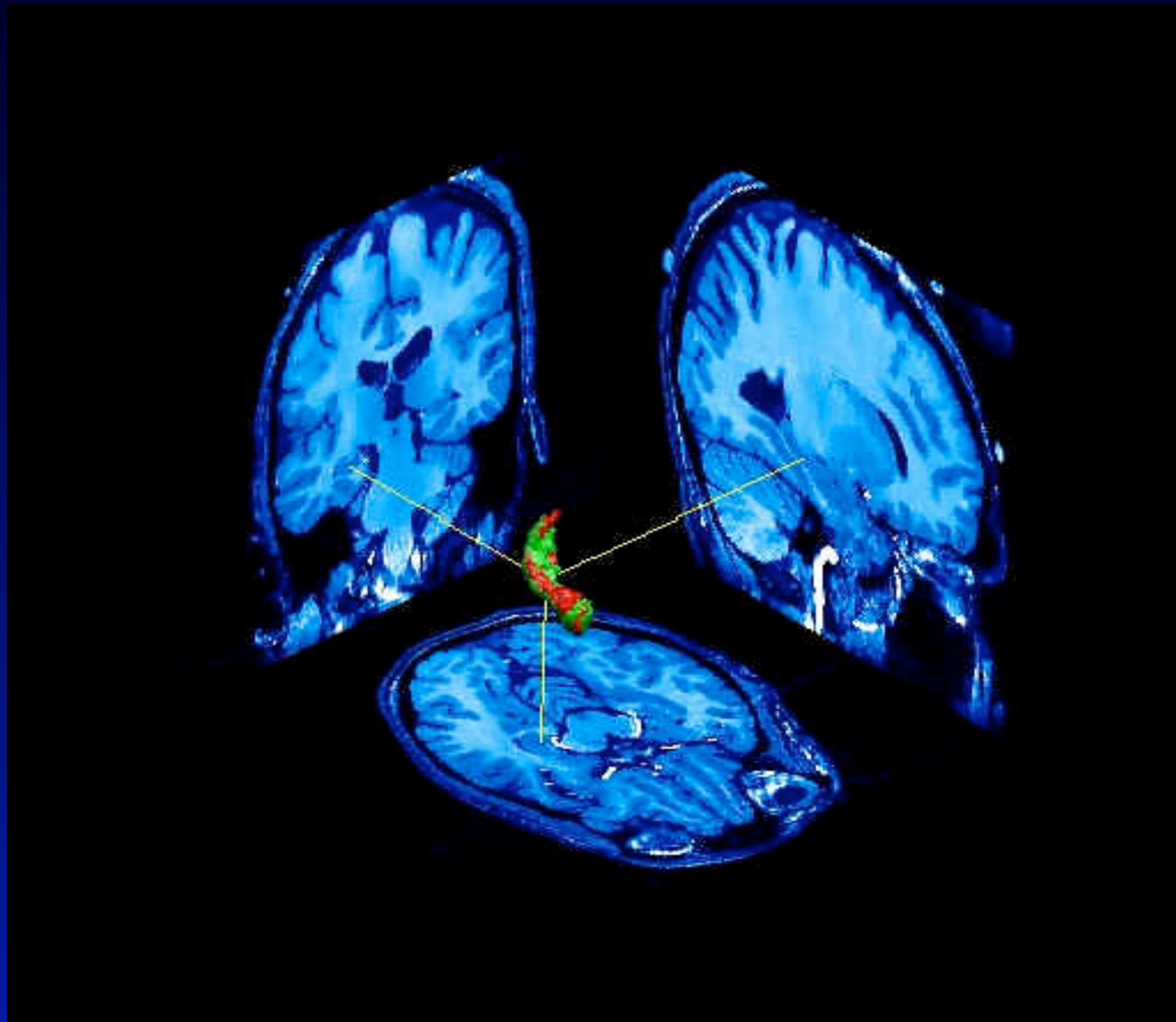
ROI Analysis: Morphometry

Measuring the volume of an anatomic structure.



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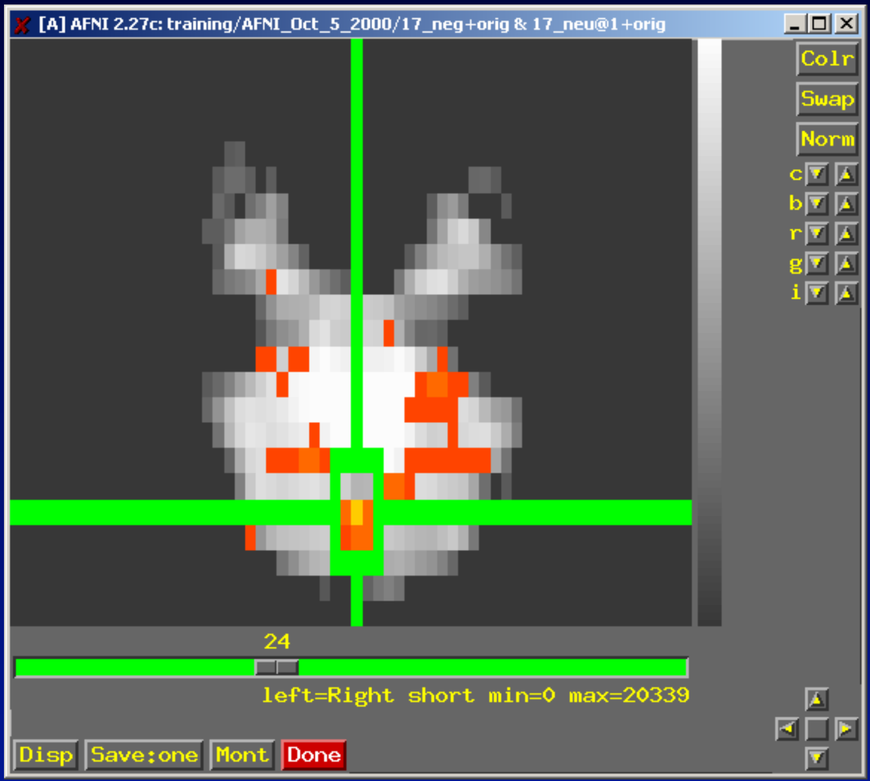
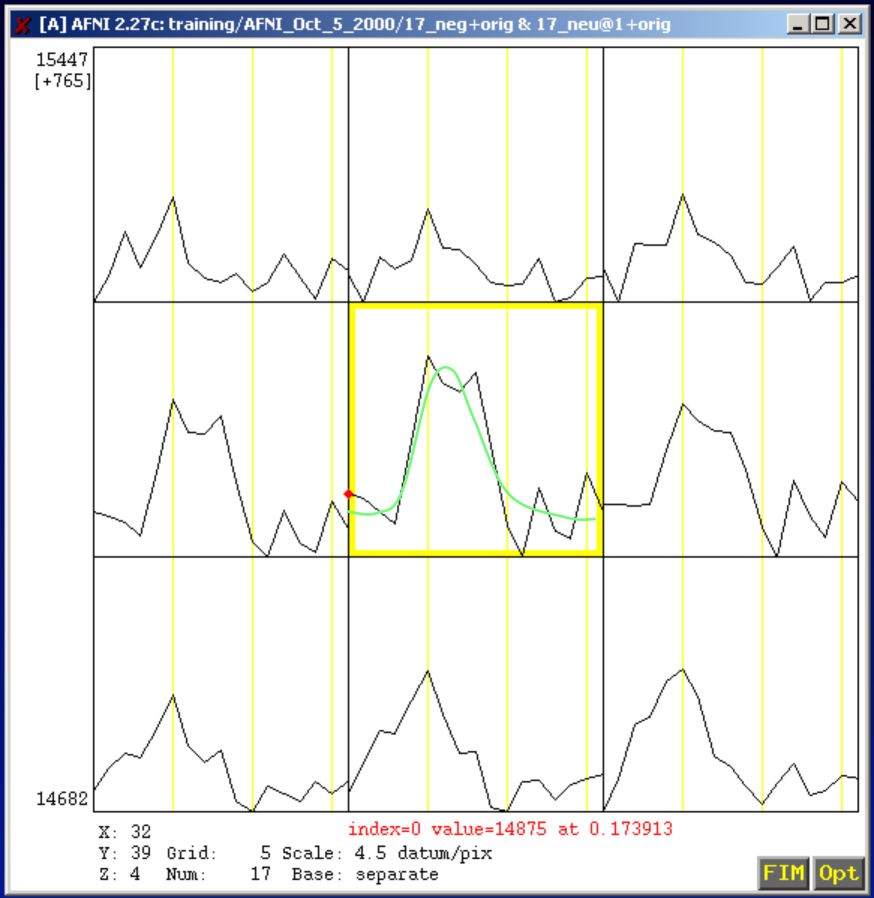
Extracting Data from Images

Time series: examining how data in a voxel changes over time.



fMRI image with overlay showing degree of correlation to ideal response function.



Time series over 17 sec for 9 voxels shown inside green rectangle. (Ideal response function shown in green.)

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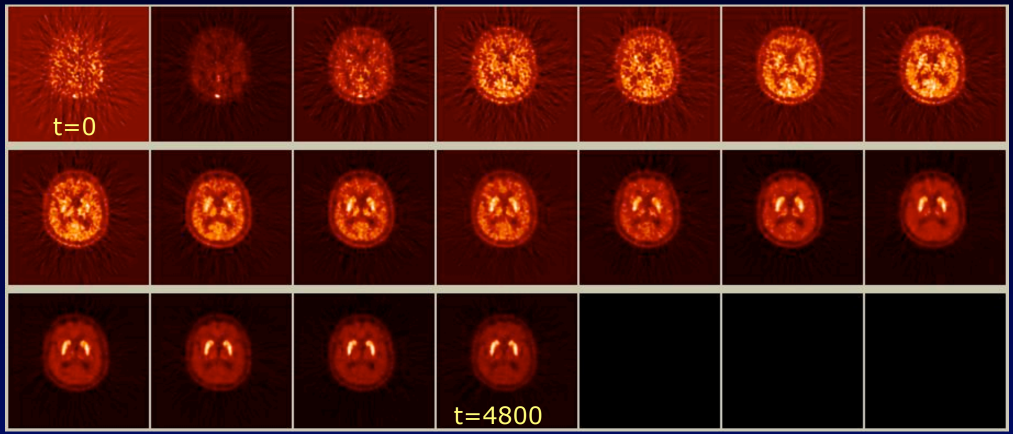
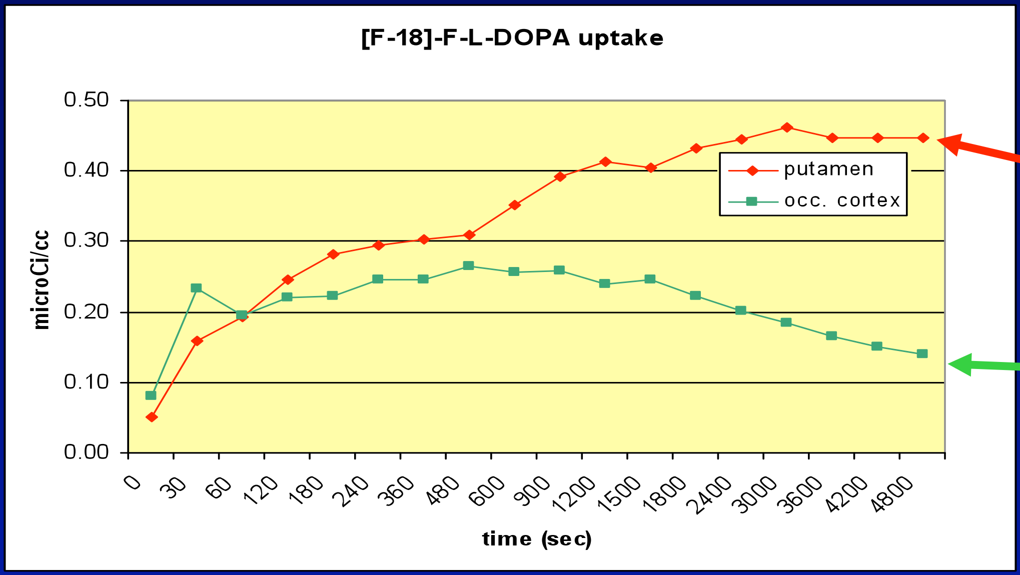
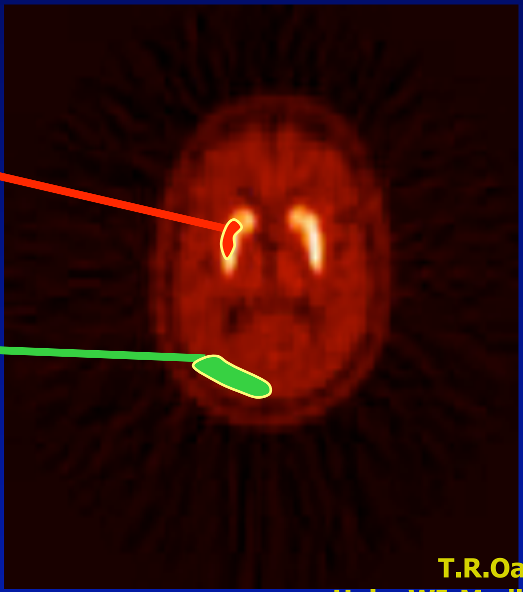
Extracting Data from Images

ROI time series: examining how data in a ROI changes over time.







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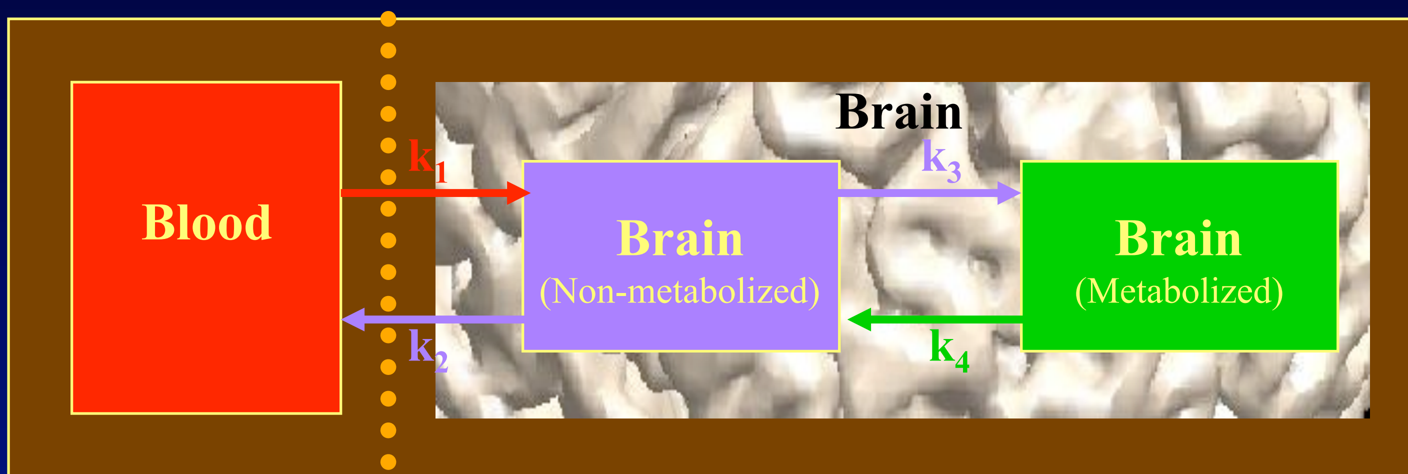
Quantitative Images

Some modalities (PET) are said to be quantitative because the values are in terms of basic physical units, and these can be directly compared across time and/or subjects.

Furthermore, these images can be converted into other (more interesting) units, such as a biochemical or physiological rate-constant.



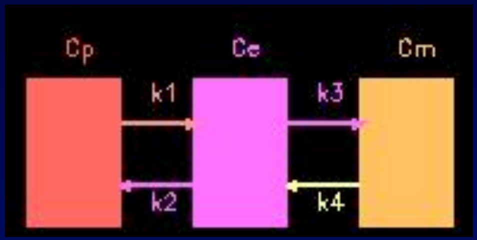
$$ICMRglu = \left(\frac{C_g}{LC}\right)\left(\frac{k_1 k_3}{k_2 + k_3}\right)\left(\frac{C_i(T) - C_e(T)}{C_m(T)}\right)$$

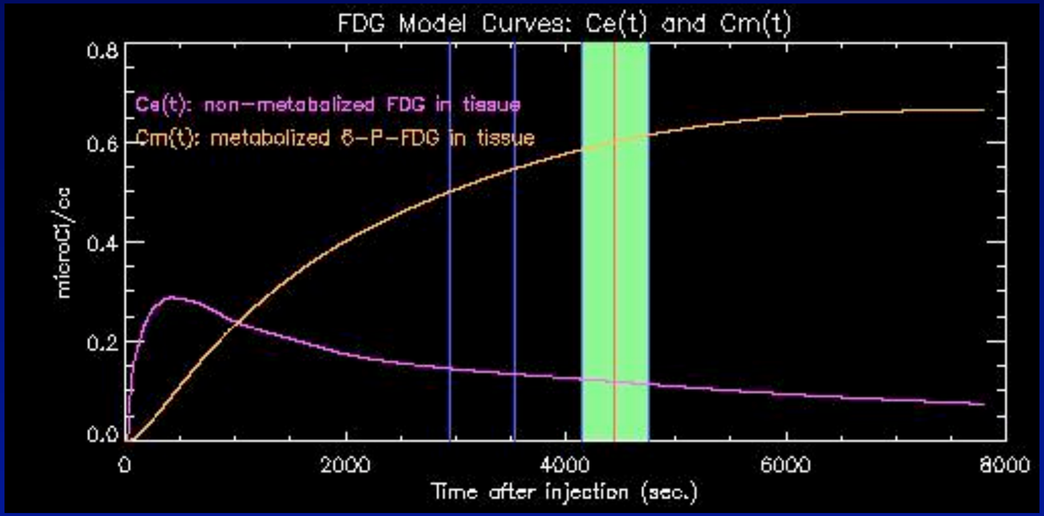
$$ICMRglu = L * C_g\left(\frac{C_i(T) - C_e(T)}{C_m(T)}\right)$$

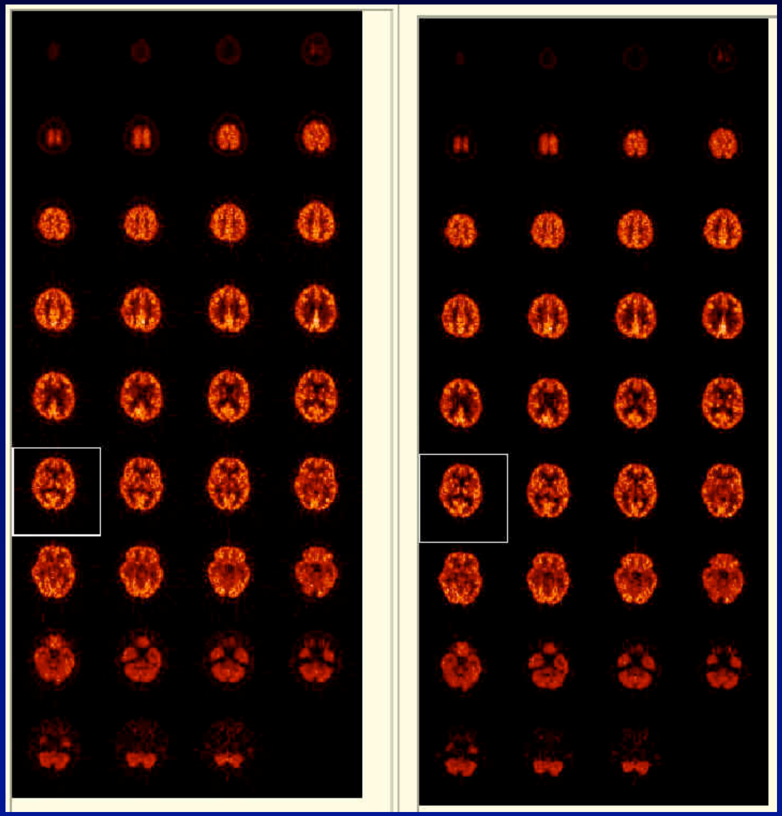
Quantitative Images

Images which represent an underlying physiological process are (usually) more interesting than images of the "raw" measured data.

There may be little visual difference between raw and quantitated images, but it is the underlying values that are important.







Raw FDG (microCi/cc)

Quantitated FDG (1/sec)

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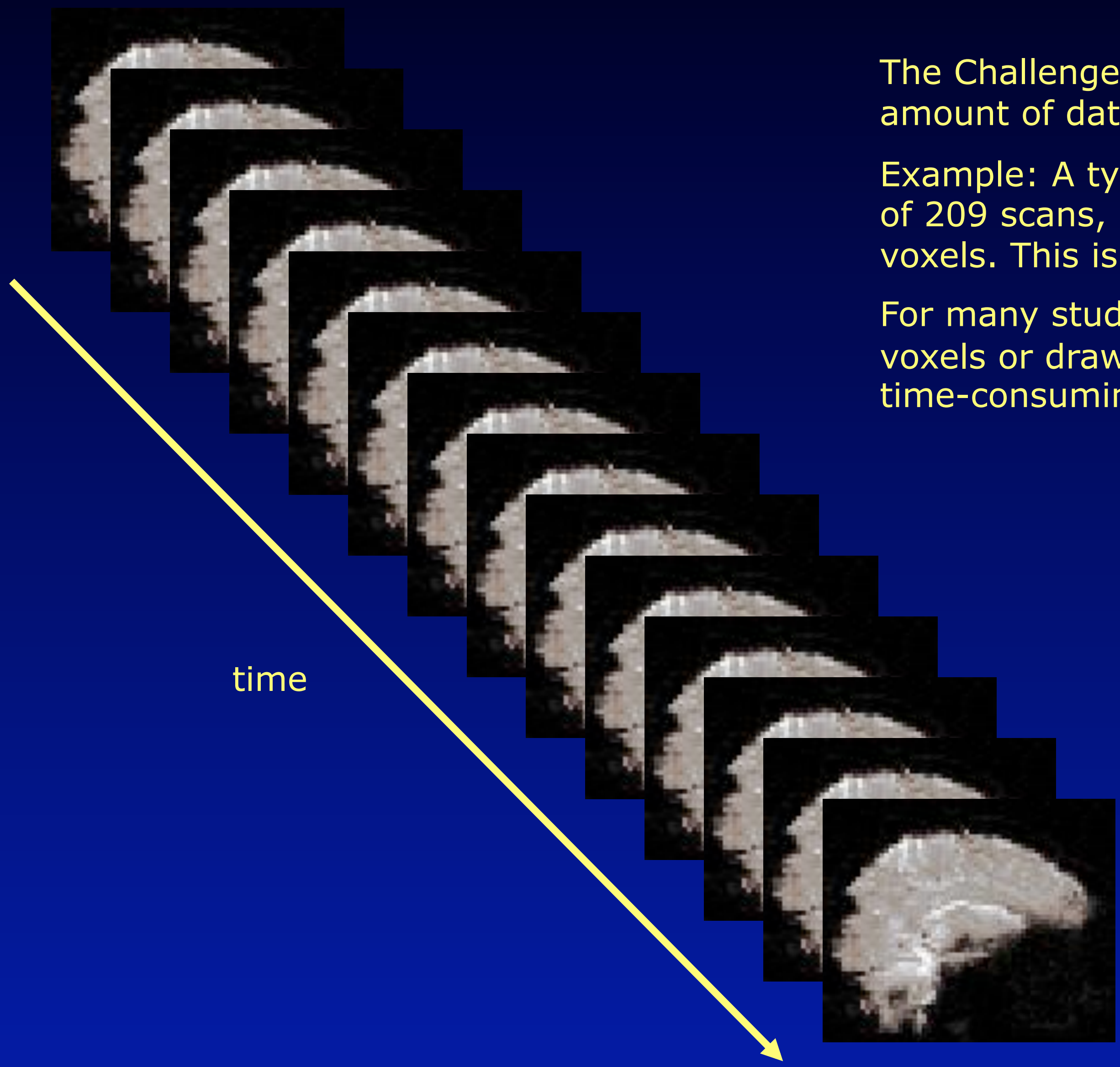
Data Reduction



The Challenge: how to reduce a vast amount of data to a few pithy numbers.

Example: A typical fMRI study consists of 209 scans, each with 64x64x23 voxels. This is 20 million pieces of data!

For many studies, examining individual voxels or drawing ROIs is prohibitively time-consuming.

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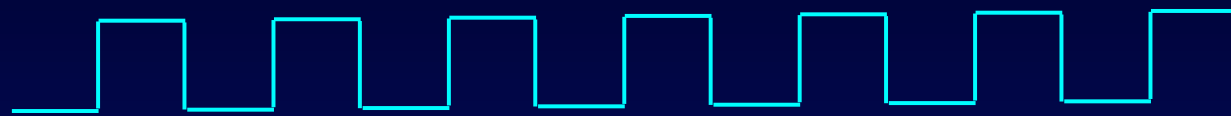
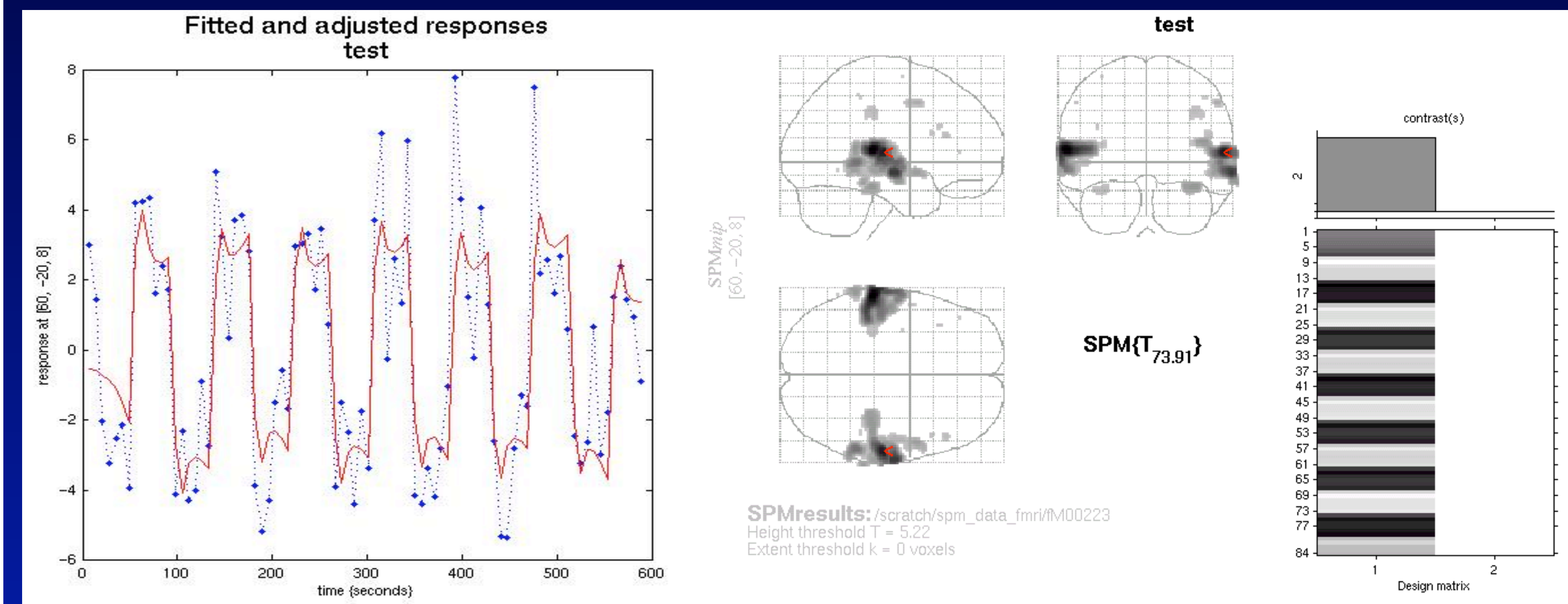
Data Reduction: Statistical Parametric Map (SPM)

Goal: Find brain regions that are activated by a tone.

Model for Listening task:



tone is: off on off on off on off on off on off on off on



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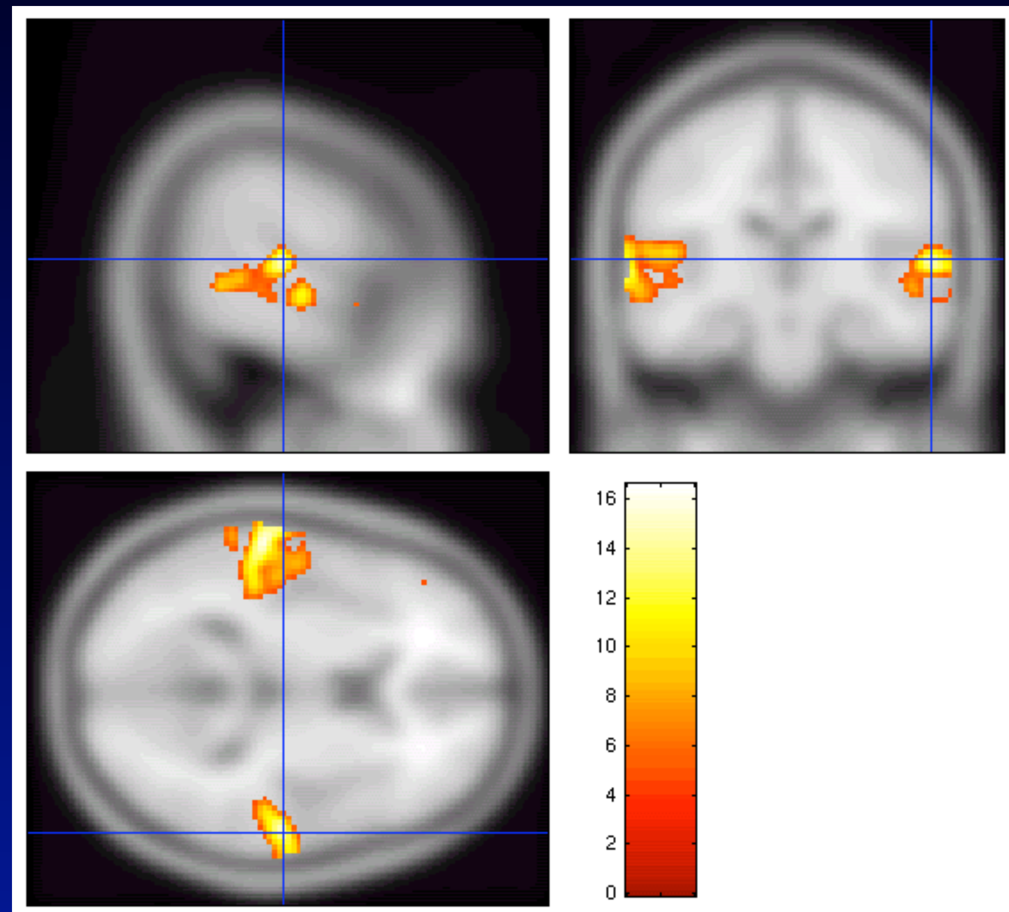
Data Reduction: Statistical Parametric Map (SPM)

- Where is the activation?
- How strong is it?
- How significant is it?
- Is it repeatable?
- Can these results be generalized to a larger population?



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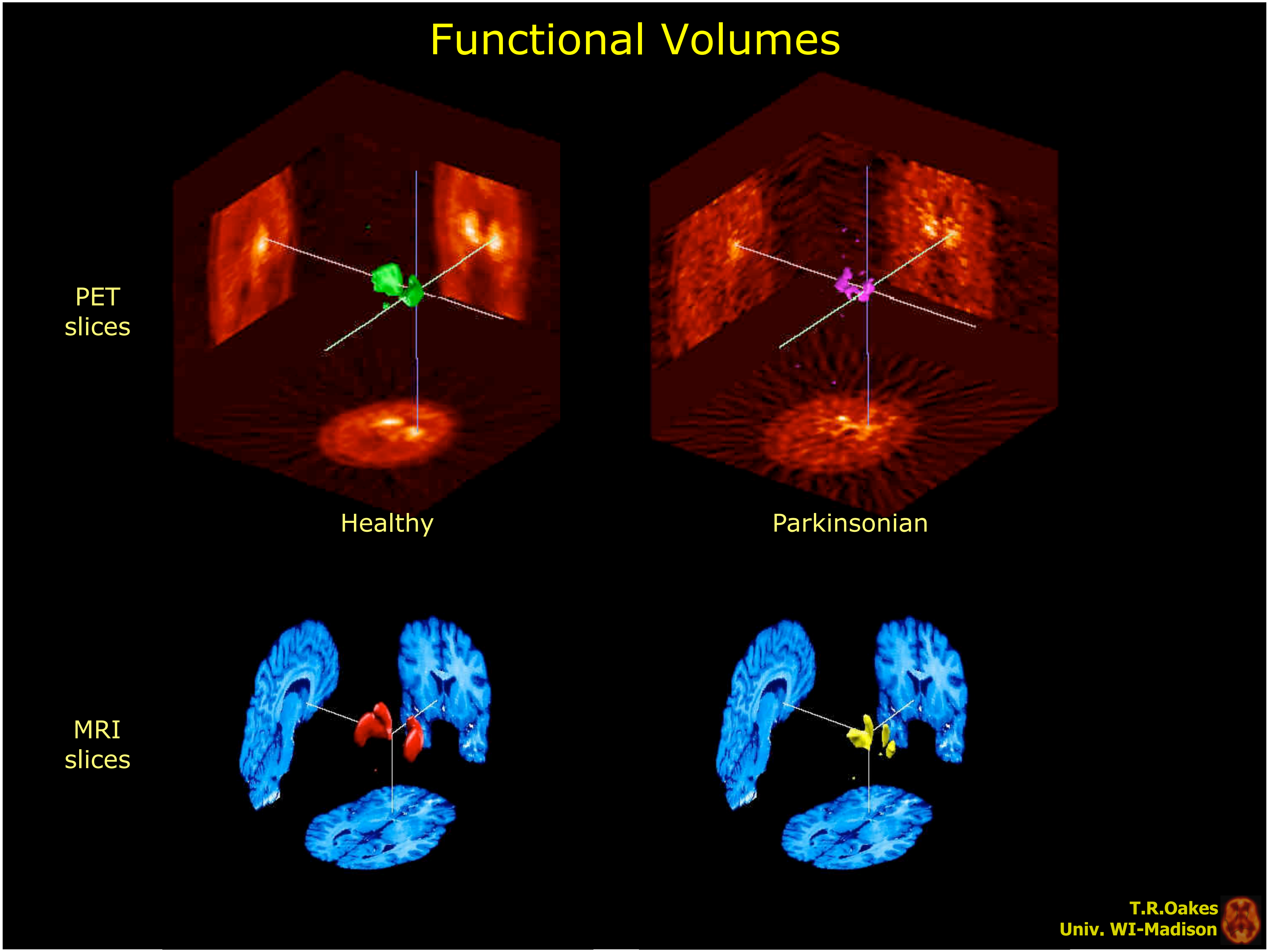
Functional Volumes
PET
slices
Healthy
Parkinsonian
MRI
slices
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Visualisation: 4D

Areas of the brain activated when mothers view pictures of their own infants (red) and of other infants (blue)

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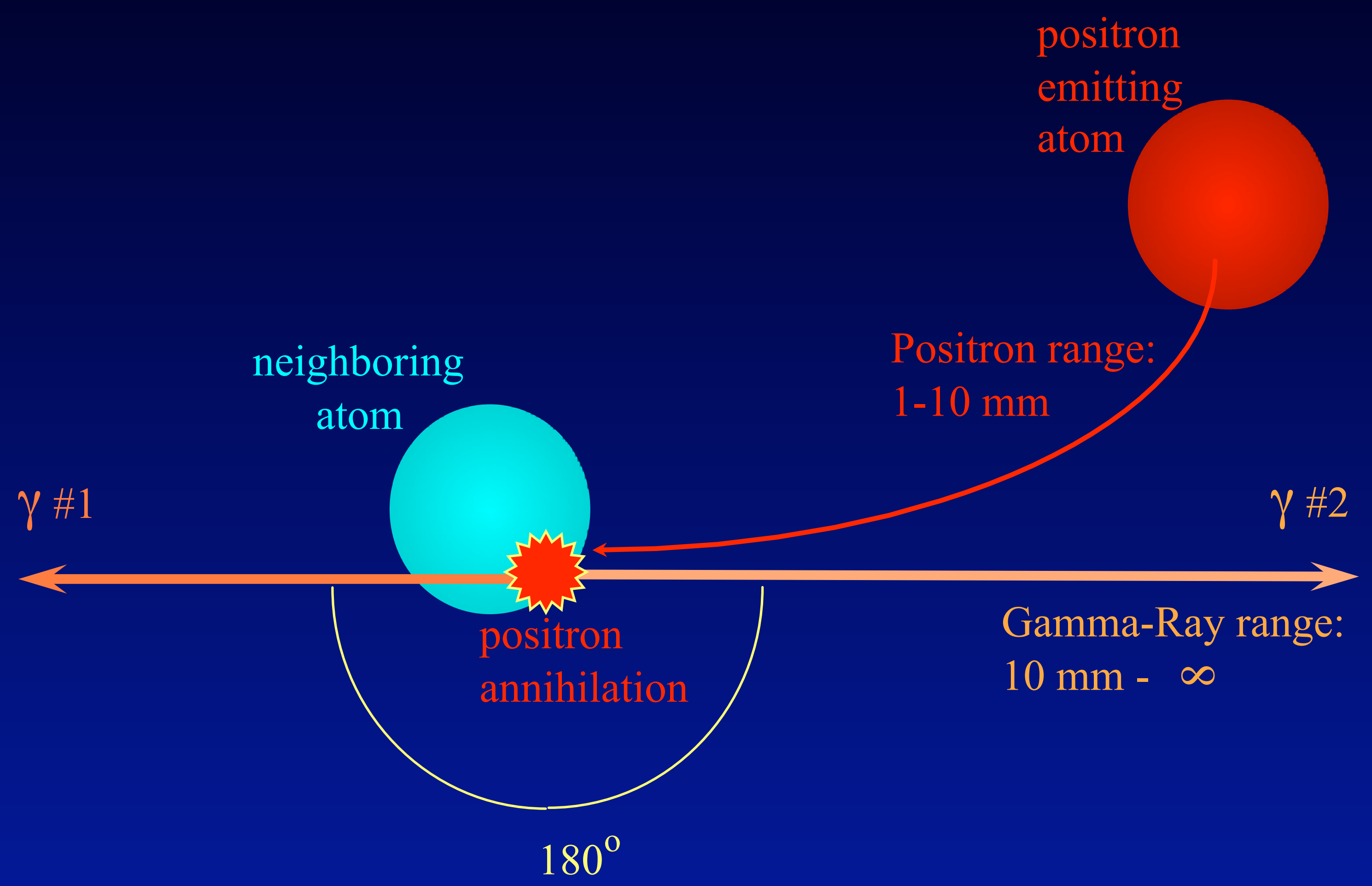
Part II: PET Particulars

•How does the PET scanner work?

•What is a tracer?
•How do you make a tracer?
•What types of tracers do we have?

•What types of studies do we do?
•What types of studies COULD we do?

Positron Annihilation



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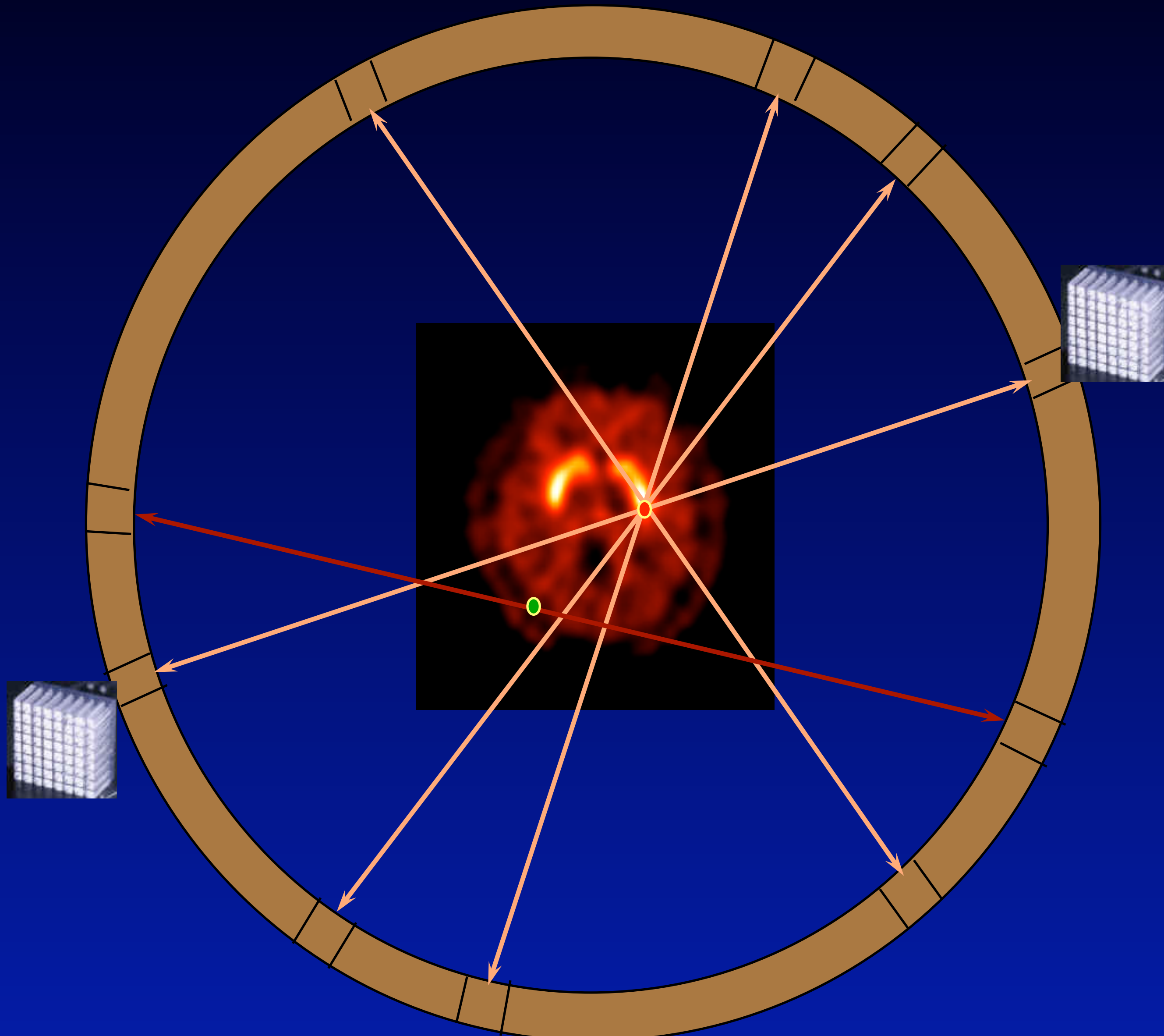
A Functional Image starts with a Measurement



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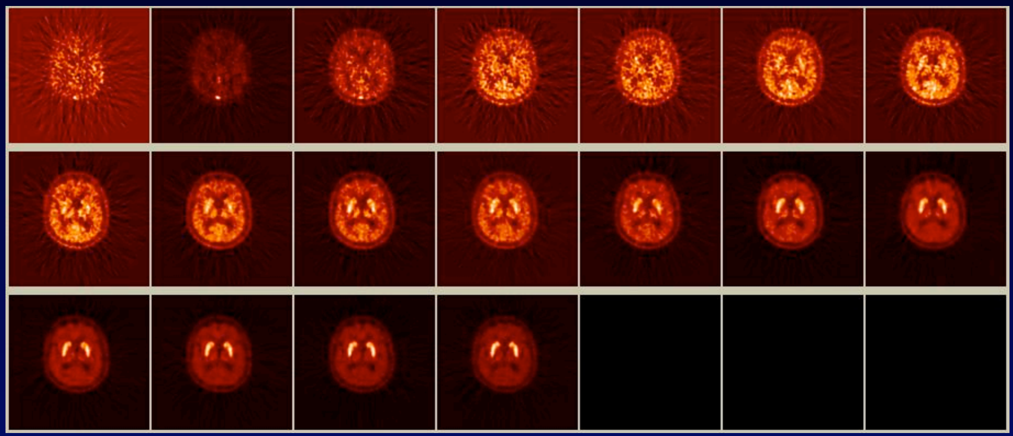
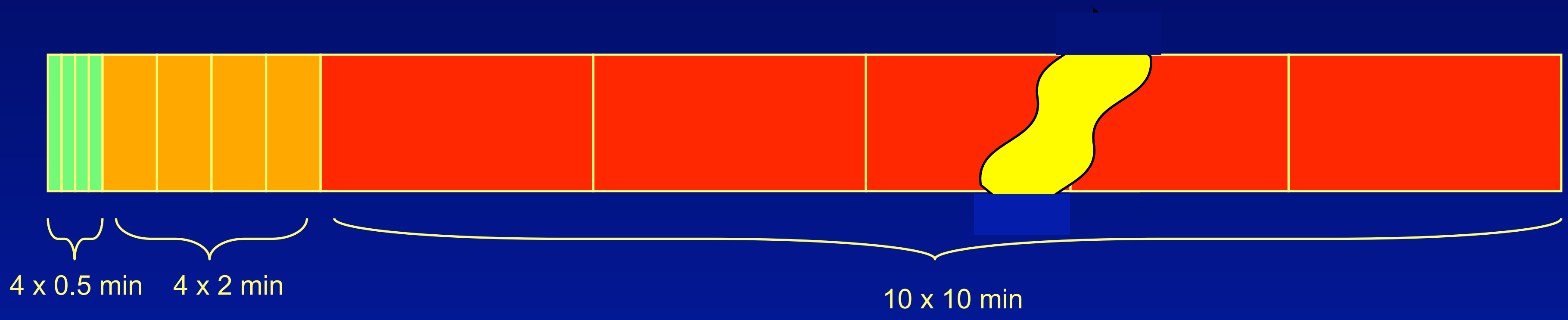
Dynamic Scan





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A Tracer…

- Mimics (follows, traces) a physiologically interesting molecule or process
- Is related in a known way to a naturally-occurring analog
- Does not alter the process being studied
  - it is inert, or
  - it is present in extremely low concentrations.
- Must yield a concentration measurement in tissue.
  - Tracer molecule must be labeled with a special atom or molecule.

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So many tracers, so little time…

Physiological Processes

- Blood Flow
- Blood volume
- Perfusion
- Metabolism

brain, cardiac, muscle, etc.

- Lung, liver, kidney function
- Cardiac output
- DNA / RNA and protein biosynthesis
- Neurotransmission

Physiologically relevant positron emitters

- ^{17}F ($t_{1/2}$ = 1 min)
- ^{15}O ($t_{1/2}$ = 2 min)
- ^{13}N ($t_{1/2}$ = 10 min)
- ^{11}C ($t_{1/2}$ = 22 min)
- ^{18}F ($t_{1/2}$ = 110 min)

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Neurotransmission

Processes:

- •Postsynaptic / Presynaptic
- •Agonist / Antagonist
- •Specific neurotransmitter sub-types
- •Synthesis
- •Transport across cell membranes
- •Reuptake
- •Displacement
- •Vesicular storage

•Systems

- •Dopamine
- •Seratonin
- •Choline
- •Opiate
- •Benzodiazepine

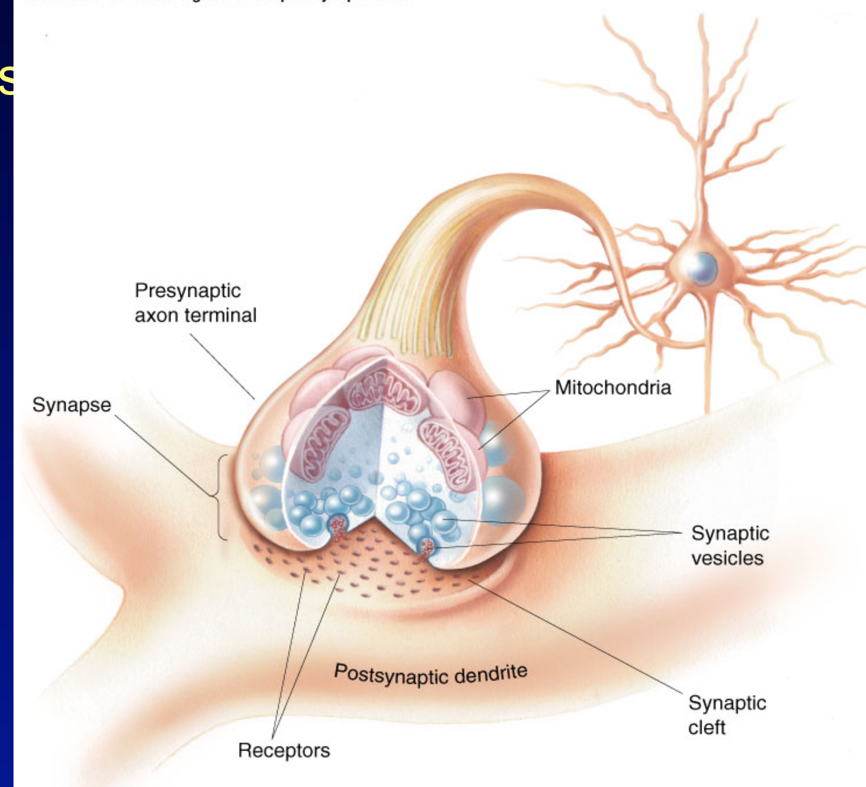

Figure 2.15
The axon terminal and the synapse. Axon terminals form synapses with the dendrites or somata of other neurons. When a nerve impulse arrives in the presynaptic axon terminal, neurotransmitter molecules are released from synaptic vesicles into the synaptic cleft. Neurotransmitter then binds to specific receptor proteins, causing the generation of electrical or chemical signals in the postsynaptic cell.

How to make a PET tracer

1. Make a positron emitter
2. Label a precursor

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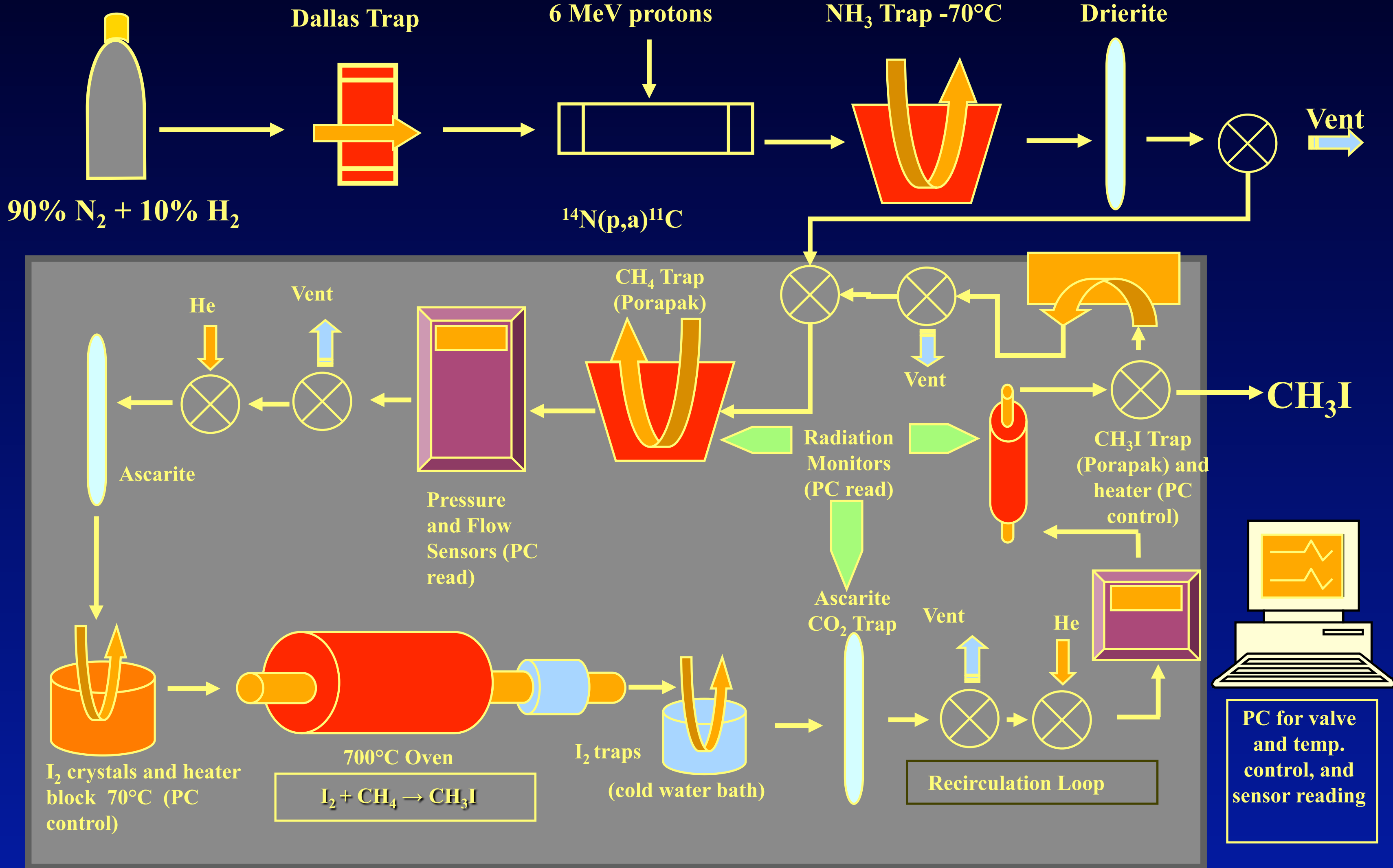
Radiosynthesis rig for [^{11}C]-methyl iodide



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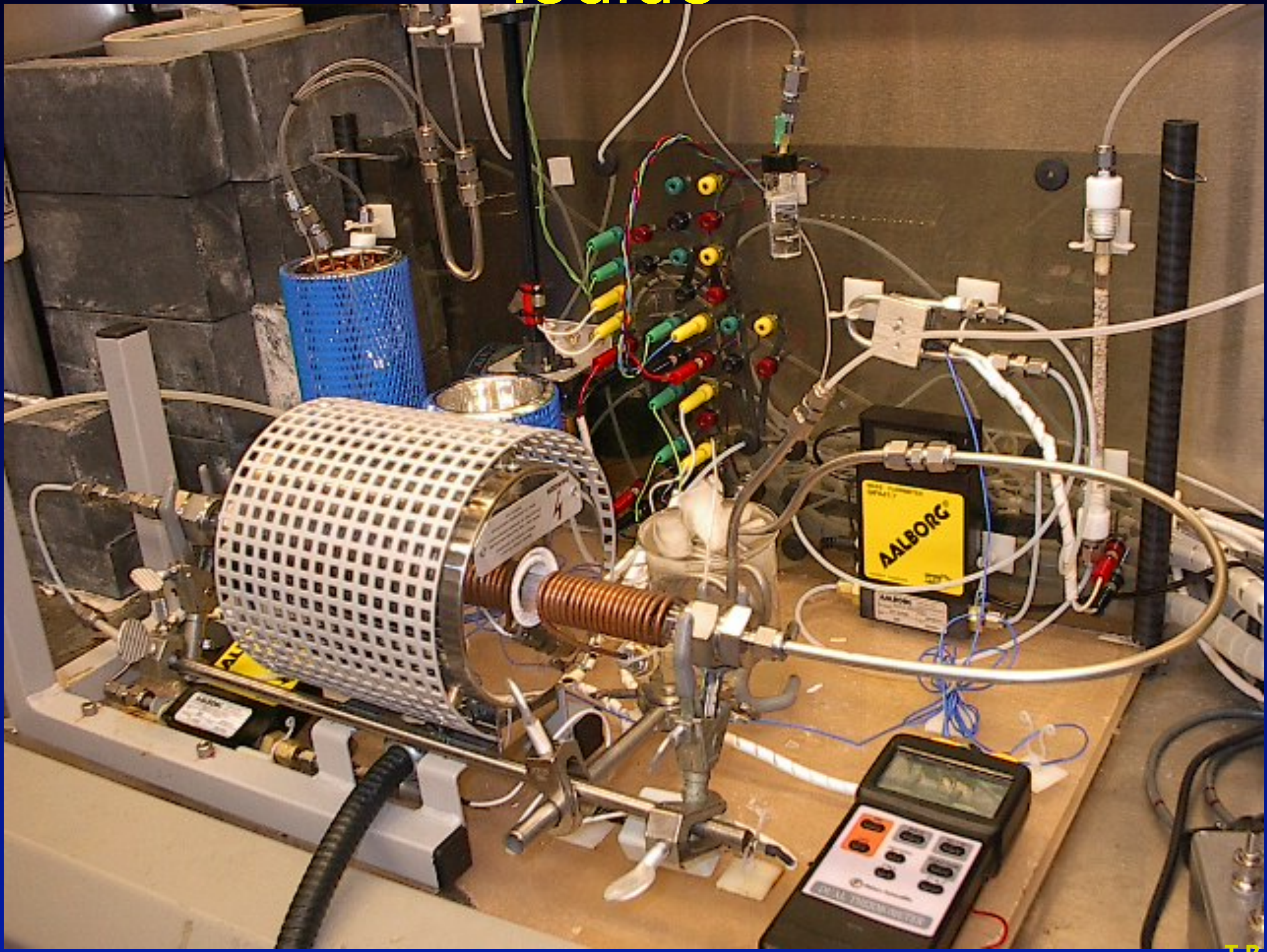
Radiosynthesis rig for [^{11}C]-methyl iodide



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Current PET studies

- Metabolism:
  - $[^{18}F]$-FDG (glucose analog): the workhorse
  - $[^{15}O]$-O_2
  - $[^{18}F]$-FLT (fluoro-levo-tyrosine: DNA synthesis => oncology)
- Blood flow
  - $[^{15}O]$-H_2O
  - $[^{15}O]$-CO (blood volume)
  - $[^{17}F]$-CH_3, $[^{18}F]$-CH_3
- Dopaminergic system
  - $[^{18}F]$-fluoro-L-DOPA (vesicular storage)
  - $[^{18}F]$-FMT (fluoro-meta-tyrosine: dopamine synthesis)
  - $[^{18}F]$-fallypride (high-affinity post-synaptic D2 receptor)
  - $[^{18}F]$-desfallypride (medium-affinity post-synaptic D2 receptor)
  - $[^{11}C]$-raclopride (low-affinity post-synaptic D2 receptor)
- Benzodiazepine
  - $[^{11}C]$-PK11195 (activated macrophages)