New Technologies for Molecular Imaging of Brain Function

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MIT Department of Biological Engineering

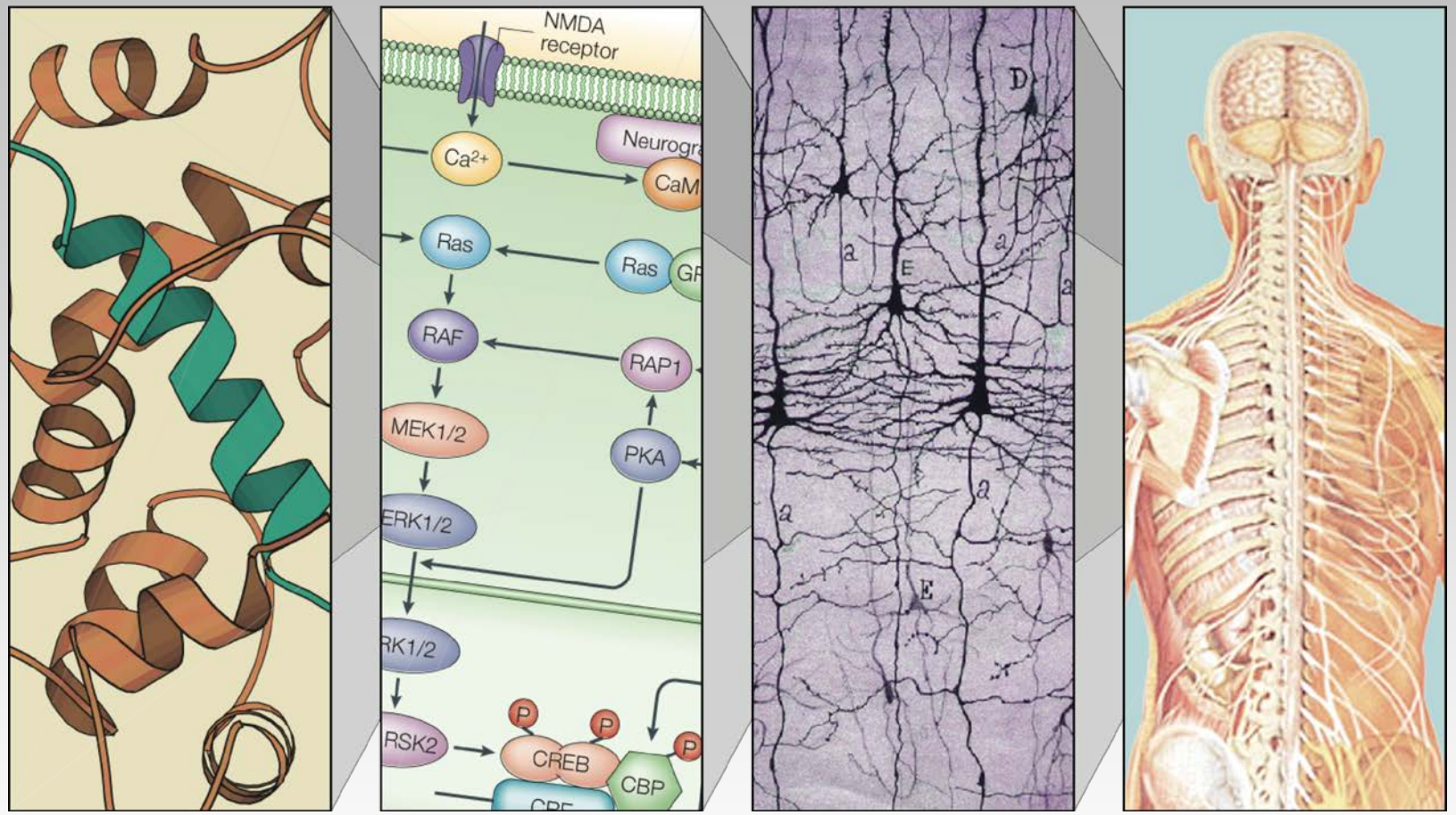
Outline

introduction to molecular imaging

some current frontiers

functional molecular imaging in the brain

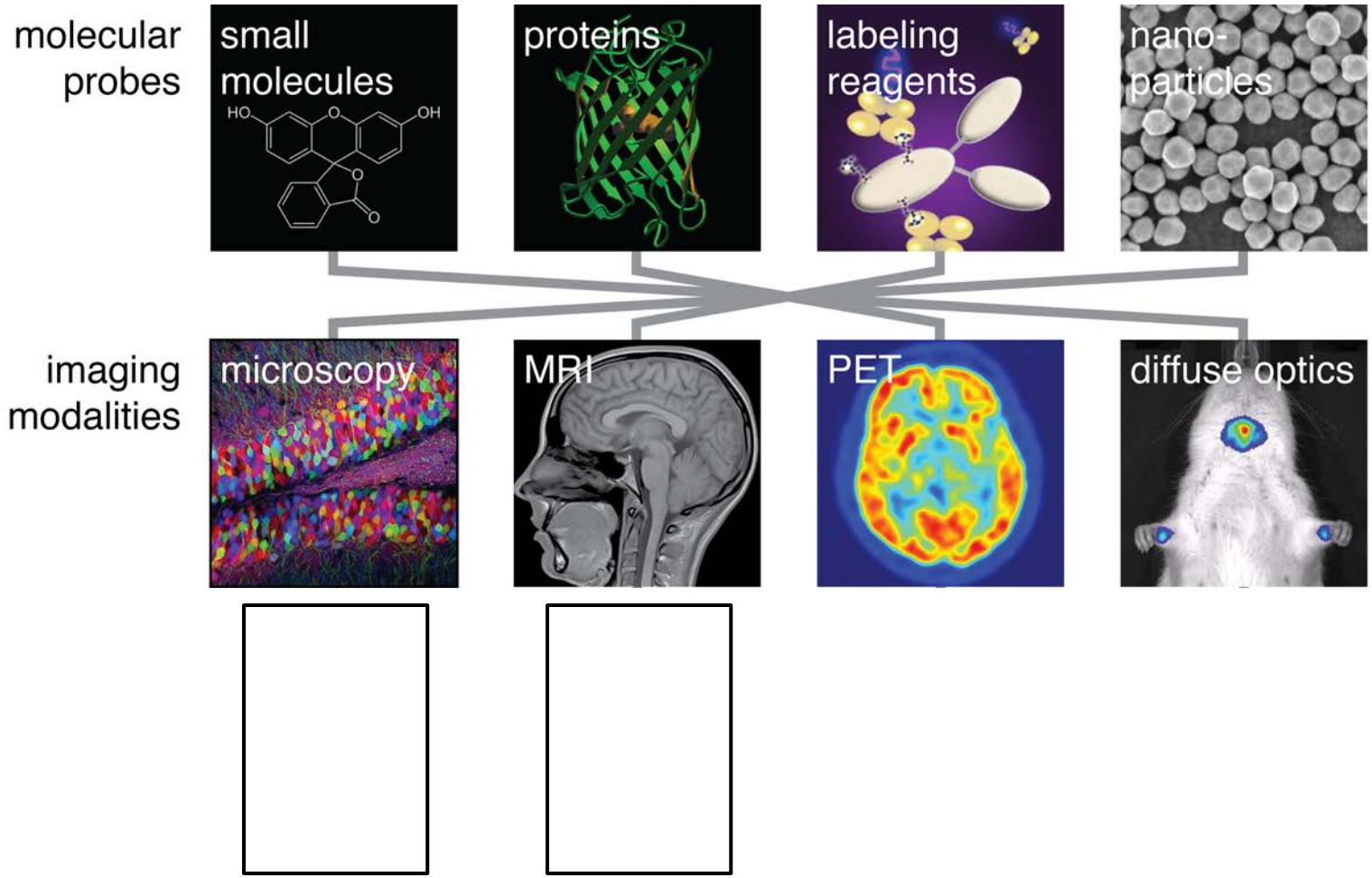
future perspective



molecules pathways/cells cellular networks organ(ism)s

molecular imaging

combination of molecular probes with noninvasive imaging



www.wikipedia.com, www.scienceblogs.de, www.biolegend.com, www.cytodiagnostics.com, cbs.fas.harvard.edu, www.healthcare.siemens.com, www.wikipedia.com, www.cvs.ed.ac.uk

Camillo Golgi (1873)

M. Phelps & M. Ter-Pogossian (1974)

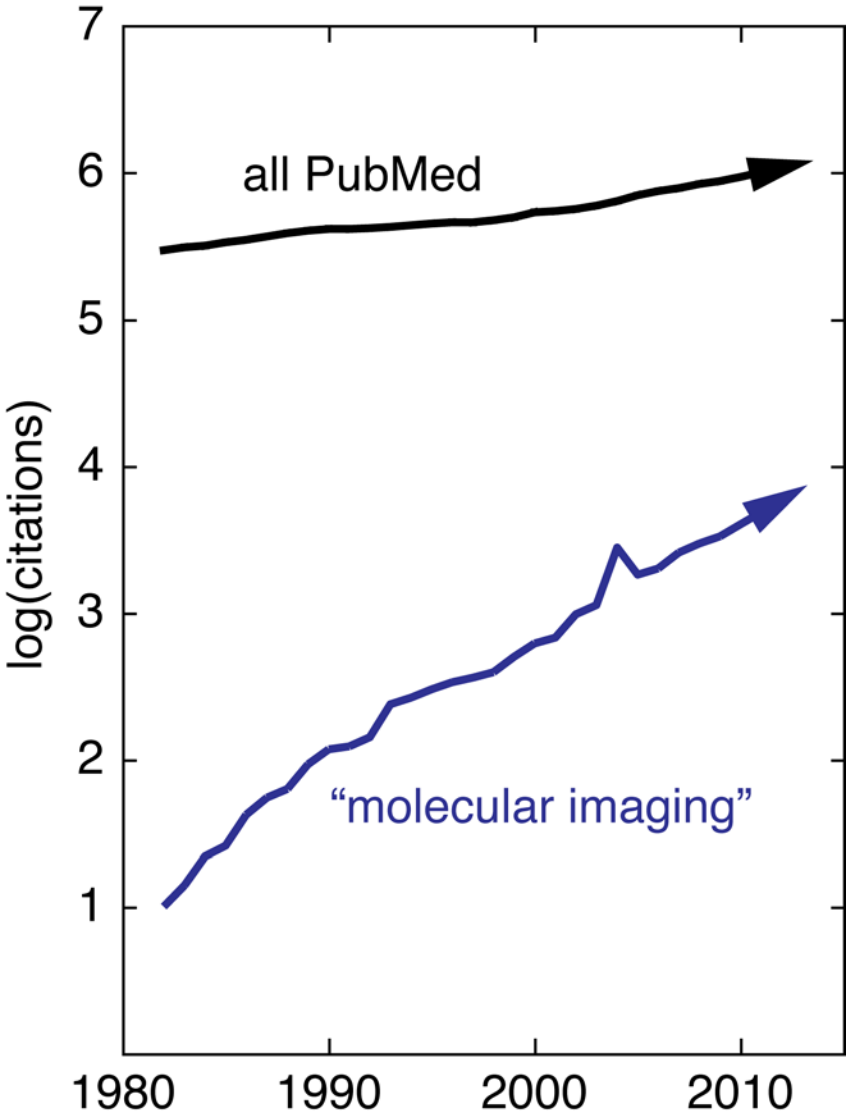
De Carlos & Borrell (2007) *Brain Res. Rev.*

www.bnl.gov

continuing innovation

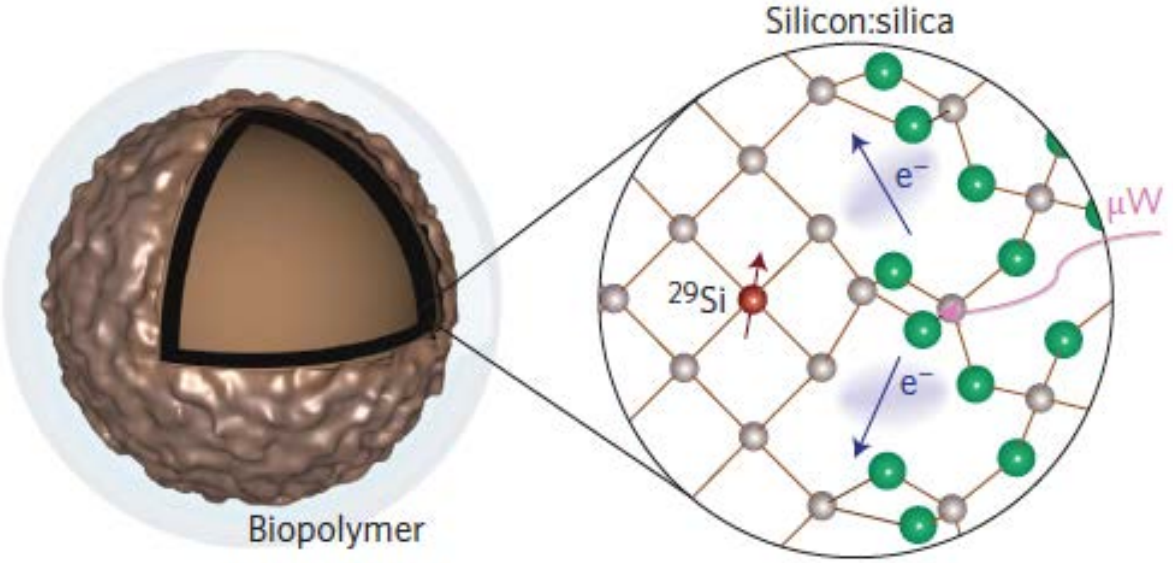
(diversity wanted)

rapid growth

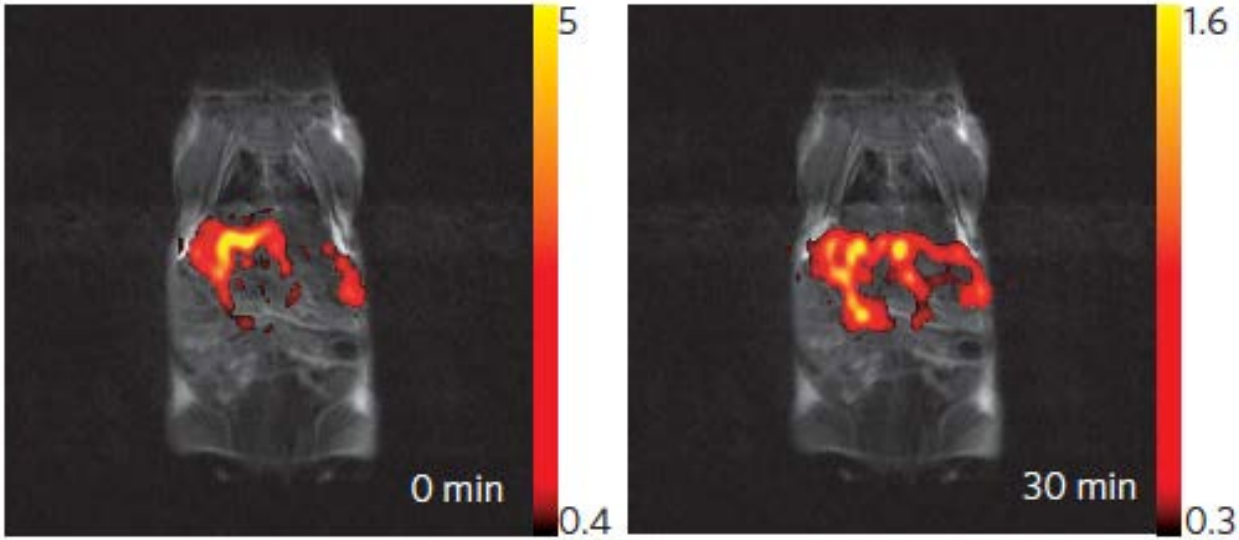


new physics: hyperpolarized probes for MRI

dynamic nuclear polarization of silicon nanoparticles

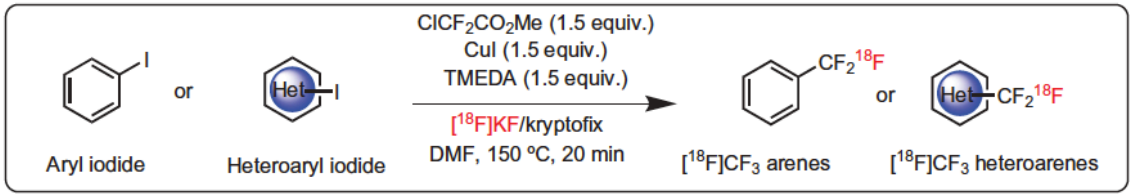


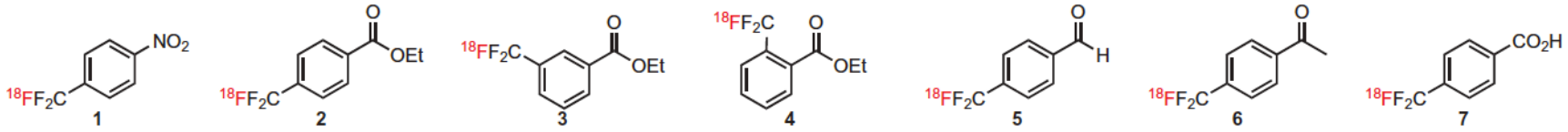
long term imaging in cancer model (pM particles)

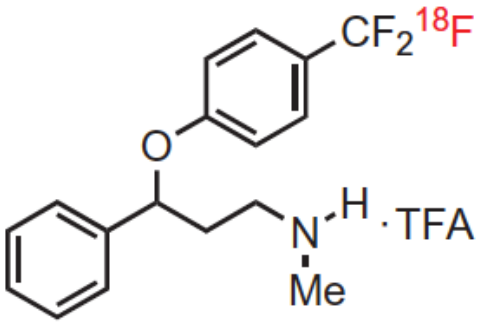


Cassidy *et al.* (2013) *Nat. Nanotechnol.*

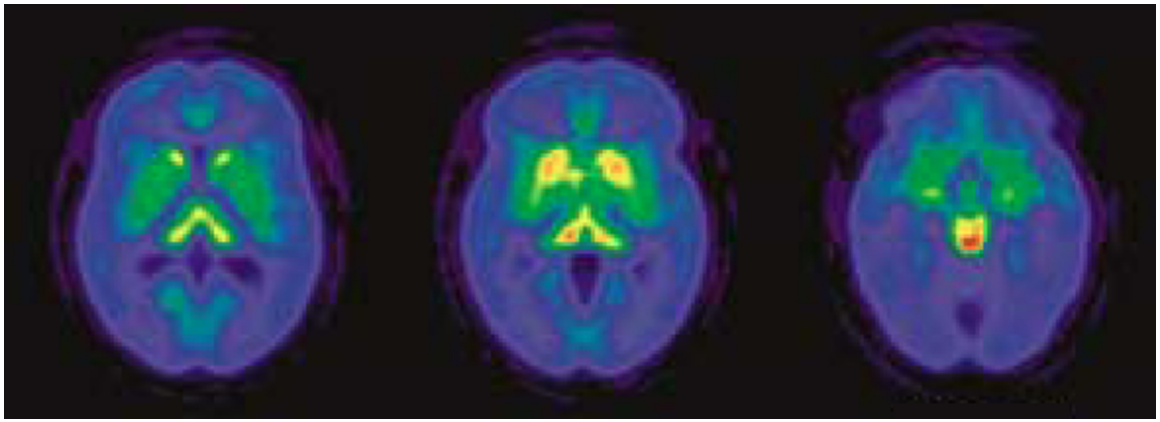
new chemistry: efficient synthesis of ^{18}F PET agents







fluoxetine



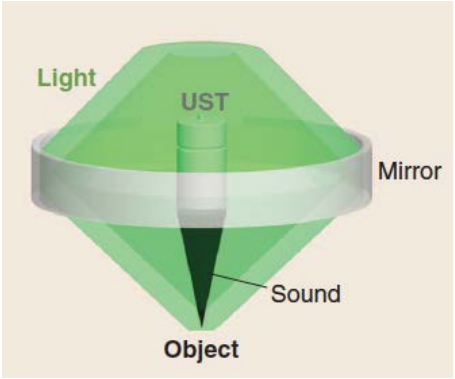
serotonin transporter

Albin *et al.* (2008) *J. Cereb. Blood Flow Metab.*

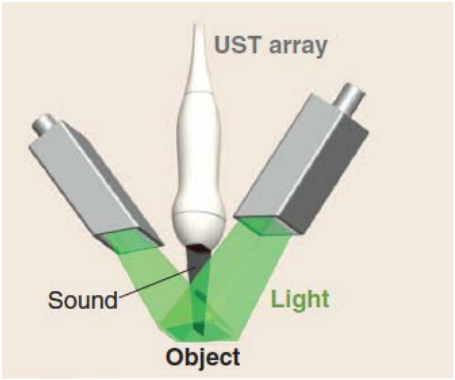
Huiban *et al.* (2013) *Nat. Chem.*

new instrumentation: photoacoustic tomography *in vivo*

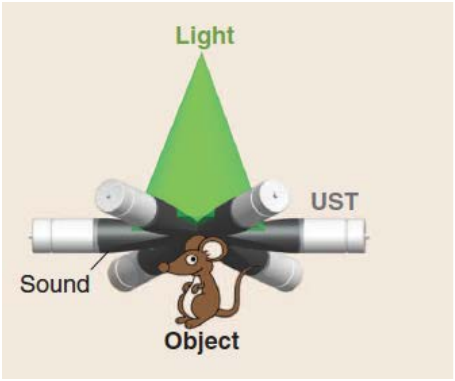
imaging human skin vasculature



molecular dye localized in rat lymph node



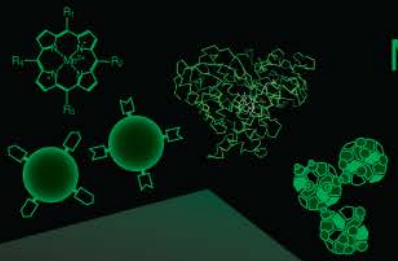
functional imaging in rat brain



Wang & Hu (2013) *Science*

1 cm (rat)
5 mm (mouse)

molecular imaging

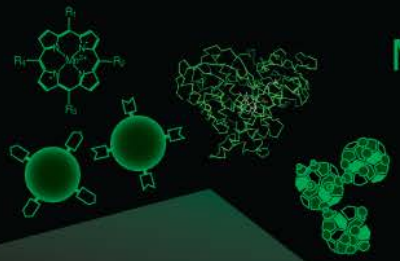


MRI contrast agents that sense neuronal activity

>10 billion neurons
~10^3 synapses/neuron
cell types defined by gene expression, neurotransmitters, *etc.*
highly complex anatomy, connectivity

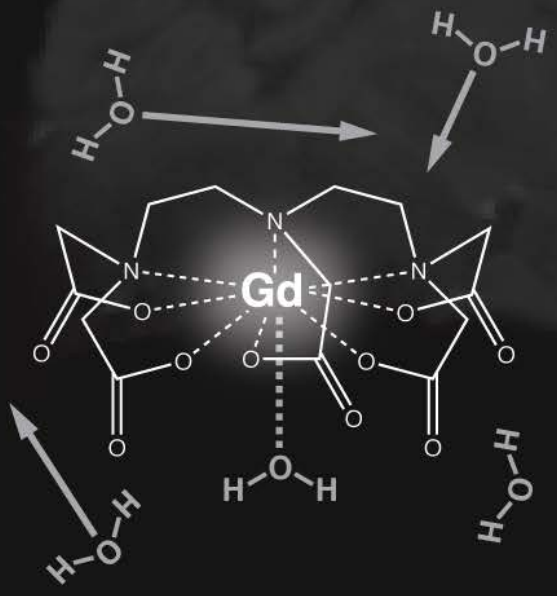
1 cm (rat)
5 mm (mouse)

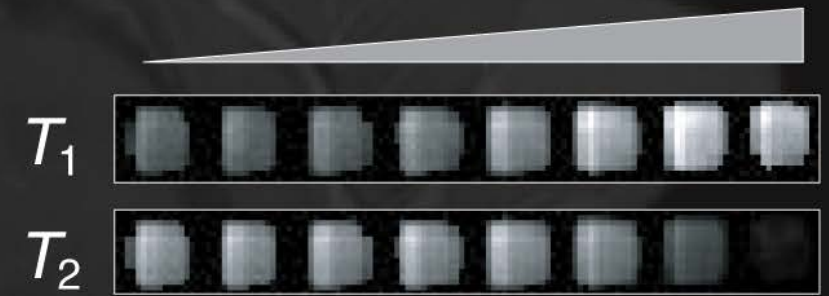
molecular imaging

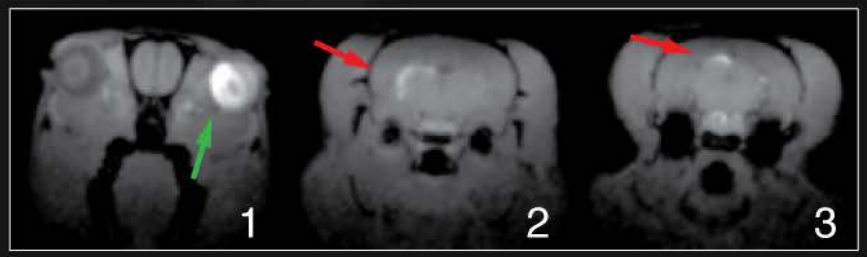


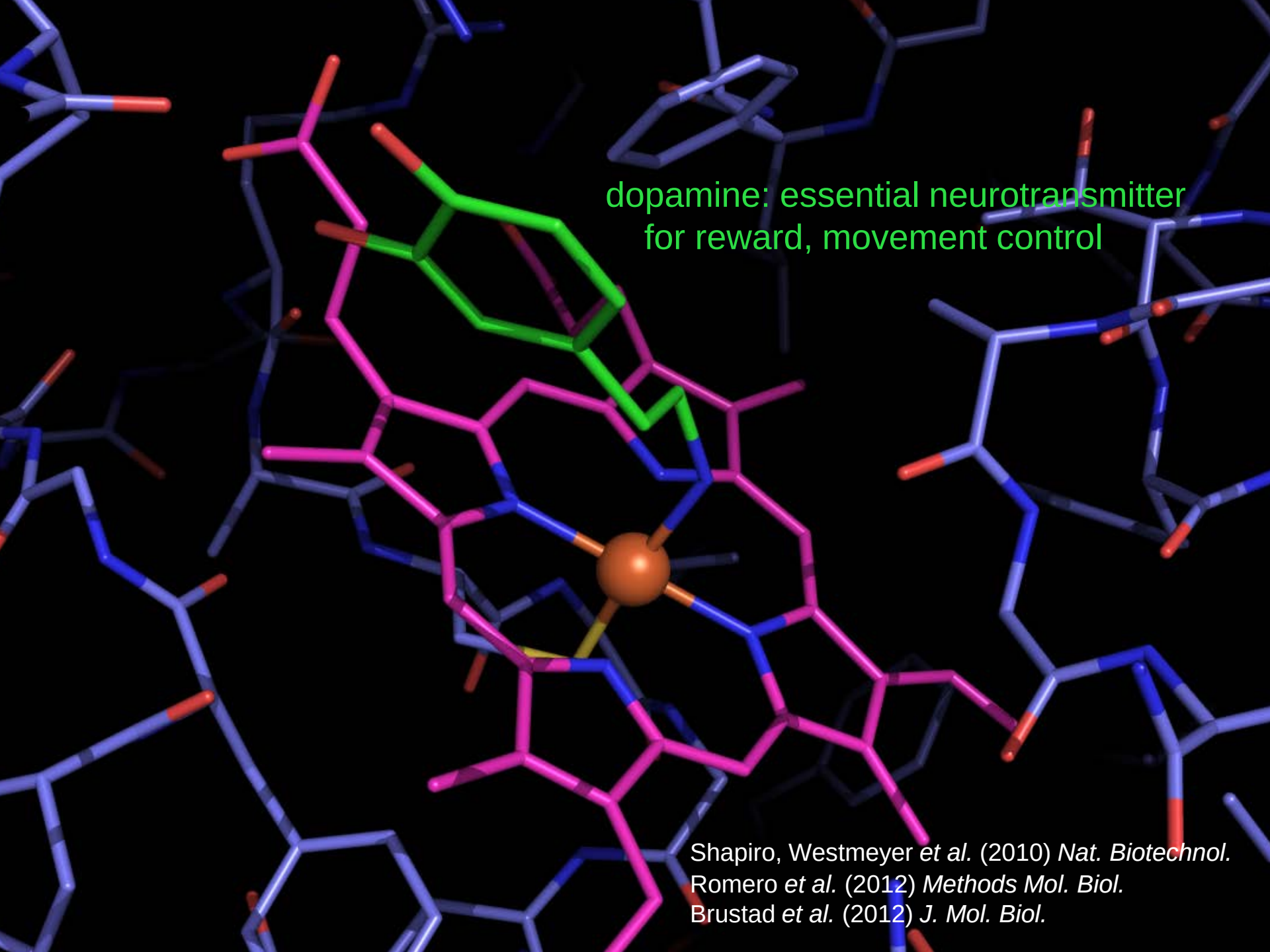
MRI contrast agents that sense neuronal activity

What are MRI contrast agents?

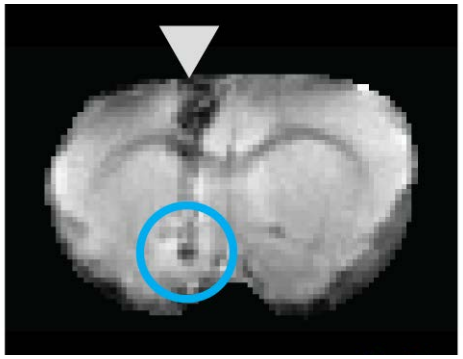




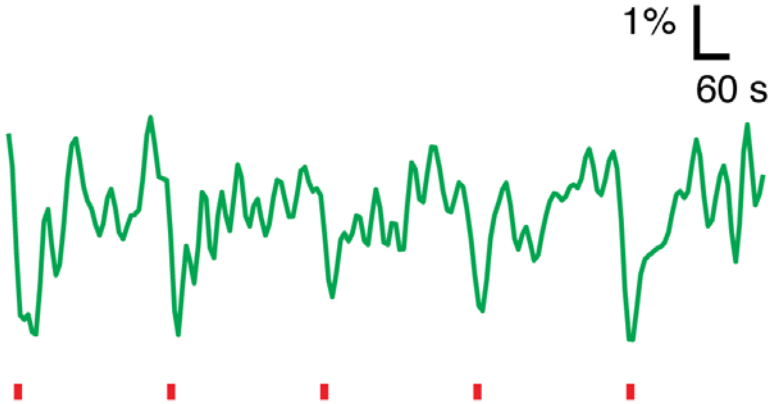




Shapiro, Westmeyer *et al.* (2010) *Nat. Biotechnol.*
Romero *et al.* (2012) *Methods Mol. Biol.*
Brustad *et al.* (2012) *J. Mol. Biol.*

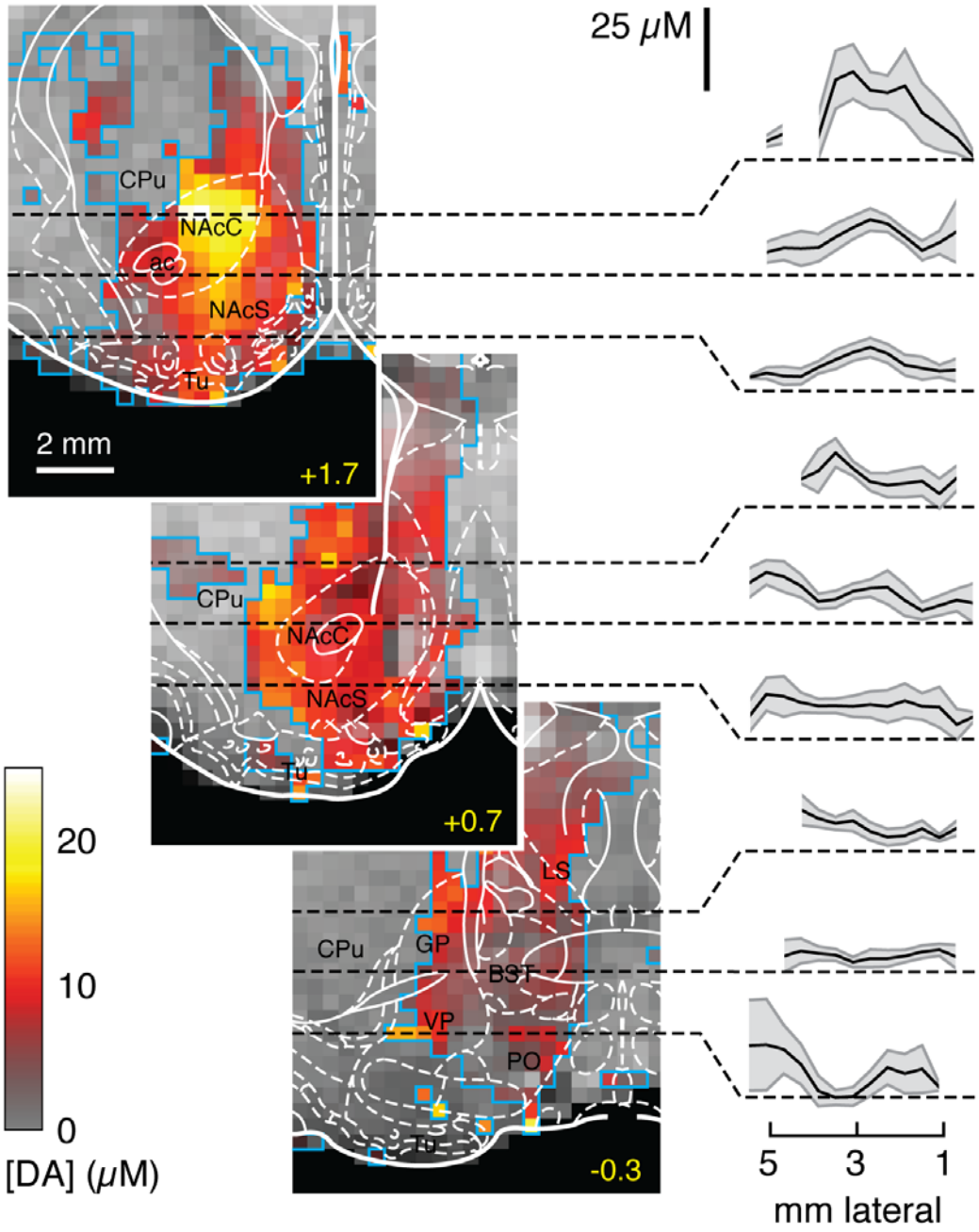


sensor binds dopamine *in vivo*
and produces expected signal changes



amperometry

Lee *et al.* (2014) *Science*

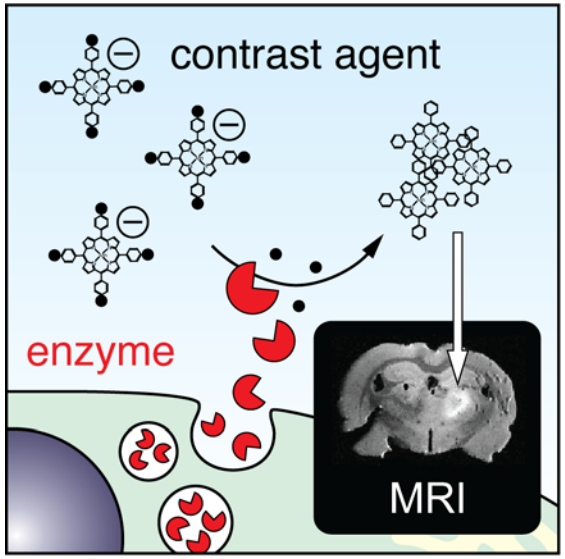


patterned signaling apparent; DA strongest in NAc core

first functional MRI at molecular level

Lee *et al.* (2014) *Science*

How can we boost biomolecular MRI signals?



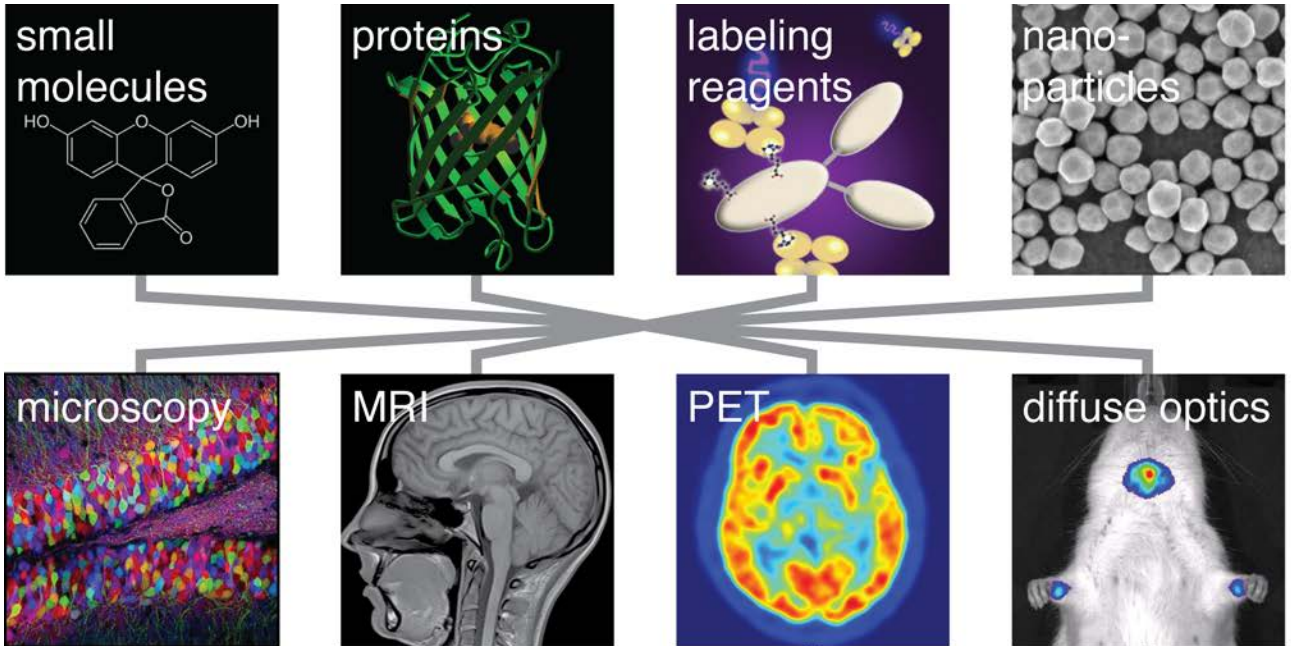
enzyme catalyzes probe accumulation

enzymatic contrast detected in live brains

towards detection of diverse molecular processes involved in neurobiology and medicine...

Westmeyer *et al.* (2010) *Angew. Chem.*
Westmeyer *et al.* (2014) *Chem. Biol.*

frontiers of molecular imaging



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