

# Molecular Imaging

## Definition:

*Molecular imaging is* the visualization, characterization, and measurement of biological processes at the molecular and cellular levels in humans and other living systems.

## Molecular Imaging:

Permits the *noninvasive* study of cells in their natural microenvironment, without perturbing the system under investigation.

Whereas traditional in vitro approaches require cells to be removed from their native surroundings and hence can only at best, provide information on a small part of the whole picture.

# Why Study Intact Subjects?

Study intact signaling and communication pathways (e.g. mapping of brain activity due to external stimulus)

Can track movement of cells (e.g. interaction between T cells and metastatic cancer cells)

Includes effects of transport/delivery, metabolism and excretion (e.g. therapeutic potential of a drug)

Can measure biological processes in their native environment (in presence of feedback and other modulating mechanisms)

# Why In Vivo Imaging?

in vivo  $\neq$  in vitro

non-destructive\* - repeat studies in the same animal

each animal serves as its own control

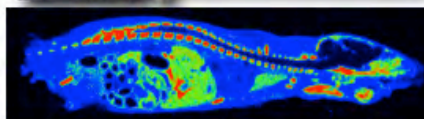
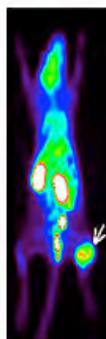
can efficiently survey whole animal

rapid in vivo screening?

provides bridge from animal studies to human studies



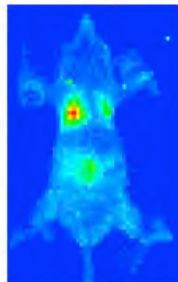
microPET



Autoradiography



microCT



Bioluminescence



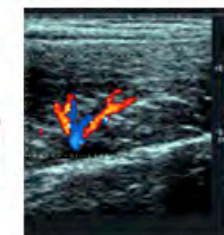
microSPECT



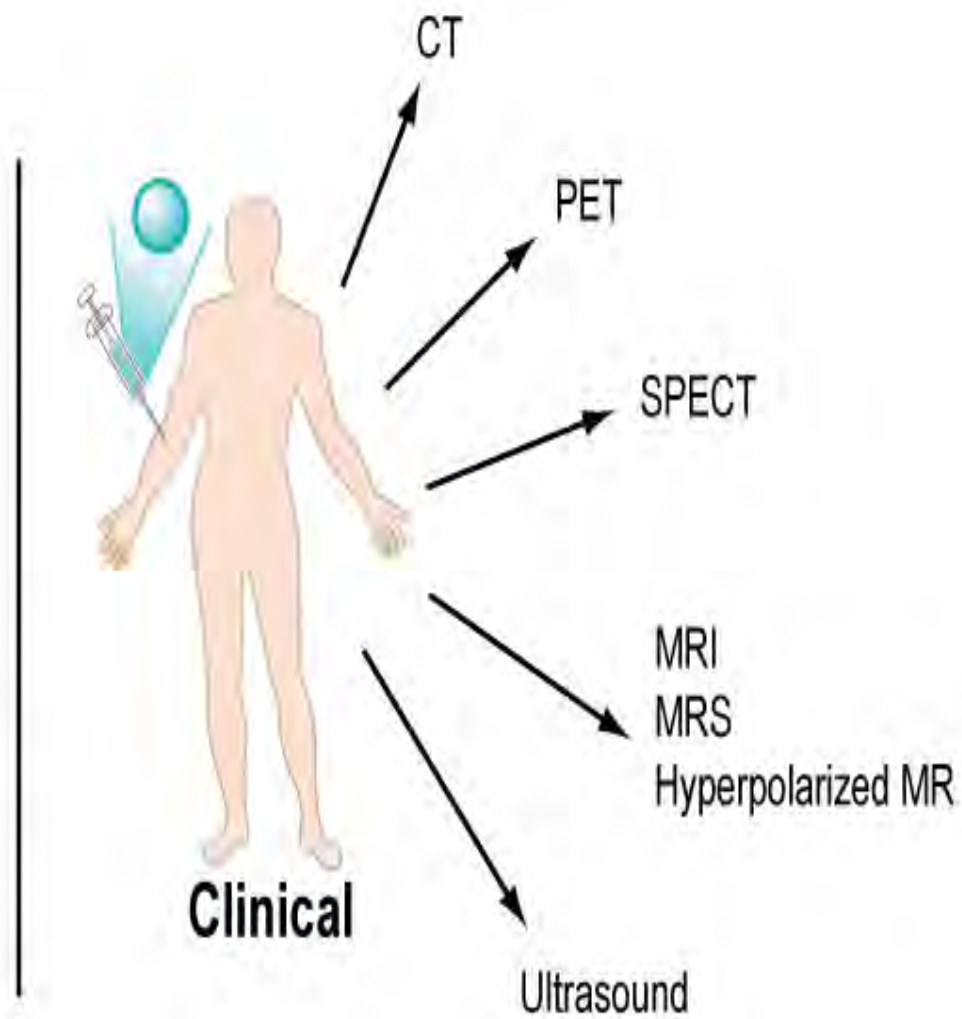
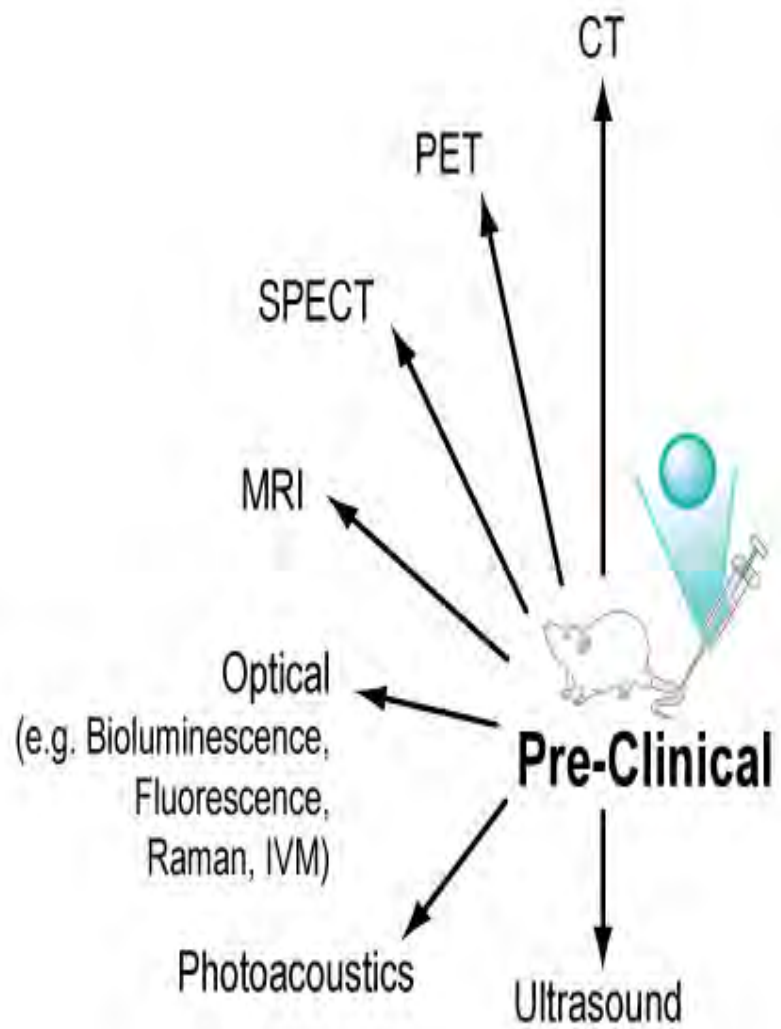
Animal MRI



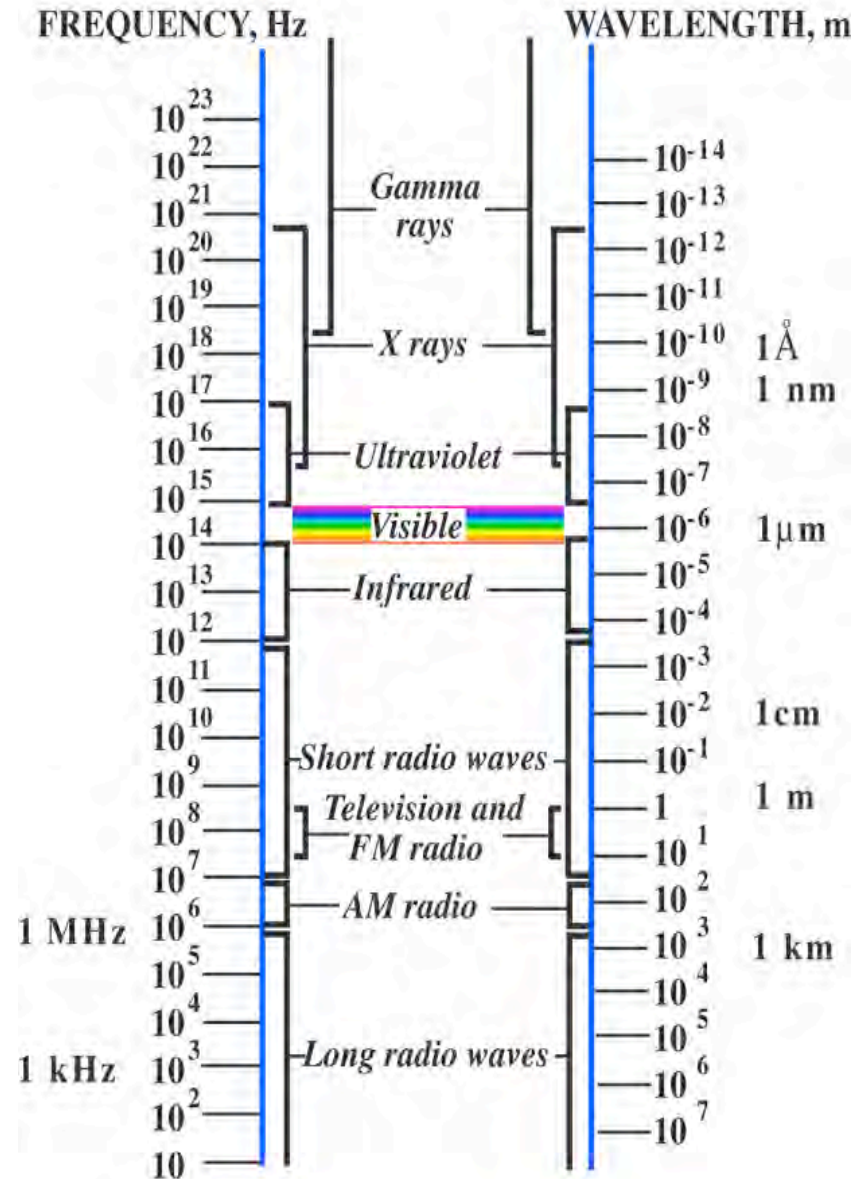
Fluorescence



Ultrasound



# Radiation Spectrum

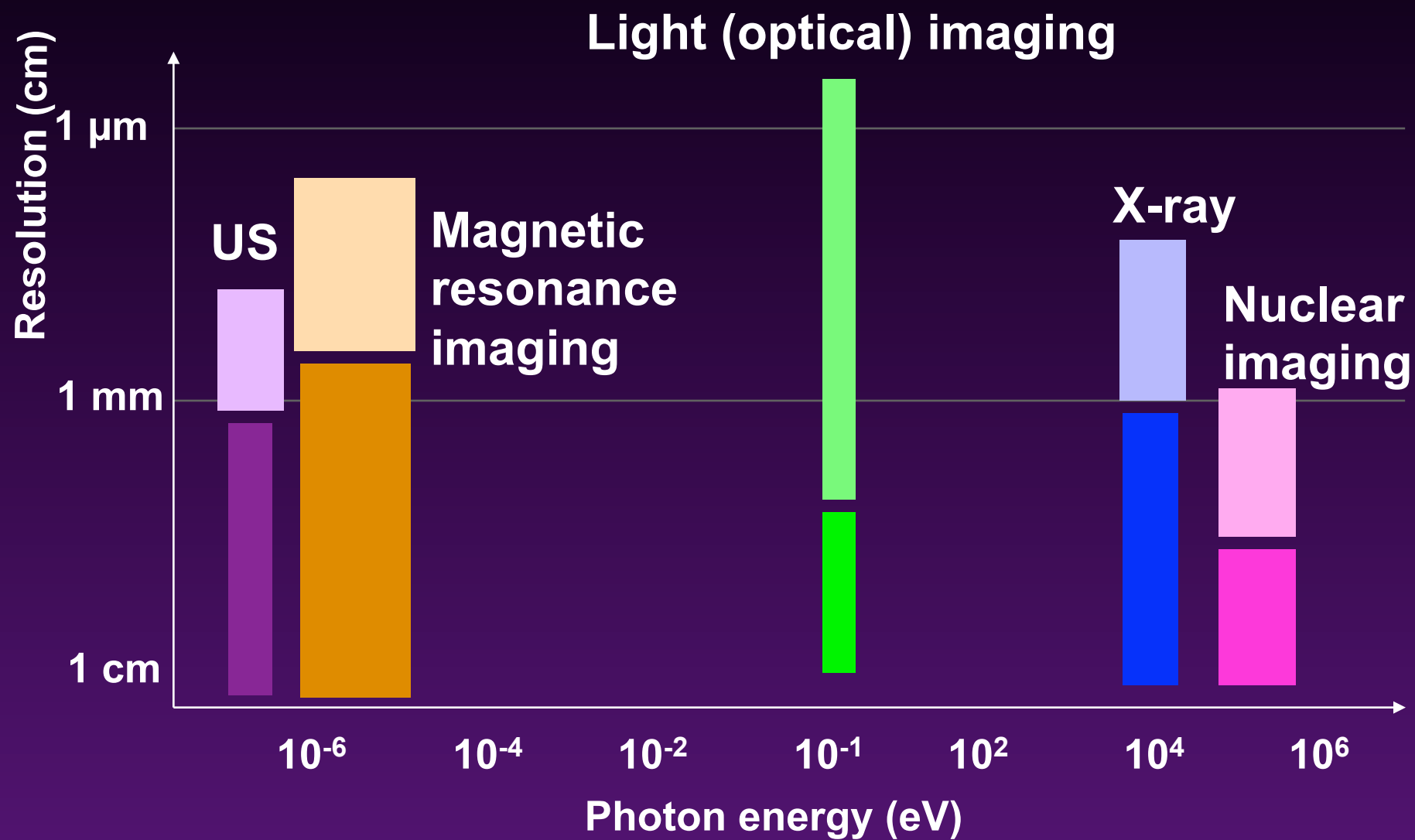


**Key advantages and disadvantages of the main available imaging modalities used in molecular imaging approaches.**

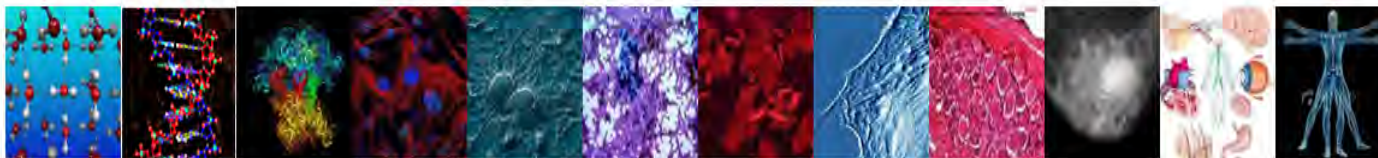
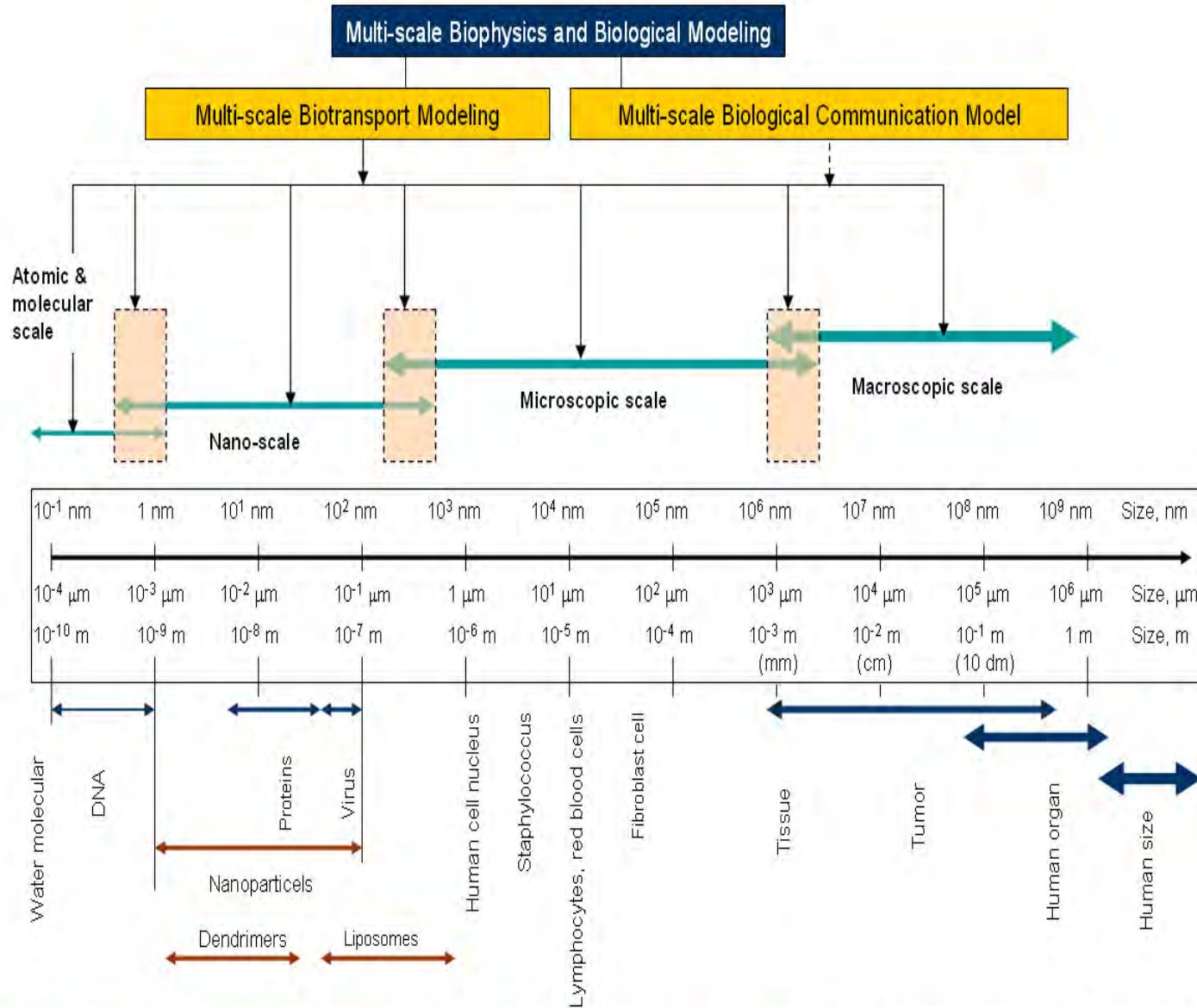
<b>Imaging Technique</b>	<b>EM Radiation Spectrum Used In Image Generation</b>	<b>Advantages</b>	<b>Disadvantages</b>
Positron emission tomography (PET)	High energy gamma rays	High sensitivity; isotopes can substitute for naturally occurring atoms; quantitative; translational research	PET cyclotron or generator needed; relatively low spatial resolution; radiation of subject
Single photon emission computed tomography (SPECT)	Lower energy gamma rays	Many molecular probes available; can image multiple probes simultaneously; may be adapted to clinical imaging systems	Relatively low spatial resolution; radiation
Optical bioluminescence imaging	Visible light	Highest sensitivity; quick, easy, low cost, and relatively high throughput	Low spatial resolution; current 2-D imaging only; relatively surface-weighted; limited translational research
Optical fluorescence imaging	Visible light or near-infrared	High sensitivity; detects fluorochrome in live and dead cells	Relatively low spatial resolution; relatively surface-weighted
Magnetic resonance imaging (MRI)	Radio waves	Highest spatial resolution; combines morphologic and functional imaging	Relatively low sensitivity; long scan and postprocessing time; mass quantity of probe may be needed
Computed tomography (CT)	X-rays	Bone and tumor imaging; anatomic imaging	Limited 'molecular' applications; limited soft tissue resolution; radiation
Ultrasound	High-frequency sound	Real time; low cost	Limited spatial resolution; mostly morphologic although targeted microbubbles under development



# Overview of imaging modalities



# Scale



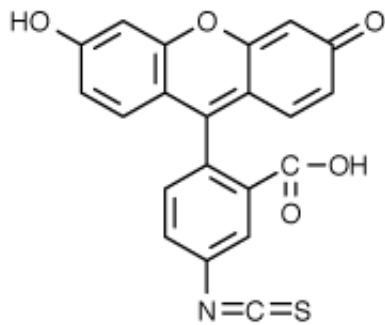
# Molecular Imaging Strategies

## (Imaging Probes)

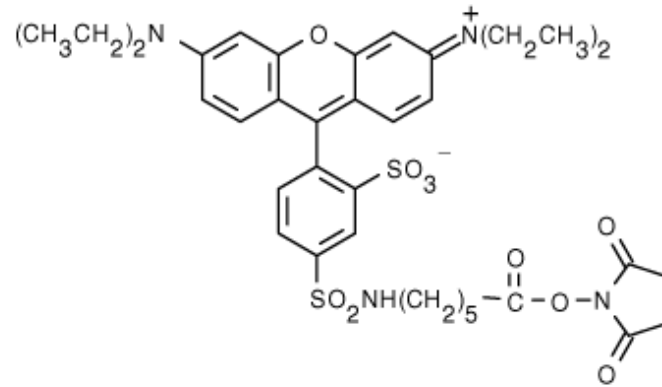
	Injectable Agents	Genetically encoded reporters
Endogenous Genes Proteins	<p>Radiopharmaceuticals PET, SPECT, MRI, U/S, Optical, QDots</p> <p>(Clinical)</p>	<p>Endogenous fluorophores, Metabolites/MRS, pH, O<sub>2</sub> content</p>
Exogenous Transgenes Proteins	<p>Gene Therapy, HSV-TK/ 18FHBG, Transferrin Receptor/MION</p>	<p>GFP, Luciferase, Signal transduction fusions, Protein-protein interactions, Transgenic reporter mice</p> <p>(Basic)</p>

# Fluorophores

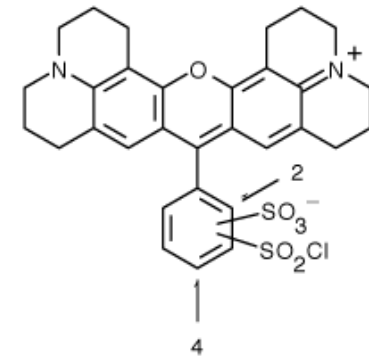
Generally some form of polyaromatic hydrocarbons or heterocycles



FITC



RHODAMINE RED



TEXAS RED

Process is cyclical unless molecule is destroyed (bleaching)

For in vivo use want absorption/emission in red/near IR to maximize fluorescence emissions