1.What is MRI?

Non-invasive method to form a picture of the anatomy but also physiology of processes in the body, better contrast of soft tissues

2. DTI?

（1）anisotropic diffusion: restrict the movement direction of water

(2) isotropic diffusion: no restriction

Measures the restricted diffusion of water molecules in tissue

Maps the structure of fiber tracts to model brain connectivity

3. fMRI, watching brain activity in real time: detects blood flow and Blood oxygenation level.

4.schizophrenia: cognitive disorder (brain volume reduction and loss of neurons): medial pulvinar(pm)



6.Describe the principles of the following imaging techniques:

• Microcomputed tomography (MicroCT): allow 3d visual reconstruction

1. X-rays are generated

2. X-rays are transmitted through sample

3. X-rays are absorbed/attenuated by tissue and transmitted x-rays are detected

4. Sample is rotated and iterative projection images are obtained

5. The projection images are reconstructed with software to give virtual slices

Use of agents to increase contrast and attenuation: Iodine based; nanoparticle based; lanthanide-based-> different types of agents have different targets

Application: 3D bone (bone marrow) architecture; analysis of bone mass and bone formation/resorption; in vivo monitoring vascularization in bone cancer; tumor imaging

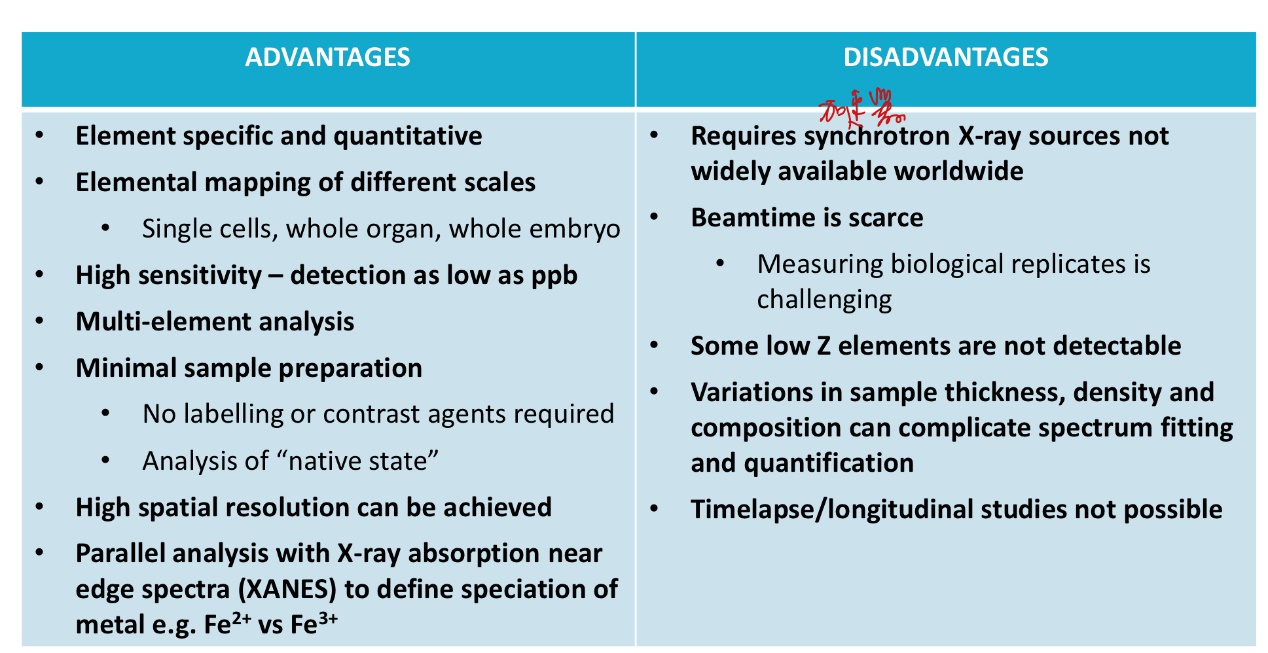
Analysis in normal and disease models: the attenuation of them varies result in significant MicroCT imaging.

• X-ray fluorescence microscopy (XFM)

Excites unique low-energy light by emitting high-energy light(X-ray).

Analysis of muti-elemental X-ray(different tissues have different concentration of elements): K lines of several elements show unique X-ray fluorescence peaks. Energies of X-ray lines are only dependent on atomic energy levels and will always be the same.

Advantages and disadvantages of synchrotron based XFM:



• Bioluminescence imaging (BLI):production and emission of light by a living organism via a chemical reaction.

Application: trans genetic mouse using fluorescent genes from firefly to monitor infection dynamics.

Advantages: build animal disease models, low cost, high sensitivity

Disadvantages: absorb short wavelength of light; route of administration will influence; hair will absorb the light.

7.light microscopy - brightfield: uses white light and detects contrast in sample originating from variable densities in sample that attenuates light.

Advantages: Excellent for colored samples

Disadvantages: Staining methods often incompatible with living cells and organisms.

8.light microscopy – contrast techniques: phase contrast and DIC/ darkfield/ birefringence

9.phase contrast and DIC: rely on the specimen changing of the phase of the light. (require specific optics)

Suitable for high resolution imaging of unstained cells and transparent small organisms.

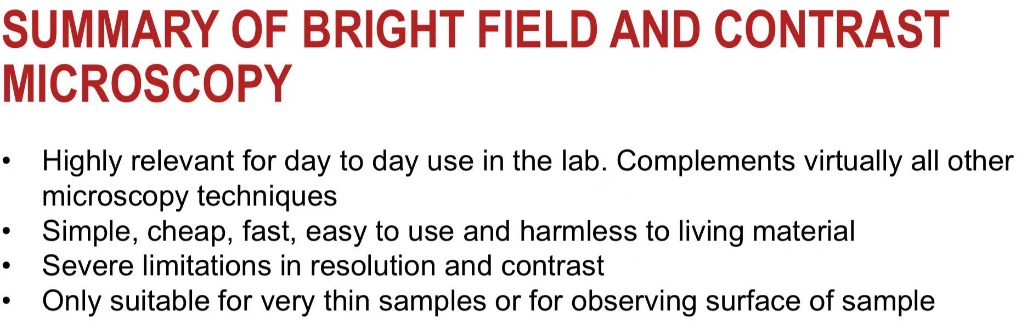
Visualize cells in culture.

10. darkfield: give “inverse” negative image of specimen against black background.

Useful for very transparent samples and low resolution.

11. polarized light (birefringence microscopy): use polarizer to induce single orientation in the light path.

Detect changes in stereotypic patterns



12.Fluorescence microscopy: Property of molecule to absorb light of one wavelength and emit light of another wavelength; Enable ways to specifically distinguish structures in cells and tissue with high spatial resolution using endogenous properties “autofluorescence” or labelling techniques (fluorophores).

Increase contrast and resolution in biological samples.

Advantages: high lateral resolution

Disadvantages: axial resolution limited. Only suitable for thin samples.

Colorized:

13. Autofluorescence: Cells and tissues have different fluorescent properties (caused by metabolites, pigments and structural proteins)

14.Fluorophores: uses small molecules absorbing light of one wavelength and emit light of another wavelength.

label biomolecules in vitro and in vivo(immunofluorescence)

15.Fluorecent proteins: jellyfish fluorescent proteins: GFP

Techniques in observing of fluorescence microscopy

16.confocal microscopy: use optical sectioning to remove out-of-focus information

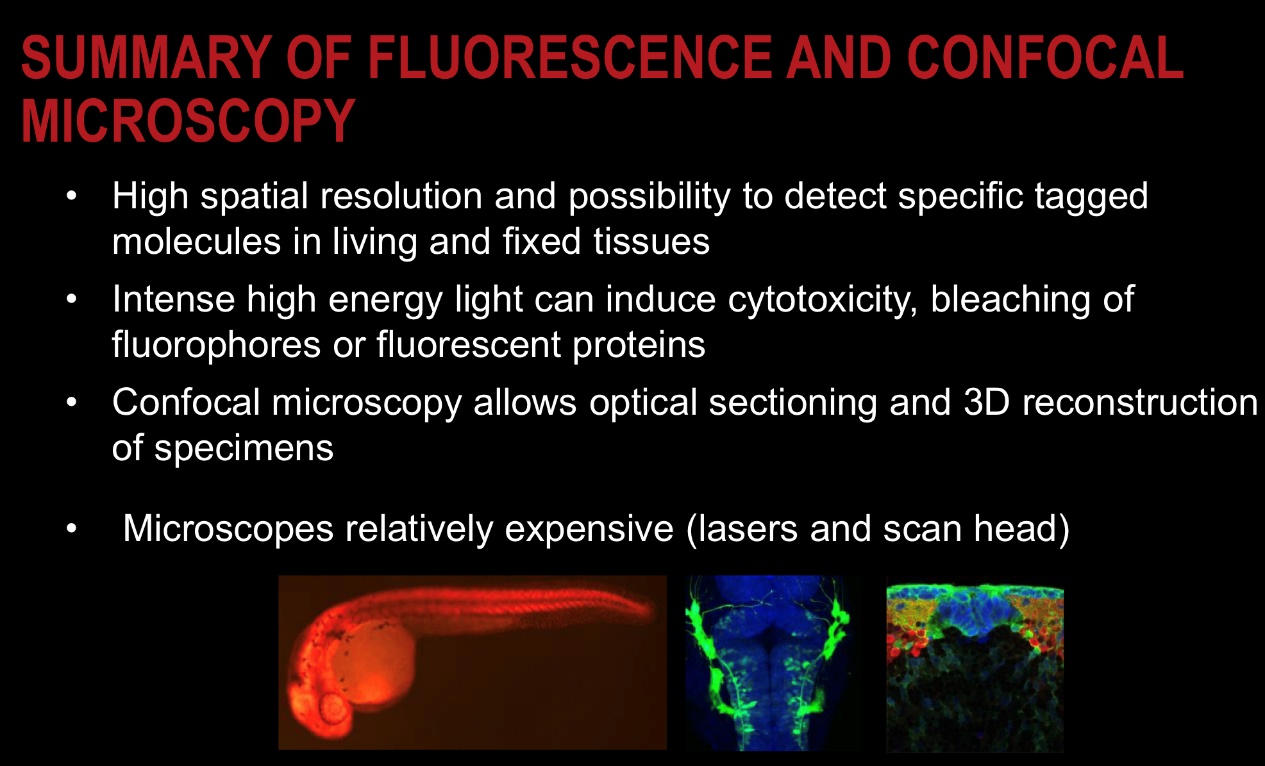
Point scanning (pixel by pixel and row by row)

Advantages: accurate and sensitive, higher lateral resolution

Disadvantages: bleaching and cytotoxicity; thickness of objectives is required

Point scanner rather than digital camera.

3D reconstruction



17.Judgements of image: resolution; depth; sensitivity and acquisition speed.

Imaging methods that specialize & excel on each of these aspects:

Resolution(higher) energy(lower) speed(faster)

18.Speed:

19.spinning disk confocal microscopy: using multiple pinholes (digital camera) capture entire field at the same time.

Advantages: fast -> good for living imaging and small samples

Disadvantages: reduced resolution; expensive; bleaching

20. light sheet microscopy: thin sheet of light to detection (resolution determined by thickness of light sheet) camera required

Can maximize benefit by rotation of samples

Advantages: Fast and homogenous imaging from large samples; less bleaching and cytotoxicity; imaging from multiple angles of targets

Disadvantages: lower resolution; require significant computational resources to decode.

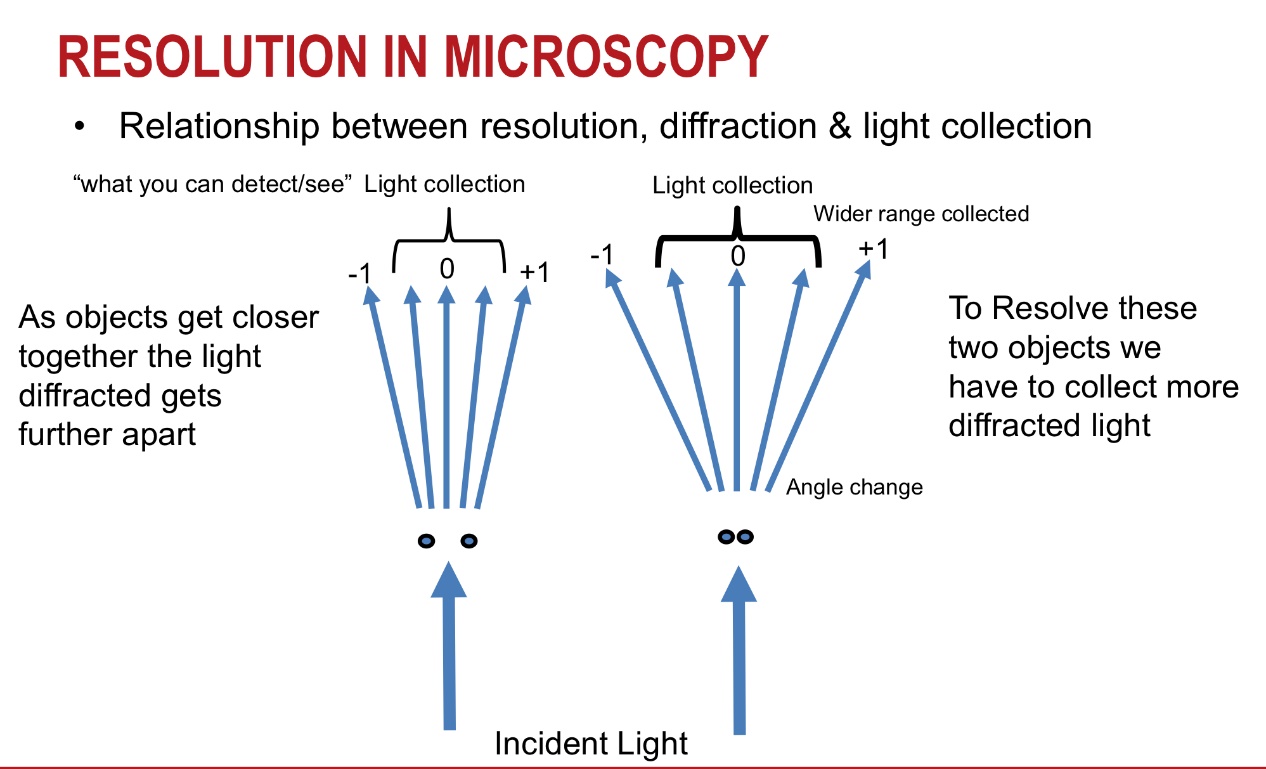
21.Energy:

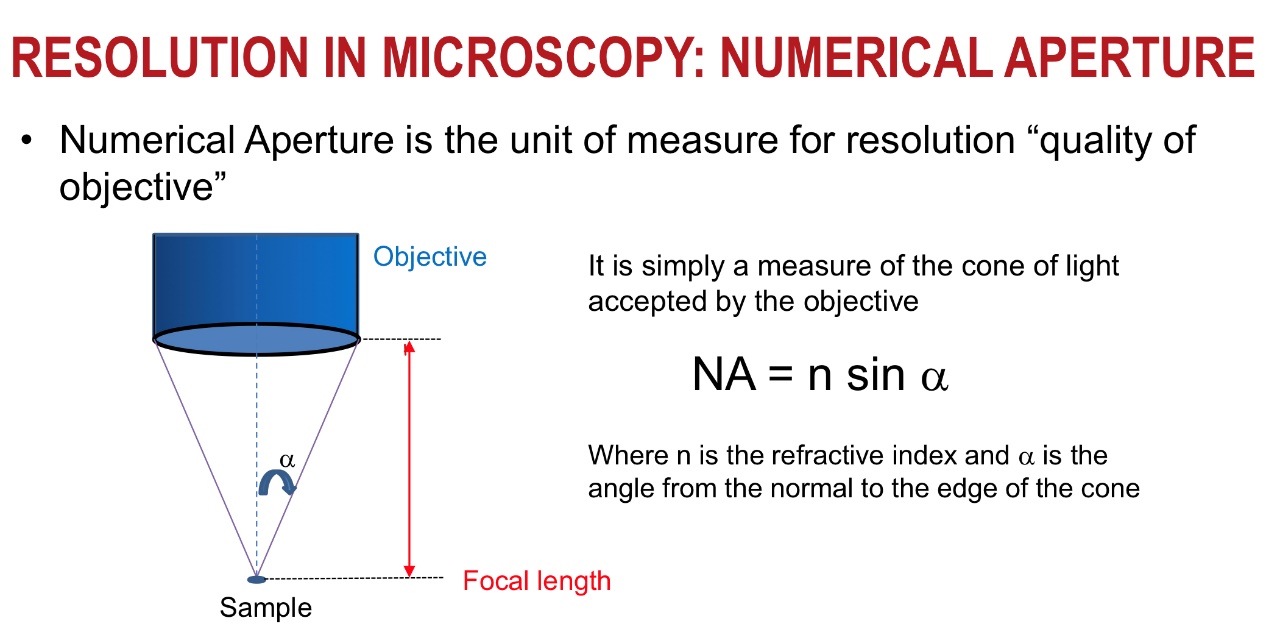
22.multiphoton microscopy: use long wavelength (high concentration and low cytotoxicity) light precise illumination (minimizes out of focus light). Based on multiphoton excitation principle. Equals advantages.

Disadvantages: complex lasers and temperamental to operate; expensive; unpredictable excitation max

23.Resolution:

Magnification: enlarge the pictures/ Resolution: make it clear.





Higher NA->more light captured->higher resolution(by shortening the distance to sample, no closer than working distance; get bigger objective glass; change refractive index)

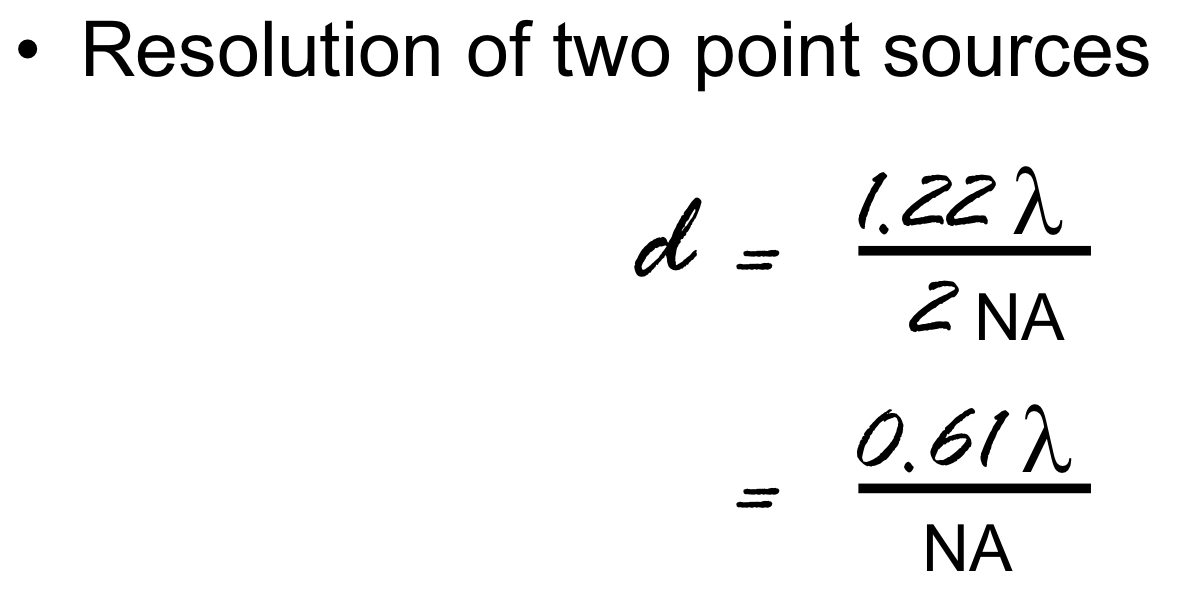
Objective limitations:

Weight and size limitations

Photons are lost at each optical element(lens)

Complexity and number of optical elements increases with magnification

d(lower)



24. super resolution:

STED (overcome the limits resolution of light microscopy): suppress surrounded fluorescence (reducing excitation and increasing resolution) with suppression laser without impact on central dose.

Applied to living cells and fixed tissues

Advantages: superior resolution

Disadvantages: limited to few fluorophores and fluorescent proteins; expensive

STORM: different fluorophores emit light at different times.

Applied to fixed tissues.

Advantages: superior resolution

Disadvantages: slow; repeated illuminated; limited to few fluorophores and fluorescent proteins

Resolution improved by deconvolution: uses mathematical/ computational process to correct for reproducible artifacts.

Advantages: good in thin and less complex samples with little PSF; widely applicable to methods before.

Disadvantages: artificially alter data; intense computation

Registration: adjust location

Quantitative approach: colocalization

Judgements: number, location, brightness