

#### Outline

- Detector resolution and other specs
- Modular cameras and integrating detectors
- · Scintillator materials and statistics
- Optical coupling
- Photodetectors
- CCD/CMOS-based gamma cameras
- MLE in scintillation cameras
- Likelihood theory and camera design
- Summary and conclusions

#### **Detector resolution**

Conventional wisdom: Detector resolution is irrelevant since you are always limited by the collimator anyway





# S mm resolution 6 mm resolution 3.2M counts 4 mm resolution 4 mm resolution 100k counts

Gerd Muehllehner, Phys. Med. Biol. (30)2:163-173, (1985).

(b)

mage quality





#### Need for high detection efficiency?

In both SPECT and PET, objective performance measures improve with better system resolution, even at the expense of counts

Useful single-number characterization for detectors:

Space-bandwidth-efficiency product (coincidence efficiency for PET)

Count-rate capability Do we need fast detectors?

- No we can use lots of slower ones
- We can even use integrating detectors!

#### Modular detectors

- Modular detectors are:
  - Electrically and mechanically independent
  - Relatively low cost
  - Small (compared to object size)
- Advantages:
  - Inexpensive

  - Easily interchanged for service
    Reconfigurable for different imaging applications
    High countrate capability
    Parallel collection of projection data, high sensitivity

#### Examples of modular detectors









#### Photon counting and energy resolution with integrating detectors



Barber et al., Physica Medica, 1993; Trans. Med. Imag. 1993

#### A scintillation camera consists of:

- Scintillator material
   Monolithic crystal
   Segmented crystal

  - Columnar
- Optical coupling mechanism
   Proximity coupling ("light guide" in an Anger camera)
   Lenses and mirrors
- Lenses and mirrors
   Fiber optics
   Optical sensors
   PMTs
   MAPMTs, PSPMTs
   Si PIN diodes, APDs, SPMs, etc.
   CCD or CMOS sensors
   Data processing
   Event detection
   Appret arithmetic

  - Anger arithmetic
     ML methods

#### **Scintillators**

- Key requirements for scintillation cameras:
  - Large crystals
  - High light output
  - Good proportionality
  - Low Fano factor!



Candidate scintillators for SPECT

Material	Density (g/cm³)	Attenuation coefficient @140keV (cm <sup>-1</sup> )	Light yield (phot/MeV)	Peak emission (nm)	Non- Proportionality (10-200 keV)
Nal(TI)	3.67	2.64	45,000	415	20%
LaBr <sub>3</sub> (Ce)	5.1	2.89	74,000	375	15%
Srl <sub>2</sub> (Eu)	4.6	3.28	90,000	435	5%
Yl <sub>3</sub> (Ce)	4.6	3.44	99,000	549	<2%
Lul <sub>3</sub> (Ce)	5.6	6.16	115,000	522	< 2%
Elpasolites	4.2	3.95	Up to 60,000	445	< 2%

Nonproportionality degrades energy *and* spatial resolution (Correlated signals reduce Fisher information)



#### What everyone knows about Fano Factor: $\sigma_n^2 = \overline{N}_{opt} \eta F$

But it is also true (Barrett and Swindell, 1981) that:

#### $\langle \Delta n_1 \Delta n_2 \rangle = \eta_1 \eta_2 \overline{N}_{opt} (F-1)$

So Fano factor can be measured by observing correlations in two different photodetectors viewing the same scintillation event.

Positive correlations are caused by: F > 1

Multiple energy deposition pathways + nonproportionality Variation of light collection as function of random position Random energy deposition, other nuisance parameters PMT gain noise, electronic noise Negative correlations are caused by F < 1

Photon anti-bunching, sub-Poisson (sub-Moses) statistics









## Estimates of Fano factor Unpublished work of Vaibhav Bora et al.

Crystal	Correlation coefficent	Photoelectron Fano factor (F <sub>n</sub> )	Photon Fano Factor (F <sub>N</sub> )
Srl <sub>2</sub> :Eu	-0.3336 ± 0.2384	0.7324 ± 0.0604	0.0441 ± 0.2157
YAP:Ce	0.1036 ± 0.0691	1.1237 ± 0.0042	1.4419 ± 0.0151
Csl:Na	0.3643 ± 0.2292	1.6132 ± 0.1960	3.1899 ± 0.6999
LaBr <sub>3</sub> :Ce	-0.32 ± 0.17	0.72 ± 0.06	0.10 ± 0.16

Optical coupling in Scintillation cameras



#### Imaging optics: lenses and fibers



#### Fiber optic tapers



Schott Glass



Roper Scientific

#### The demagnification problem

Both lenses and fiber tapers have numerical apertures

Collection efficiency varies as m<sup>2</sup> for both (m = magnification; usually m < 1)

Large FOV + small CCD => small coupling efficiency



#### Seeing the light (optical sensors)

- Photomultiplier tubes
   Conventional

  - Multi-anode (MAPMT)
     Position-sensitive (PSPMT)
- Photodiodes
  - Si PiN
     Silicon drift detectors

  - Hgl<sub>2</sub>
     Avalanche photodiodes (APDs)
     Geiger-mode APD arrays (SPMs)
- CCD and CMOS sensors

#### Advances in Photocathodes PECTRAL RESPONSE CHARACTERISTICS Metal Package PMT (TO-8 Type) STANDARD SUPER CLARITY gth (nm) 200 250 400 450 600 550 400 WAVELENGTH (nm) Hamamatsu

#### Multianode PMTs and SPM arrays



Hamamatsu H8500 MAPMT



SensL SPM array

#### PMTs: Pluses and minuses

- Pluses
  - Familiar technology
  - Large gain before electronic noise
  - Modest (but improving) quantum efficiency
  - Dark current negligible (with blue scintillators)
  - Large sensor size (reduces processing req)
- Minuses
  - Bulky, fragile
  - Gain depends on voltage, temperature, time
  - Sensitive to magnetic fieldsLarge sensor size (affects spatial and DOI resol)

#### Silicon photodiodes: Pluses and minuses

#### Pluses

- High quantum efficiency
- Long-wavelength sensitivity
- Stable, robust
- Small sensor size

#### Minuses

- No gain before electronic noise
  Dark current
- Small sensor size

#### Avalanche Photodiodes (APDs) and Silicon Photomultipliers (SPMs, Geiger-mode APDs): Pluses and minuses

- Pluses
  - High quantum efficiency

  - Internal gain before electronic noise
    Small sensor size (potentially high spatial resolution)
- Minuses

  - Noisy gain (APDs)
    Gain depends strongly on voltage (APDs)
    Low fill factor partially negates QE advantage (SPMs)
    Small sensor size (costly to cover large area)

- Recent advances in CCDs
- Larger sensor area - Less light loss
- Back-thinning and AR coating
  - Higher QE
- Cooling
- Lower dark current
- Electron multiplication
- Smaller read noise (at expense of dynamic range) Parallel readout
  - Shorter frame time

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	O SPECTROSCOPY	Higher Throughput     Compact Housing			Server Server		
CCD		Kodak KAF-09000		-			
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Pixel Size		12 x 12 microns					
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Dynamic Ra	ange	84 dB		Poor			
QE at 400 n	m	37%		Real			
Peak QE (5:	50 nm)	64%					
Anti-bloomi	ing	>100X					



### Leica M-Monochrom

Rangefinder CCD



## Recent advances in CMOS (active pixel) sensors

- Signal processing circuitry at each pixel
- Greatly reduced readout noise at high pixel rates
- Microlenses to concentrate light on active area
- "Digital" lenses (telecentric in image space)
- Larger sensors
- Parallel readout
- Ultrafast frame rates

#### "Prosumer" DSLR cameras 24 X 36 mm CMOS sensors



Nikon D700, 12 MP, ~\$2400



Canon EOS 5D Mk II, 22 MP, ~ \$2500 Canon EOS 5D, 12 MP, ~ \$2000

#### Two new sCMOS cameras from Andor



## CMOS chip layout





http://micro.magnet.fsu.edu/primer/digitalimaging/cmosimagesensors.html









#### CCD/CMOS-based scintillation cameras Photon counting with integrating detectors

- Lens-coupling to scientific-grade CCD

   LumiSPECT (Taylor 2004, Miller 2007)
- Image intensification
  - EMCCD (DeVree 2004, Nagarkar 2005, Teo 2006, Miller 2006, Lewis 2007)
  - Microchannel plates (Miller 2006)
  - Vacuum intensifier + EMCCD (Meng 2006)



#### LumiSPECT CCD properties

Detector Type	VersArray 1300B, scientific grade	
CCD Format	$1340 \times 1340 \times 20 \mu m$ Pixels	
Dark Current	$0.1e^{-}/\text{pixels/sec}@-40^{\circ}C,$ $0.5e^{-}\text{pixels/hr}@-110^{\circ}C$	
Read Noise	$3e^{-}$ @50kHz scan rate, $12e^{-}$ @1MHz scan rate	
Binning Modes	$2 \times 2, 3 \times 3, 4 \times 4$	
Full-frame Readout	36sec@50kHz, 1.8sec@1MHz	
Thermal Precision	$\pm 0.1$ degrees Celsius over entire temperature range	
Nonuniformity	$\leq 4\%$ over active area of CCD	

#### LumiSPECT Photon-Counting Mode Brian Miller, 2007





2x2 binning to sample at 40µm pixels
 Tc99m γ-rays
 RMD columnar Csl(Tl), 270µm thick







## Hicrochannel-plate detectors (work of Brian Miller)





## Data acquisition and processing for scintillation detectors

- · Conventional approach:
  - Immediately apply Anger arithmetic
  - Patch up the problems that result
- Recommended approach:
  - Collect all possible data in list mode
  - Apply rigorous ML estimation methods

#### Maximum-likelihood estimation

Likelihood = probability ( data | parameters )

Maximum likelihood: choose the parameter values that maximize the likelihood for the observed data

Advantages

Accounts for data statistics

Enforces agreement with data in a statistical sense

Nice asymptotic properties (as you get better data) Best possible variance Unbiased (right answer on average)

#### Maximum-likelihood estimation

• MLE maximizes the probability of the data given the parameter :

 $\hat{ heta}_{\mathsf{ML}} \equiv egin{argmax}{l} \mathsf{argmax} & \mathsf{pr}(\mathbf{g}|m{ heta}) \\ m{ heta} \end{array}$ 

• Equivalently, maximizes the logarithm of this conditional probability:

 $\hat{ heta}_{\mathsf{ML}} = egin{argmax}{l} \mathsf{argmax} & \mathsf{ln}[\mathsf{pr}(\mathbf{g}| heta)] \\ eta \end{array}$ 

#### Fisher information matrix

#### Definition

$$F_{jk} = \left\langle \left[ \frac{\partial}{\partial \theta_j} \ln \mathsf{pr}(\mathbf{g}|\boldsymbol{\theta}) \right] \left[ \frac{\partial}{\partial \theta_k} \ln \mathsf{pr}(\mathbf{g}|\boldsymbol{\theta}) \right] \right\rangle_{\mathbf{g}}$$

Cramer-Rao lower bound (for unbiased estimator)

$$\operatorname{Var}\{\hat{\theta}_n\} \geq \left[\mathbf{F}^{-1}\right]_n$$

Off-diagonal elements of inverse relate to covariances of estimates

An *efficient estimator* is one that is unbiased and for which the CR bound become an equality

In any problem, the ML estimator is efficient if an efficient estimator exists

The ML estimator is always asymptotically efficient ...

... as you get more or better data

....thereby increasing the (Fisher) information content

## Log-likelihood and FIM for Poisson statistics

$$\ln \Pr(\mathbf{g}|\boldsymbol{\theta}) = \sum_{m=1}^{M} \{-\overline{g}_m(\boldsymbol{\theta}) + g_m \ln[\overline{g}_m(\boldsymbol{\theta})] - \ln g_m!\}$$

$$F_{jk} = \sum_{m=1}^{M} \frac{1}{\overline{g}_m(\boldsymbol{\theta})} \frac{\partial \overline{g}_m(\boldsymbol{\theta})}{\partial \theta_j} \frac{\partial \overline{g}_m(\boldsymbol{\theta})}{\partial \theta_k}$$

Key point: likelihood and FIM can be computed from knowledge of mean data only

#### Independent Gaussian noise (usual model for electronic noise)

$$\ln \operatorname{pr}(\mathbf{g}|\boldsymbol{\theta}) = constant - \frac{1}{2\sigma^2} \sum_{m=1}^{M} [g_m - \overline{g}_m(\boldsymbol{\theta})]^2$$

$$F_{jk} = \frac{1}{\sigma^2} \sum_{m=1}^{M} \frac{\partial \overline{g}_m(\theta)}{\partial \theta_j} \frac{\partial \overline{g}_m(\theta)}{\partial \theta_k}$$

Again, log-likelihood and FIM can be computed from knowledge of mean data only

#### ML Methods for processing signals from gamma-ray detectors

H. H. Barrett et al., IEEE Trans. Nucl. Sci., 56:725-735, 2009.

#### Event-by-event gamma-ray imaging

- Why gamma-ray photons are different from optical photons:
  - Gamma-ray photons arrive at slow rate, compared to resolving time of electronics
  - Large energy per photon
  - Get a lot of information from each photon
- From one photon, can estimate up to five attributes:
  - 2D position on detector face (x, y)
  - Depth of interaction (z)
  - Energy
  - Time of arrival

#### 2D position estimation for a 3X3 modular camera

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#### Experimental validation Work of Stephen Moore (IEEE MIC 2007)







#### Contracting-Grid Search Algorithm

Example for position estimation for a single experimental event:



L. Furenlid et al., 2005

J. Hesterman et al., IEEE Trans.Nucl. Sci., 57(3), 1077-1084 2010

#### ML position estimation in practice Jacob Hesterman, Luca Caucci, Steve Moore

- Modeling and calibration
  - Optics
  - Poisson noise
  - PMT gain noiseNonproportionality
- Hardware
  - Cell processors
  - GPUs
  - Gate arrays
- Software
  - Native cell processing
  - CUDA
  - Gate array programming

Image: Note of the sector of

~ 10<sup>6</sup> events/sec on one PlayStation 3 3D position estimation, 64-anode MAPMT: ~64,000 events/sec on one GeForce 9800

## Statistics of scintillation detectors based on CCD or CMOS cameras:

A case study in detector design

B. W. Miller et al., Proc. SPIE, 7450-24, 2009

#### CCD/CMOS-based scintillation cameras Photon counting with integrating detectors

- Lens-coupling to scientific-grade CCD

   LumiSPECT (Taylor 2004, Miller 2007)
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  - Microchannel plates + CMOS (Miller 2006)
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#### Random effects in this class of gamma cameras

- Random light collection and production of photoelectrons
- Dark current
- Random amplification
- Readout noise after the amplification

#### Mean signal

Mean number of optical photons produced by gamma photon of energy  $\mathcal{E}\colon$ 

 $\overline{N}_{opt} = A\mathcal{E}$ ,

The mean number of electrons generated in the  $m^{th}$  pixel;

 $\overline{n}_m(x,y,z,\mathcal{E}) = A \, \mathcal{E} \, \eta_{QE} \, \eta_m(x,y,z) + \overline{n}_m^{dark} \, ,$ 

where  $\overline{n}_{dark}^{dark}$  is the mean number generated in the dark by thermal excitation and  $A \mathcal{E} \eta_{QE}$  is the mean number generated by the scintillation flash.

Mean of the final pixel value  $g_m$ :

 $\overline{g}_m(x,y,z,\mathcal{E}) = \overline{G}\overline{n}_m(x,y,z,\mathcal{E})$ 

where  $\overline{G}$  is the overall mean gain, including all components between the photon-to-electron conversion and the final readout.

#### Variance and covariance

The variance, conditional on the interaction location and energy, is given by

 $\operatorname{Var}\{g_m | x, y, z, \mathcal{E}\} = \overline{n}_m(x, y, z, \mathcal{E}) \left[\operatorname{Var} G + \overline{G}^2\right] + \sigma^2,$ 

where Var G is the variance of the gain and  $\sigma^2$  is the variance of the readout noise, both assumed independent of m.

If the optical blur is negligible compared to pixel size, then the covariance matrix for  ${\bf g},$  denoted  ${\bf K},$  has elements given by

 $K_{mm'}(x, y, z, \mathcal{E}) = \left[\overline{n}_m(x, y, z, \mathcal{E})\overline{G}^2(1+\alpha) + \sigma^2\right]\delta_{mm'},$ 

where  $\alpha \equiv \operatorname{Var} G/\overline{G}^2$  .

In practice,  $\alpha \approx 1$  for both image intensifiers and EMCCDs.

If pre-readout gain is large enough, readout noise is negligible in all systems

#### Likelihood and log-likelihood

If we approximate the Poisson distribution for  $n_m$  by a Gaussian and assume that both the gain noise and the readout noise are Gaussian, the likelihood function is

$$\operatorname{pr}(\mathbf{g}|x, y, z, \mathcal{E}) = \frac{1}{\sqrt{(2\pi)^M \prod_{m=1}^M K_{mm}(x, y, z, \mathcal{E})}} \exp\left\{-\frac{1}{2} \sum_{m=1}^M \frac{[g_m - \overline{g}_m(x, y, z, \mathcal{E})]^2}{K_{mm}(x, y, z, \mathcal{E})}\right\}$$

and the corresponding log-likelihood becomes

$$\ln \operatorname{pr}(\mathbf{g}|x,y,z,\mathcal{E}) = -\frac{1}{2} \sum_{m=1}^{M} \ln K_{mm}(x,y,z,\mathcal{E}) - \frac{1}{2} \sum_{m=1}^{M} \frac{[g_m - \overline{g}_m(x,y,z,\mathcal{E})]^2}{K_{mm}(x,y,z,\mathcal{E})} + C \,,$$

where C is a constant, independent of the parameters to be estimated.

## Fisher information matrix and Cramér-Rao Bound

$$F_{jj'}(\boldsymbol{\theta}) \approx \frac{1}{1+\alpha} \sum_{m=1}^{M} \frac{1}{\overline{n}_m(\boldsymbol{\theta})} \frac{\partial \overline{n}_m(\boldsymbol{\theta})}{\partial \theta_j} \frac{\partial \overline{n}_m(\boldsymbol{\theta})}{\partial \theta_{j'}}.$$

$$\operatorname{Var}\left\{\hat{\theta}_{j}\right\} \geq \left[\mathbf{F}^{-1}(\boldsymbol{\theta})\right]_{jj}$$

$$F_{jj'}(\boldsymbol{\theta}) \approx \frac{1}{1+\alpha} \sum_{m=1}^{M} \frac{1}{\overline{n}_m(\boldsymbol{\theta})} \frac{\partial \overline{n}_m(\boldsymbol{\theta})}{\partial \theta_j} \frac{\partial \overline{n}_m(\boldsymbol{\theta})}{\partial \theta_{j'}}$$
$$\overline{n}_m(x, y, z, \mathcal{E}) = A \mathcal{E} \eta_{QE} \eta_m(x, y, z) + \overline{n}_m^{dark}.$$

- Mean gain unimportant, if it is large enough to override readout noise
- Gain noise reduces Fisher information ~ 2x
- Dark current reduces Fisher information
- Dark current can be reduced by use of:
- cooling
- photocathode with no red response
- faster frame rate
- Effect of dark current is reduced by more efficiently creating photoelectrons: larger QE, better optical coupling, larger PC, etc.
- MLE reduces effect of dark current by optimal weighting of pixels
- Demagnification before photocathode is deleterious

Property	Unintensified CCD	EMCCD	Vacuum II + EMCCD	MCP + CMOS
QE	Outstanding	Excellent	Good	Good
Optical collection efficiency	Poor if minification is used	Poor if minification is used	Excellent with large-area intensifier and no minification	Good to excellent, depending on area
Readout noise	Fair, reduced by slow readout (much better with CMOS DSLRs)	Negligible at high gain, but at sacrifice of dynamic range	Same as EMCCD	Negligible, no sacrifice of dynamic range
Dark current	Problematical at room temp, can be reduced by cooling	Same as CCD	Same as CCD	Fair with surplus night vision devices, excellent with custom PC, reduce with high frame rates
Readout speed	Limited by CCD, very poor for scientific CCDs	Limited by EMCCD, ~30 fps	Limited by EMCCD, ~30 fps	Can use ultrafast CMOS, to 67,500 fps

#### Conclusions

- Space-bandwidth is our most important product
- What Poisson limit?
- Count on integrating detectors
- Are CCDs obsolete?
- Likely, fast and accurate!
- Get more information!