Phantom Realism
in Virtual (pre-) Clinical Trials:
A Statistical Properties Perspective

Craig Abbey

Outline

- Phantom Realism
  - What is the goal?
  - What can we do?
- Statistical Properties
  - Power spectra
  - Laplacian Fractional Entropy

Virtual Clinical Trials

- Use simulation to assess devices and methodology instead of reader studies from acquired cases
  - Virtual Readers (Model observers)
  - Virtual Cases (Digital Phantoms)
- Overriding Goal: Get the right answer!
  - The same answer as a non-virtual clinical trial...
  - Correct sign...

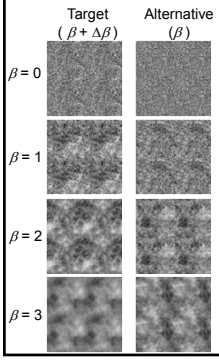
Getting the Right Answer → Validation

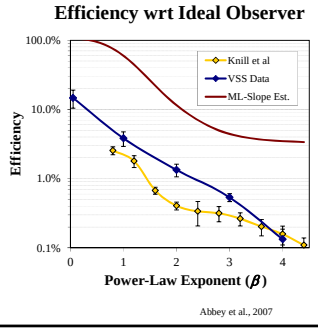
- Prospective Prediction
  - Hard
  - Can defeat the purpose
- Retrospective Prediction
  - Potential for bias
  - Limited data...
- Independent Laboratory Validation for Phantoms
  - Psychophysical validation
  - Statistical validation

Psychophysical Validation

- A visual "Turing Test": Is this a real patient?
- May get clinician buy-in
- Really hard to simulate an entire scan!
  - Less difficult for "virtual" components added to clinical images
- Study design is important:
- Not clear that what looks real spans all the features that influence decision making

Psychophysical Discrimination of Gaussian Textures





Statistical Validation

- Match statistical properties (Mean, power spectrum, etc.)
- Eventually, statistical and psychophysical validations should converge
- Advantage: Very clear what the comparison is...
- Disadvantage: Not clear what is enough...

Non-Gaussian statistical properties of virtual breast phantoms

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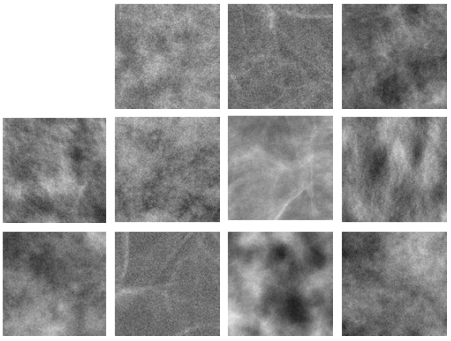
Main Points

- Virtual Breast Phantoms
  - Software programs that simulate the breast for the purpose of evaluating imaging systems
  - Capture limiting sources of variability in the object
- What is a good phantom?
  - How does one validate the "realism" of a virtual phantom
  - One Approach: Match statistical properties of breast images
- Power spectra
  - All phantoms approximately power-law + noise
  - This is good for the power law, but bad for validation
- Higher-order statistics
  - Laplacian Fractional Entropy (LFE)
  - Substantial differences between phantoms

How realistic are simulations of breast tissue?



Study Design

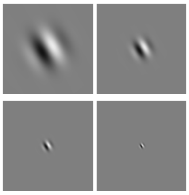
- Virtual Breast Phantoms
  - Clustered-Blob Lumpy Backgrounds (Bochud et al. 1995, 2008)
  - Truncated Binary Processes (Abbey & Boone 2008, Reiser and Nishikawa 2010)
  - UPenn Breast Phantom (Bakic, Maidment, Pokrajac, 2002, 2011, 2012)
- Full field digital mammograms
  - Hologic Selenia Dimesions system at UC Davis Medical Center
  - 19 Women selected from biopsy population
  - Acquired the "For Processing" images. Log-converted to density.
- Endpoints
  - Comparisons of power spectra
  - Comparisons of Laplacian Fractional Entropy

Gaussian and non-Gaussian Statistics

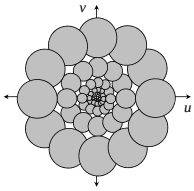
- Stationary Gaussian Process
- Fully described by mean and power spectrum
- Gaussian response histogram for any linear filter
  - Limit of a large enough ROI
- Maximum Entropy
  - Most uncertainty you can fit into 2nd-order statistics
- non-Gaussian Statistics
  - Represent higher-order statistical structure
  - Associated with "sparsity" and "tails"
  - Less uncertainty
  - Lots of them!

Octave Bandwidth Gabor Filters

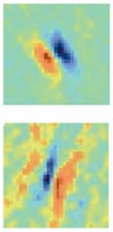
A. Filter Kernels



B. Filter Supports



C. Receptive Fields[1]

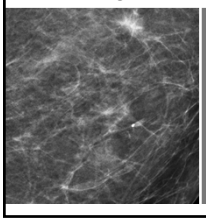


[1]Ringach et al. *J. Vis.* 2002

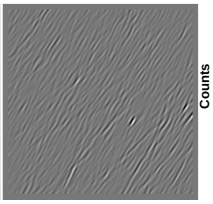
Gabor Filter Responses

Octave Bandwidth Filter (magnified)

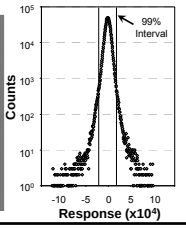
Mammogram



Convolution



Response Histogram



Definition of LFE

- Min relative entropy of histogram to Gaussian

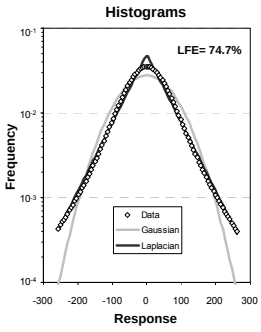
$$\mathrm{E}_{\text{Rel-Gauss}} = \min_{\mu,\sigma}\left(\sum_{n=1}^{N_{\text{Bin}}} p_n \ln\left(\frac{p_n}{q_n(\mu,\sigma)}\right)\right)$$

- Min relative entropy of Laplacian to Gaussian

$$\mathrm{E}_{\text{Rel-Lap}} = \min_{a,b}\left(\sum_{n=1}^{N_{\text{Bin}}} y_n(a,b) \ln\left(\frac{y_n(a,b)}{q_n(\mu_{\min},\sigma_{\min})}\right)\right)$$

- Ratio

$$\text{LFE} = \mathrm{E}_{\text{Rel-Gauss}} / \mathrm{E}_{\text{Rel-Lap}}$$

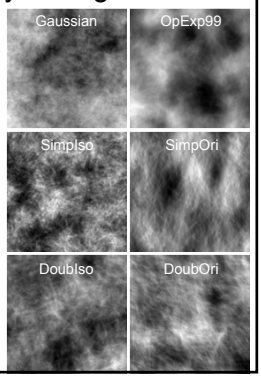


Clustered-Blob Lumpy Backgrounds

- Based on Type I Lumpy Backgrounds (Rolland and Barrett, 1992)
- Developed by Bochud and colleagues (Bochud et al. 99, Castella et al 2008)
- Randomly located clusters of random blobs

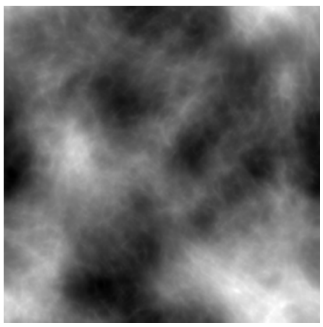
$$f_{\text{CLB}}(\mathbf{x}) = \sum_{k=0}^{K_{\text{CB}}} \sum_{n=0}^{N_k} b\left(R_{v_{k,n}}\left(\mathbf{x} - \mathbf{x}_k - \mathbf{x}_{k,n}\right)\right)$$

- Can be oriented (ORI) or isotropic (ISO)
- Can be a single process (SIMP) or a combination of two (DOUB)



CLB Simulation Process

~ 600 clusters



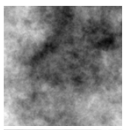
Binary Truncation Processes

- Developed for breast CT by Abbey and Boone (IWDM 2008), and for tomo-synthesis by Reiser and Nishikawa (2010).
- Simulate a 3D volume, with truncation to adipose and glandular components
- Then project to two dimensions

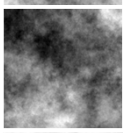
$$f_{\text{BTP}}(\mathbf{x}) = P_{\text{Proj}}\left(\mu_{\text{A}} + (\mu_{\text{G}} - \mu_{\text{A}})\Phi(Y(\mathbf{x}))\right)$$

- "Glandular Propensity" function, $Y(\mathbf{x})$
  - AB: Gaussian Process
  - RN: Phase Randomization
- Truncation Function: $\Phi(\ )$
  - AB: Cumulative Gaussian
  - RN: Step Function

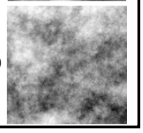
Gaussian



AB08

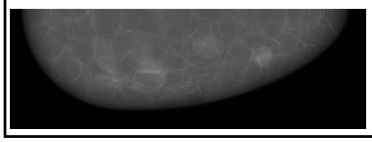


RN10

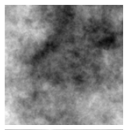


UPenn Virtual Breast Phantom

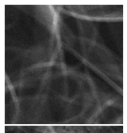
- Developed at UPenn by Maidment, Bakic, and colleagues starting in 1998.
- Based on components of gross anatomy (skin, fibroglandular tissue, adipose compartments, Cooper's ligament, etc.)
- Simulates uncompressed breast and applies FEM based compression
- Polyenergetic x-ray projection



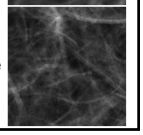
Gaussian



No-Substructure

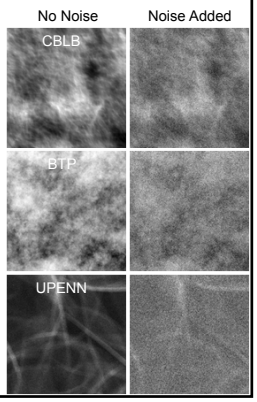


Substructure

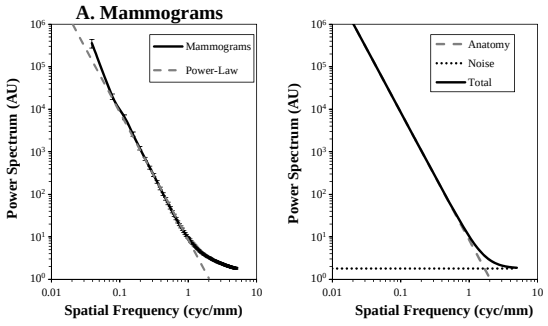


Adding noise

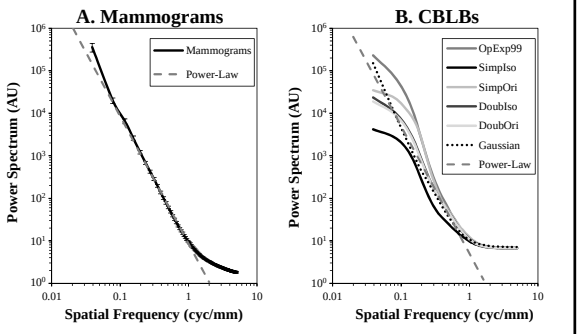
- Gaussian white noise to represent quantum and electronic noise
- Variance selected to equal power at 1cyc/mm (Burgess 2001)



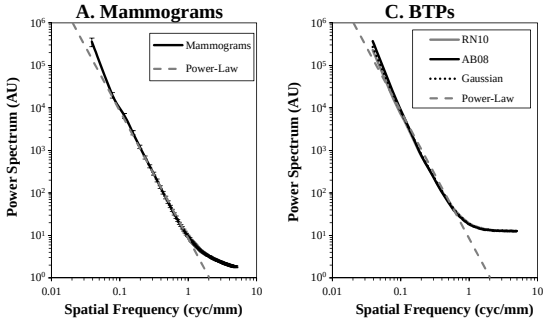
Power Spectra



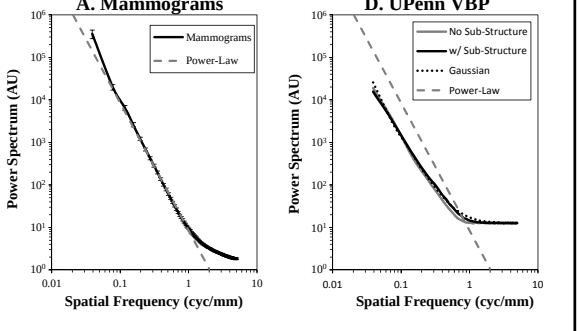
Power Spectra



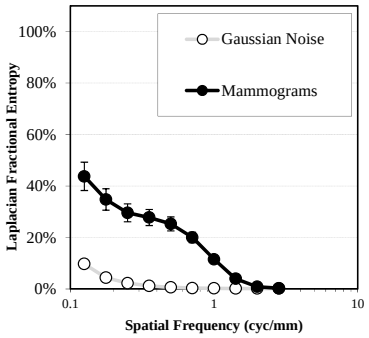
Power Spectra



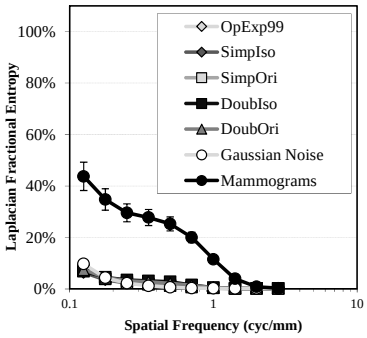
Power Spectra



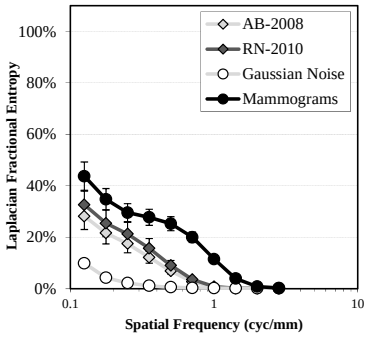
LFE Results



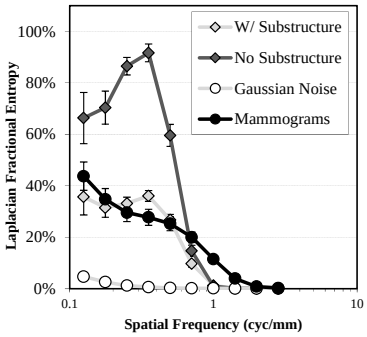
LFE: Clustered Blob Lumpy Backgrounds



LFE: Truncated Binary Processes



LFE: UPenn Virtual Phantom



Caveats

- Some strong assumptions
  - Stationarity and Ergodicity
- Smaller issues that might influence results
  - Calcium
  - Acquisition noise magnitude and spectrum
  - Patient population
  - Gabor receptive field properties

Conclusions

- Power Spectrum
  - Common to all three simulation approaches
  - A low bar...
- Laplacian fractional entropy
  - Surprisingly low for Clustered-Blob Lumpy Backgrounds
  - Low for Binary Truncation Processes
  - High for the UPenn phantom, but reduced by substructure
- A role for LFE in validating virtual breast phantoms