Super-resolution ultrasound imaging

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Outline

- Introduction and recap
- Super-resolution imaging
- Detection and localization
- Motion correction
- Tracking
- Challenges
- Advanced topics in super-resolution imaging
  - Kalman filtering and robust tracking
  - 3D super-resolution imaging
- Exercise and project
- Super-resolution imaging using red blood cells

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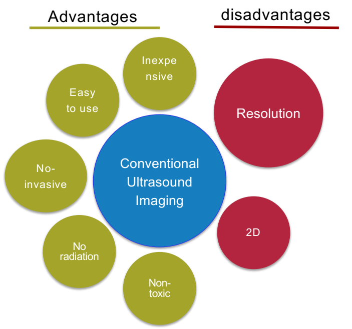
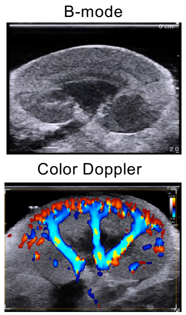
Ultrasound Imaging





Rat kidney
Size: 1x2 cm

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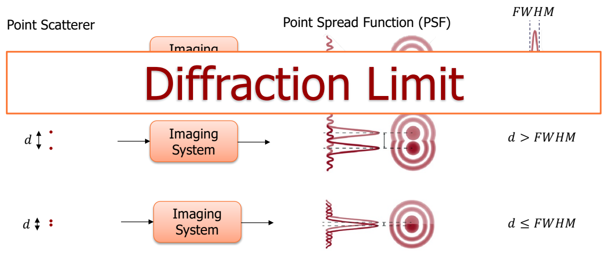
What is image resolution?



$FWHM = F_n.\lambda > \frac{\lambda}{2} = \frac{c}{2f_0}$

c: propagation speed

f_0: center frequency of wave

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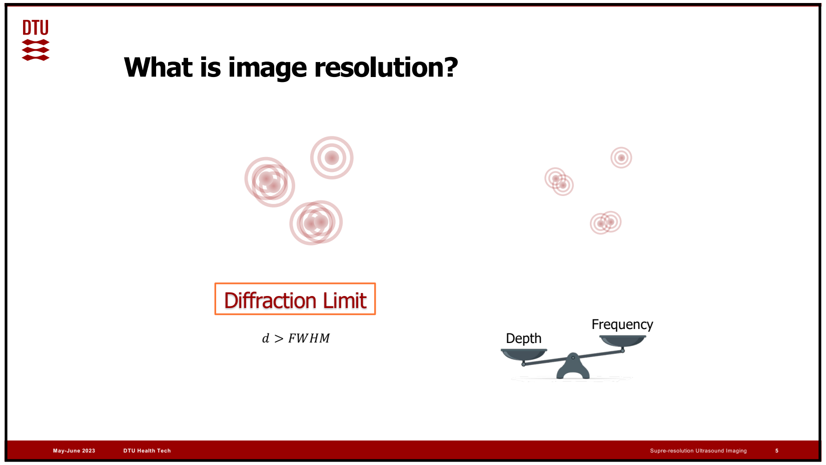
DTU
What is image resolution?
Diffraction Limit
d > FWHM
Depth
Frequency
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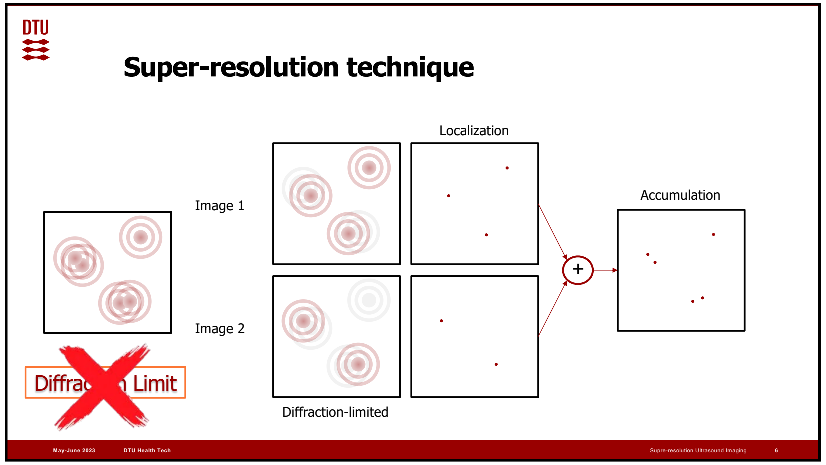
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Super-resolution technique
Localization
Image 1
Accumulation
Image 2
Diffraction Limit
Diffraction-limited
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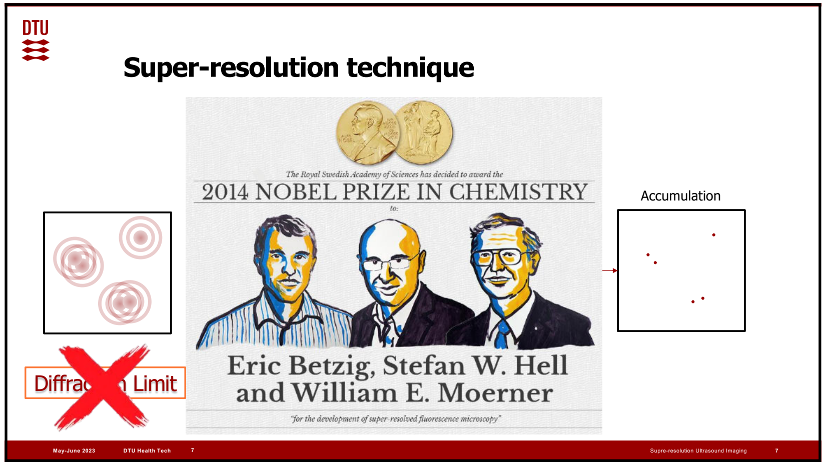
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Super-resolution technique
The Royal Swedish Academy of Sciences has decided to award the
2014 NOBEL PRIZE IN CHEMISTRY
to
Eric Betzig, Stefan W. Hell
and William E. Moerner
"for the development of super-resolved fluorescence microscopy"
Accumulation
Diffraction Limit
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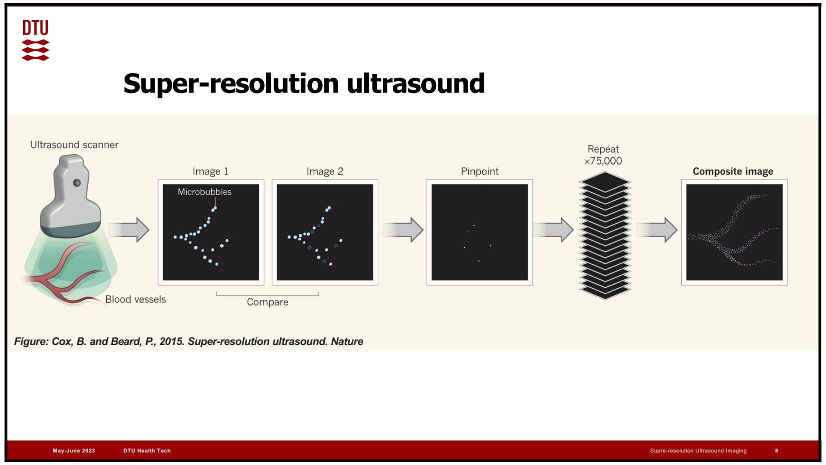
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Super-resolution ultrasound
Ultrasound scanner
Image 1
Image 2
Microbubbles
Pinpoint
Repeat ×75,000
Composite image
Blood vessels
Compare
Figure: Cox, B. and Beard, P., 2015. Super-resolution ultrasound. Nature
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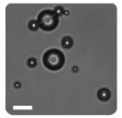
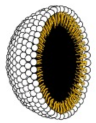
Ultrasound contrast agents (Microbubbles)

Vial of
Microbubbles (MBs)



MBs has a size of
below **1 µm** to **8 µm**
≪ wavelength
(Point scatter)



Gas filled bubbles
with lipid shell
(High impedance mismatch)

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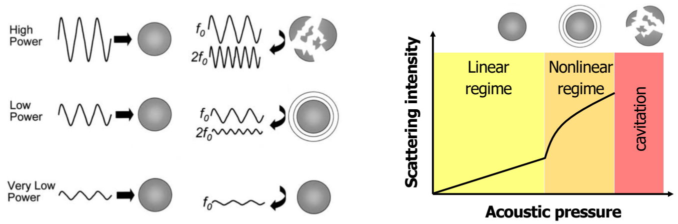
Microbubble nonlinear response



(Lindner J et al. Current Problems in Cardiology (2002); 11; 454-519)

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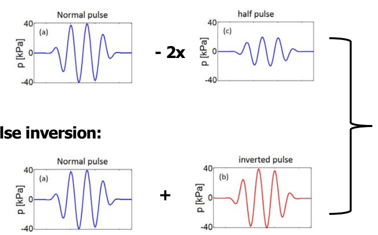
Contrast enhanced ultrasound (CEUS)

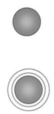
Amplitude modulation:

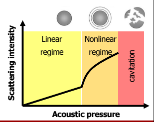
Pulse inversion:



Linear regime
= 0

Nonlinear regime
≠ 0





(Averkiou et al. Imaging methods for ultrasound contrast agents (2019); 46; 498-517)

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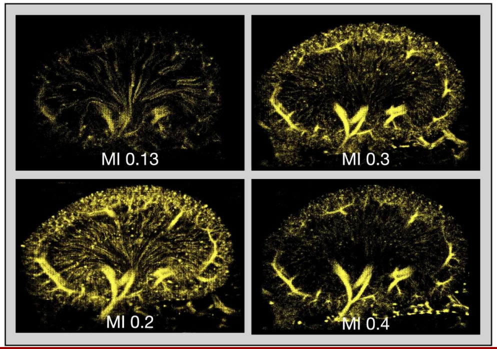
Acoustic power (depends on application)



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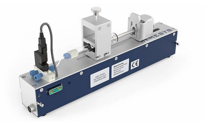
Using microbubbles

Infusion of MBs using a syringe pump



Needs approved application
Control on the concentration
Suitable for Long acquisitions

Bolus injection

FDA approved
Very high concentration at start
Short window of low concentration

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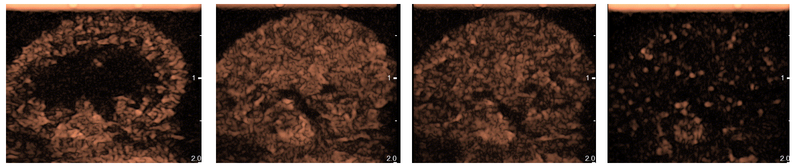
Bolus injection vs infusion



Bolus injection

Infusion

Increasing dilution ratio

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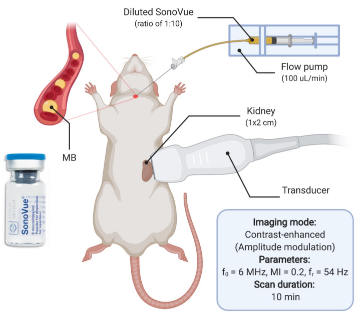
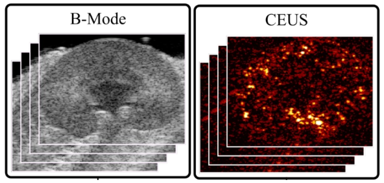
Animal experiment





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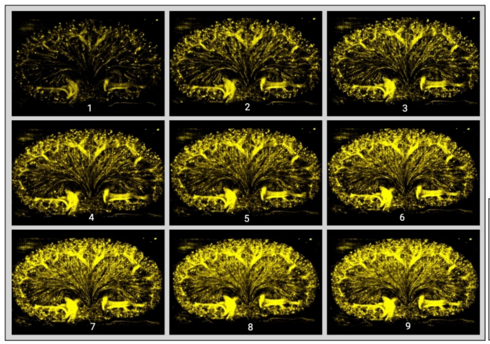
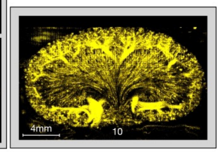
Why 10 minutes?





Numbers show time in minutes

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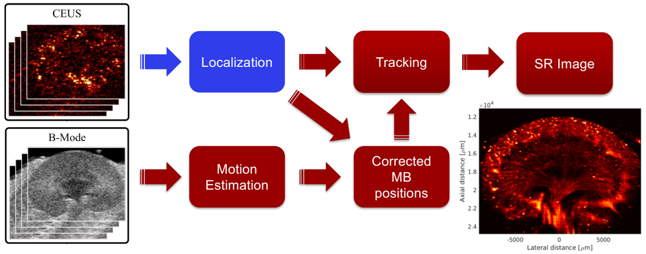
Super-resolution processing pipeline



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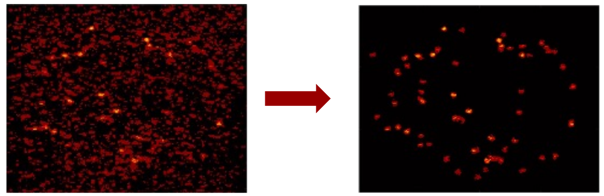
Detection of microbubbles

Applying a threshold:

- Reducing background noise
- Isolating blobs



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Detection of microbubbles

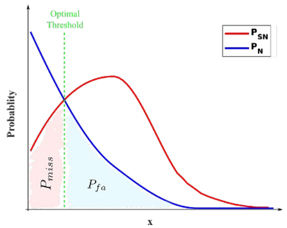
An optimal detector (ϵ):

- Maximize the generalized contrast-to-noise ratio
- Minimum miss detections
- Minimum false detections

$$gCNR = 1 - \left(\int_{-\infty}^{\epsilon} P_{SN}(x)dx + \int_{\epsilon}^{\infty} P_N(x)dx \right)$$

P_{SN}: *probability distribution of signal + noise*

P_N: *probability distribution of noise values*



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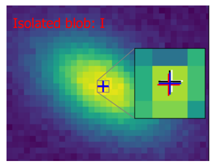
Detection of microbubbles

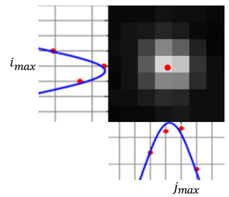
- **Weighted centroid:**



$$Centroid = \frac{1}{NM} \sum_{i=1}^{N} \sum_{j=1}^{M} (i,j)$$

$$Weighted\ Centroid = \frac{\sum_i \sum_j I(i,j) \times (i,j)}{\sum_i \sum_j I(i,j)}$$

- **Peak detection with subpixel precision**



$$(i_{max}, j_{max}) = \arg\max_{i,j} I(i,j)$$

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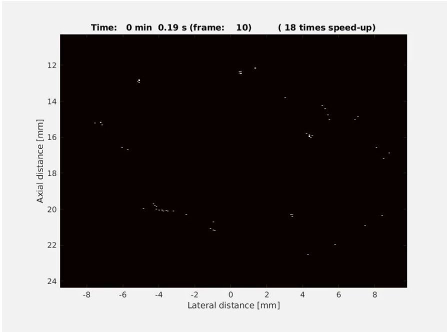
Detection density map

Inserting localized positions into a high-resolution image



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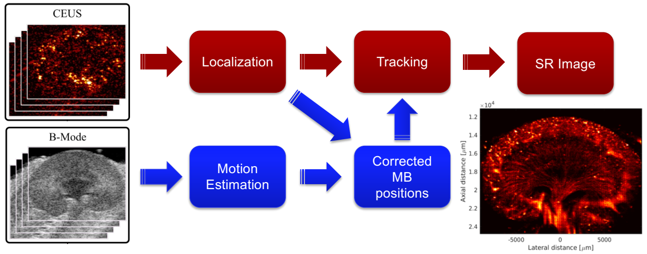
Super-resolution processing pipeline



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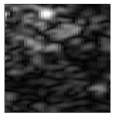
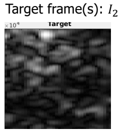
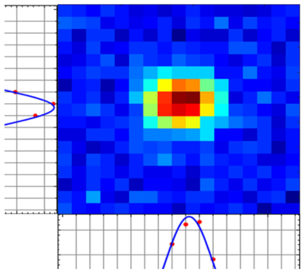
Tissue speckle tracking

Reference frame: I_1



Target frame(s): I_2





- Normalize cross correlation:

$$X(i',j') = \frac{\sum_i \sum_j I_1(i,j).I_2(i-i',j-j')}{\sqrt{\sum_i \sum_j |I_1(i,j)|^2}}$$

- Finding the peak

$$(i_{max}, j_{max}) = \arg\max_{i,j} X(i,j)$$

- Interpolation

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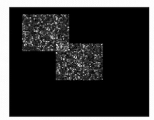
What if…

- Cross correlation consists of many shifts and multiplications
- Cross correlation of two signals is similar to a convolution that one of the signals is time reversed or flipped.
- Convolution in time/spatial domain is a multiplication in frequency domain.



Can you do speckle tracking using FFT? Any advantage?

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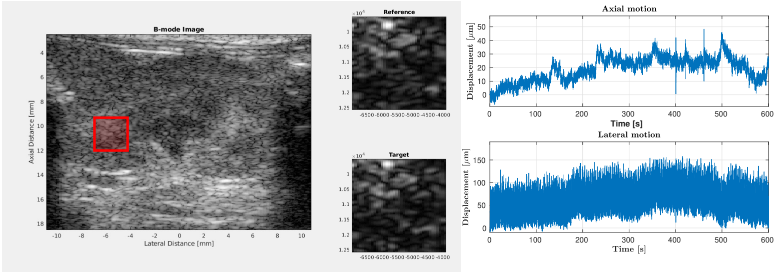
Motion estimation



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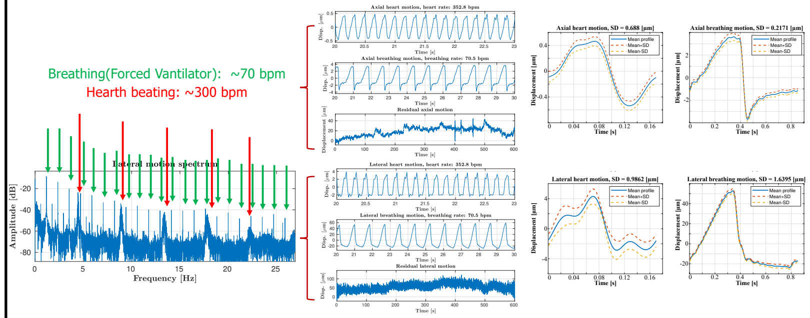
Motion estimation - precision



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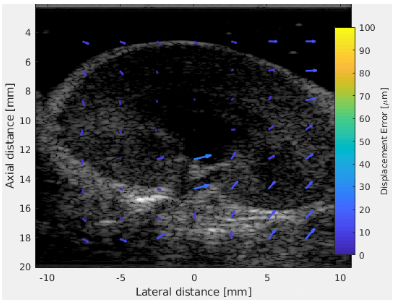
Motion estimation – Motion Field



Discrete Motion Field

$\vec{\mathcal{M}}(t_k, \vec{r}_k)$

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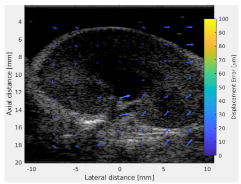
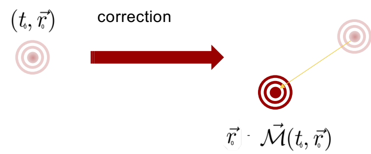
Motion correction

Motion field: $\vec{\mathcal{M}}(t, \vec{r})$





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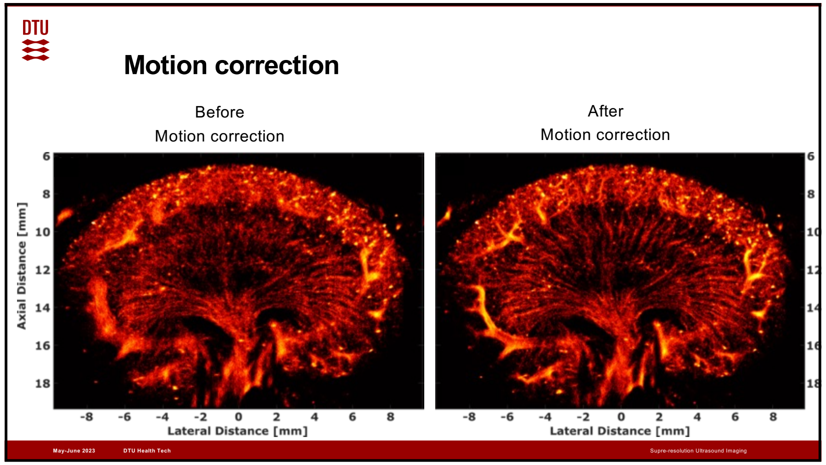
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Motion correction
Before
Motion correction
After
Motion correction
Axial Distance [mm]
Lateral Distance [mm]
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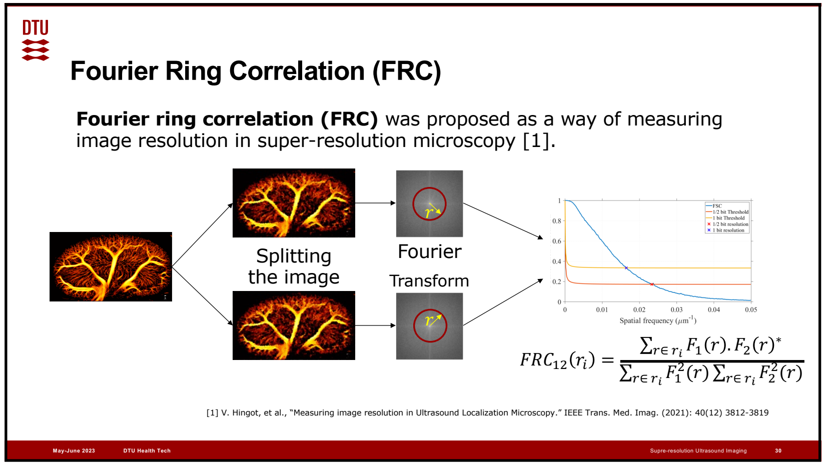
DTU
Fourier Ring Correlation (FRC)
Fourier ring correlation (FRC) was proposed as a way of measuring image resolution in super-resolution microscopy [1].
Splitting the image
Fourier Transform
$FRC_{12}(r_i) = \frac{\sum_{r \in r_i} F_1(r).F_2(r)^*}{\sum_{r \in r_i} F_1^2(r) \sum_{r \in r_i} F_2^2(r)}$
[1] V. Hingot, et al., "Measuring image resolution in Ultrasound Localization Microscopy." IEEE Trans. Med. Imag. (2021): 40(12) 3812-3819
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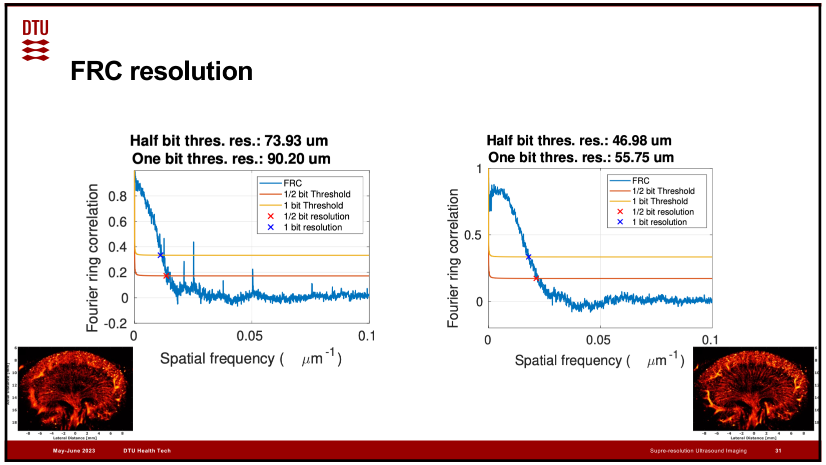
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FRC resolution
Half bit thres. res.: 73.93 um
One bit thres. res.: 90.20 um
Half bit thres. res.: 46.98 um
One bit thres. res.: 55.75 um
FRC
1/2 bit Threshold
1 bit Threshold
1/2 bit resolution
1 bit resolution
Fourier ring correlation
Spatial frequency (μm^{-1})
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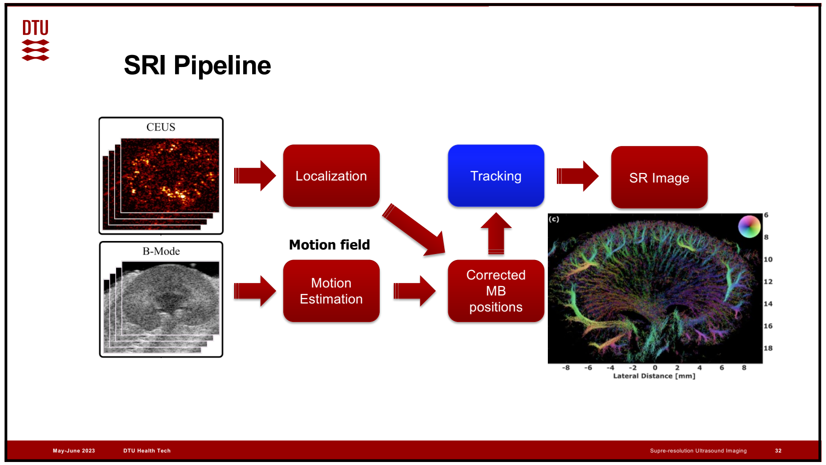
DTU
SRI Pipeline
CEUS
B-Mode
Localization
Motion field
Motion Estimation
Tracking
Corrected MB positions
SR Image
Lateral Distance [mm]
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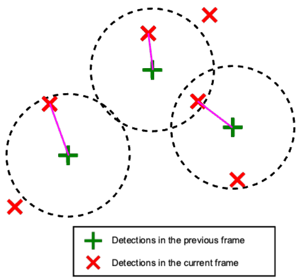
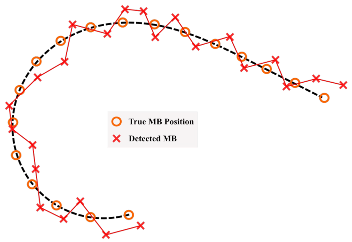
Tracking





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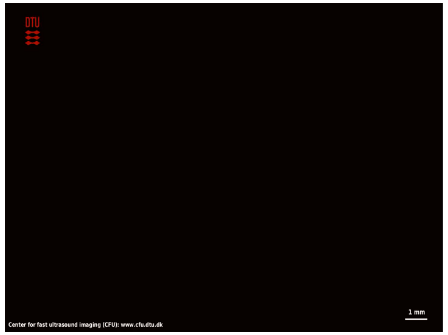
Track density images

Inserting track positions
into a high-resolution image



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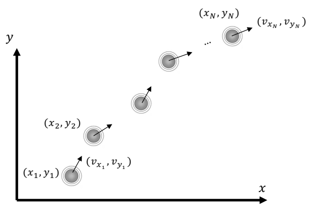
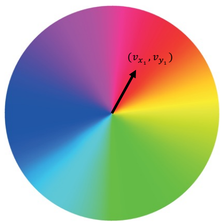
Vector velocity images

Showing 4D data (x, y, v_x, v_y) in a 2D Image – velocity encoded by colors





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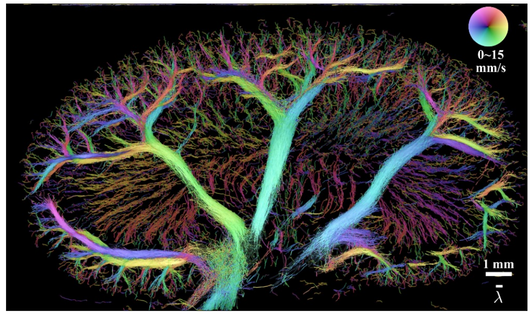
Vector velocity images



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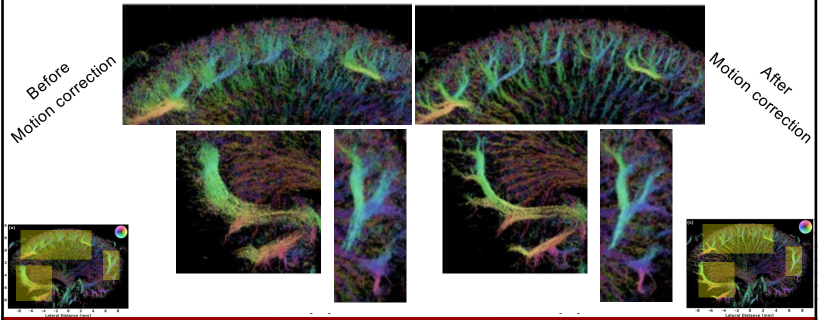
Motion correction – velocity maps



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Challenges

- Weak signal (low SNR)
- Projection ambiguities
  - Motion estimation
  - Velocity estimation
  - Complex tracking
- Require long time acquisition

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Advanced topics

Kalman filtering and robust tracking

Forward backward tracking

3D super-resolution imaging

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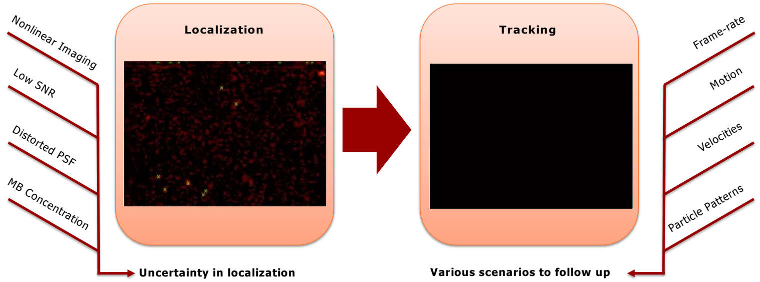
Tracking



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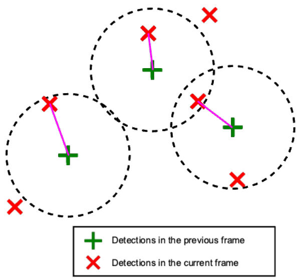
Different tracking strategy

Nearest-neighbor tracker



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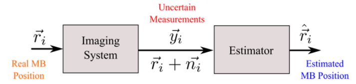
Kalman Filter

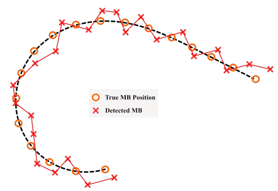


MBs motion model:

$$\vec{r}(t) = \vec{r}(t-1) + d\vec{r}(t) + \varepsilon(t)$$

MBs moves smoothly and their direction cannot change instantaneously.

Error term for the model



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Kalman framework

MBs motion model: $\vec{r}(t) = \vec{r}(t-1) + d\vec{r}(t) + \varepsilon(t)$

$$\begin{cases} \text{Prediction State:} & \bar{x}(t) = \mathbf{F}x(t-1) + \epsilon(t) \\ \text{Observation State:} & \bar{z}(t) = \mathbf{H}\bar{x}(t) + v(t), \end{cases}$$

where $x(t) = [\vec{r}(t), d\vec{r}(t)]^T = [r_z(t), r_x(t), dr_z(t), dr_x(t)]^T$,

$$\mathbf{F} = \begin{bmatrix} 1 & 0 & 1 & 0 \\ 0 & 1 & 0 & 1 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \end{bmatrix}, \quad \mathbf{H} = \begin{bmatrix} 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 \end{bmatrix},$$

$\epsilon(t) \sim \mathcal{N}(0, \sigma_\epsilon^2)$, and $v(t) \sim \mathcal{N}(0, \sigma_v^2)$ is the localization uncertainty.

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Kalman filter steps

- Prediction
  - State prediction: $x(t) = \boldsymbol{F}x(t-1) + \epsilon(t)$
  - Covariance prediction: $\boldsymbol{P}(t) = \boldsymbol{F} * \boldsymbol{P}(t-1) * \boldsymbol{F}' + \boldsymbol{Q}$, Q: model error ($\epsilon$) covariance
- Update
  - Observation: $z(t) = \boldsymbol{H}x(t) + v(t)$
  - Kalman gain: $\boldsymbol{K}(t) = \boldsymbol{P}(t) * \boldsymbol{H}' / (\boldsymbol{H} * \boldsymbol{P}(t) * \boldsymbol{H}' + \boldsymbol{R})$, R: measurement noise ($v$) covariance
  - State update: $x(t) = x(t) + \boldsymbol{K}(t) * (z(t) - \boldsymbol{H} * x(t))$
  - Covariance update: $\boldsymbol{P}(t) = (\boldsymbol{I} - \boldsymbol{K}(t) * \boldsymbol{H}) * \boldsymbol{P}(t)$

This recursive process repeats each time a new position is assigned to the MB.

Initial conditions: $x(0)$: *first position of MB*, $\boldsymbol{P}(0)$: *the challenging part*!

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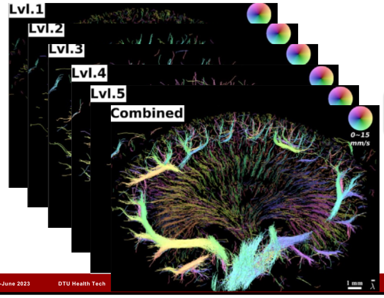
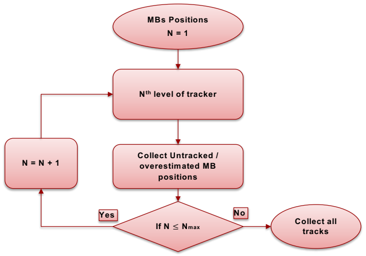
Hierarchical Kalman

– Tracking different velocity ranges with different Kalman filters





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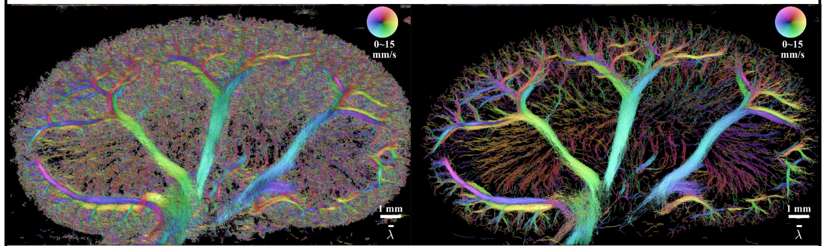
In vivo tracking results



Nearest-Neighbor

Hierarchical Kalman

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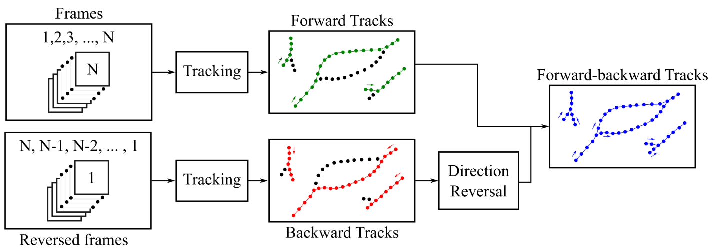
Forward Backward strategy



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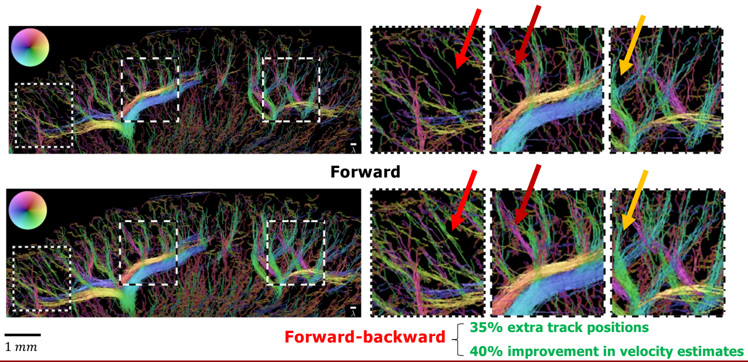
Forward-backward strategy



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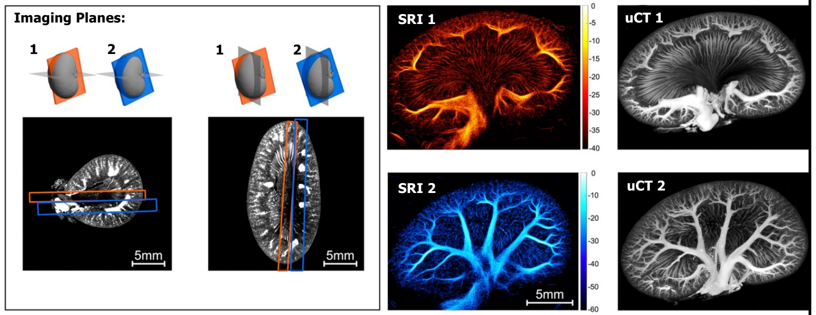
DTU

Correspondence of SRI to uCT



Andersen et. al. (2021). "Evaluation of 2D super-resolution ultrasound imaging of the rat renal vasculature using ex vivo microcomputed tomography".

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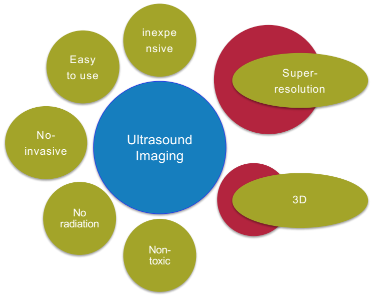
DTU

3D super-resolution imaging



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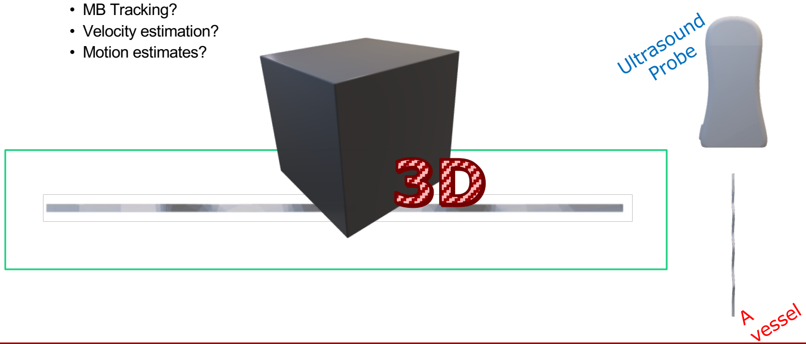
DTU

Ambiguities in 2D SRI

- MB Tracking?
- Velocity estimation?
- Motion estimates?



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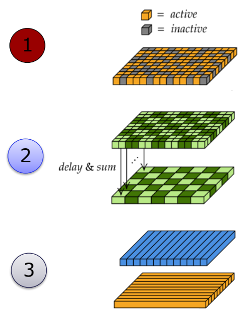
DTU

3D Ultrasound Imaging

Early concept:

Matrix array

A lot of elements and small aperture!



Sparse array

- Side-lobes
- 2x~4x less elements

Micro beamforming and multiplexing

- Low volume-rate
- Complicated circuits

Row-column array

- >100x less elements
- Larger aperture

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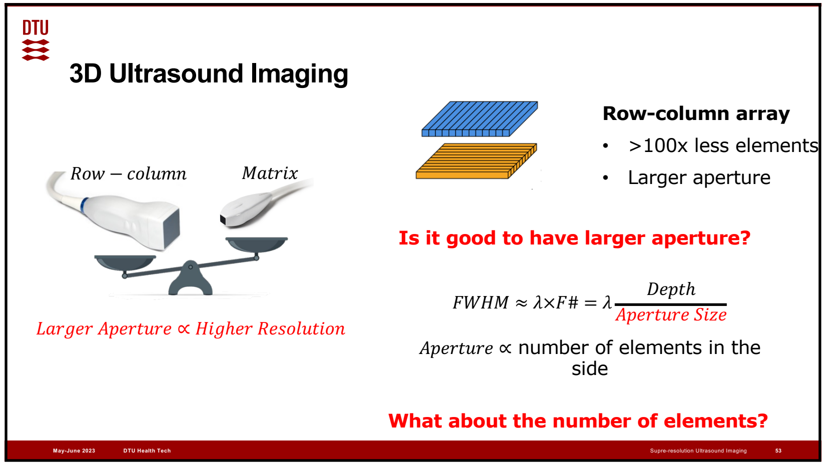
DTU
3D Ultrasound Imaging
Row – column
Matrix
Larger Aperture ∝ Higher Resolution
Row-column array
• >100x less elements
• Larger aperture
Is it good to have larger aperture?
$FWHM \approx \lambda \times F\# = \lambda \frac{Depth}{Aperture\ Size}$
$Aperture$ ∝ number of elements in the side
What about the number of elements?

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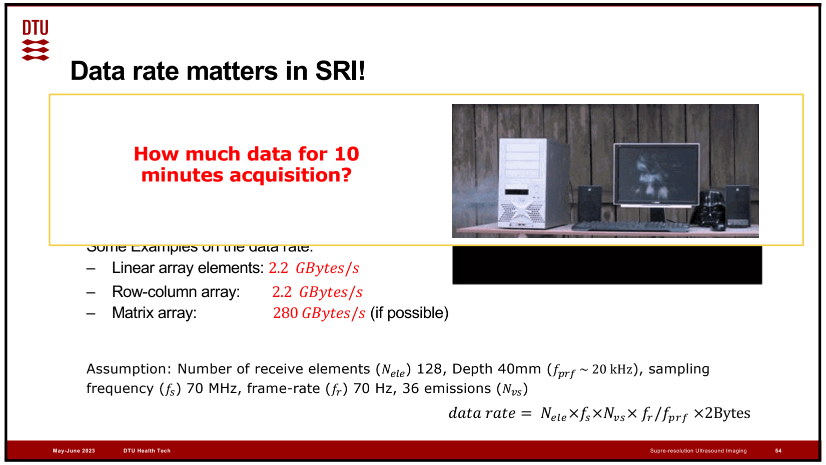
DTU
Data rate matters in SRI!
How much data for 10 minutes acquisition?
– Linear array elements: 2.2 $GBytes/s$
– Row-column array: 2.2 $GBytes/s$
– Matrix array: 280 $GBytes/s$ (if possible)
Assumption: Number of receive elements (N_{ele}) 128, Depth 40mm (f_{prf} ~ 20 kHz), sampling frequency (f_s) 70 MHz, frame-rate (f_r) 70 Hz, 36 emissions (N_{vs})
$data\ rate = N_{ele} \times f_s \times N_{vs} \times f_r / f_{prf}$ ×2Bytes

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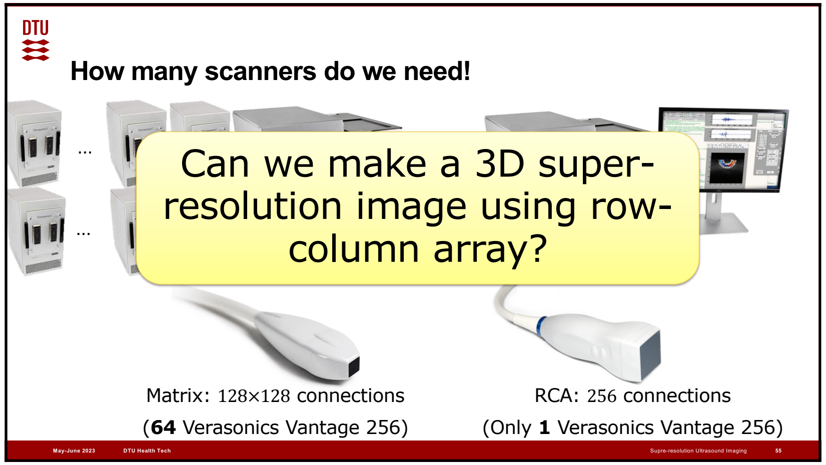
DTU
How many scanners do we need!
Can we make a 3D super-resolution image using row-column array?
Matrix: 128×128 connections
(64 Verasonics Vantage 256)
RCA: 256 connections
(Only 1 Verasonics Vantage 256)

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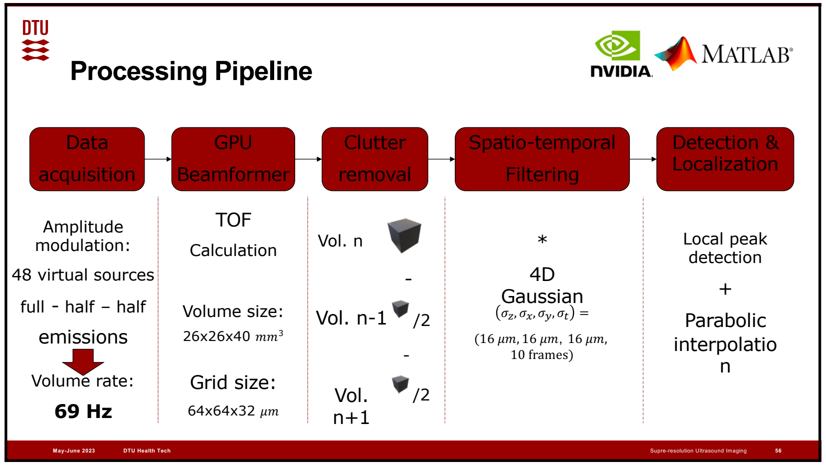
DTU
Processing Pipeline
NVIDIA
MATLAB
Data acquisition
GPU Beamformer
Clutter removal
Spatio-temporal Filtering
Detection & Localization
Amplitude modulation:
48 virtual sources
full - half - half
emissions
Volume rate:
69 Hz
TOF
Calculation
Volume size:
26x26x40 mm^3
Grid size:
64x64x32 μm
Vol. n
Vol. n-1 /2
Vol. n+1 /2
*
4D Gaussian
$(\sigma_z, \sigma_x, \sigma_y, \sigma_t)$ =
(16 μm, 16 μm, 16 μm, 10 frames)
Local peak detection
+
Parabolic interpolation

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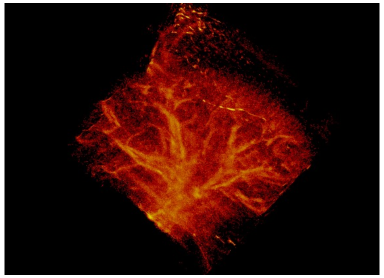
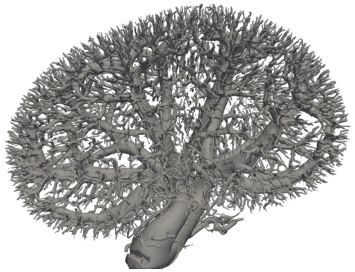
in-vivo results



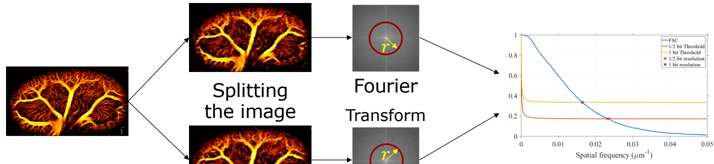


In vivo SRI
(36 seconds)

Ex vivo micro-CT
(10 hours)

Fourier ring Correlation (FSC)

Fourier ring correlation (FRC) was proposed as a way of measuring image resolution in super-resolution microscopy [1].

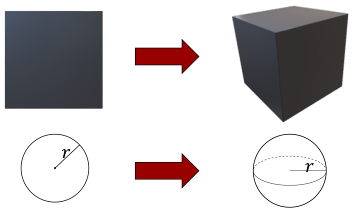


$$FRC_{12}(r_i) = \frac{\sum_{r\in r_i} F_1(r).F_2(r)^*}{\sum_{r\in r_i} F_1^2(r)\sum_{r\in r_i} F_2^2(r)}$$

[1] V. Hingot, et al., "Measuring image resolution in Ultrasound Localization Microscopy." IEEE Trans. Med. Imag. (2021): 40(12) 3812-3819

Fourier Shell Correlation (FSC)

Image



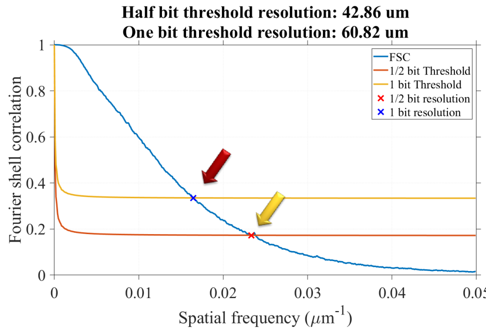
Volume

Circle
With radius r

Spherical surface
with radius r

The same concept and equation, but correlation of 3D FFT of split volumes over a shell

Resolution



Wavelength
($256\ \mu m$)

Clinical applications

- Diabetes
- Cancer
- Acute kidney injury
- Stroke
- and many other potentials

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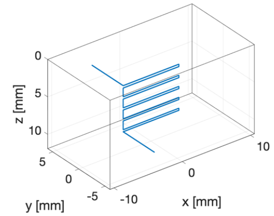
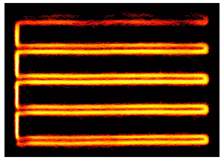
Exercise

- Working with the envelope of contrast enhanced data from a micro flow phantom
- Localization of the MBs
- Insertion of the MB positions into a high-resolution image
- Tracking of MBs (optional)
- Insertion of track positions into a high-resolution image (optional)





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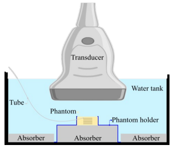
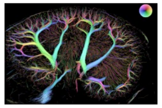
Project

- Using a 3D printed micro-flow phantom
- Acquiring contrast enhanced data using Verasonics Vantage scanner
  - Compare Linear and nonlinear sequence
  - See the effect of changing voltage (MI)
  - See the effect of different MB concentration or flow-rate
- Make a super-resolution image using localization technique on your acquired data / or a pre-aquired data from a kidney





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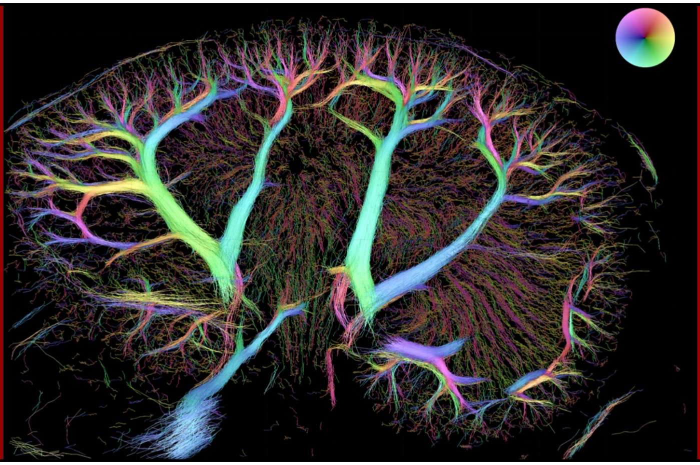

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