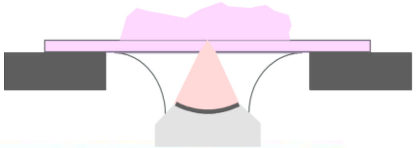
超音波顕微鏡の音場と画像



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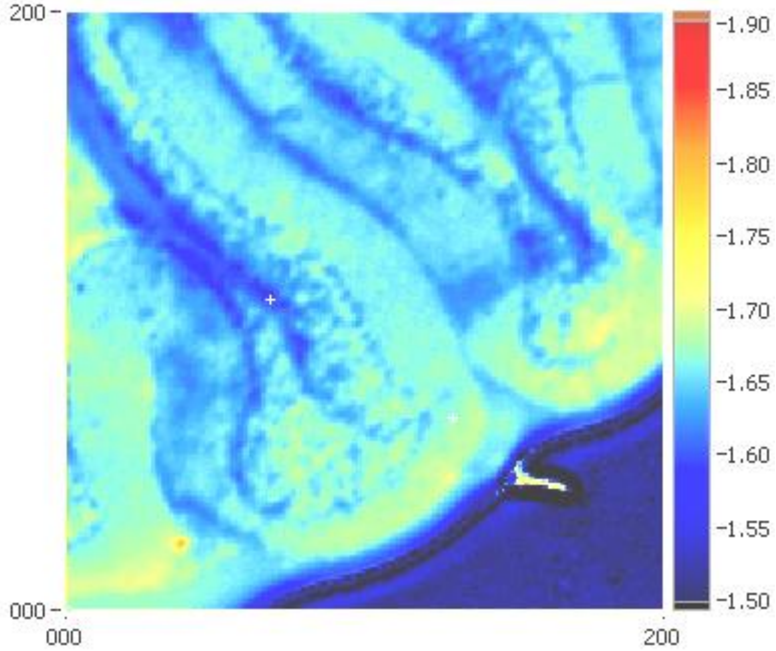
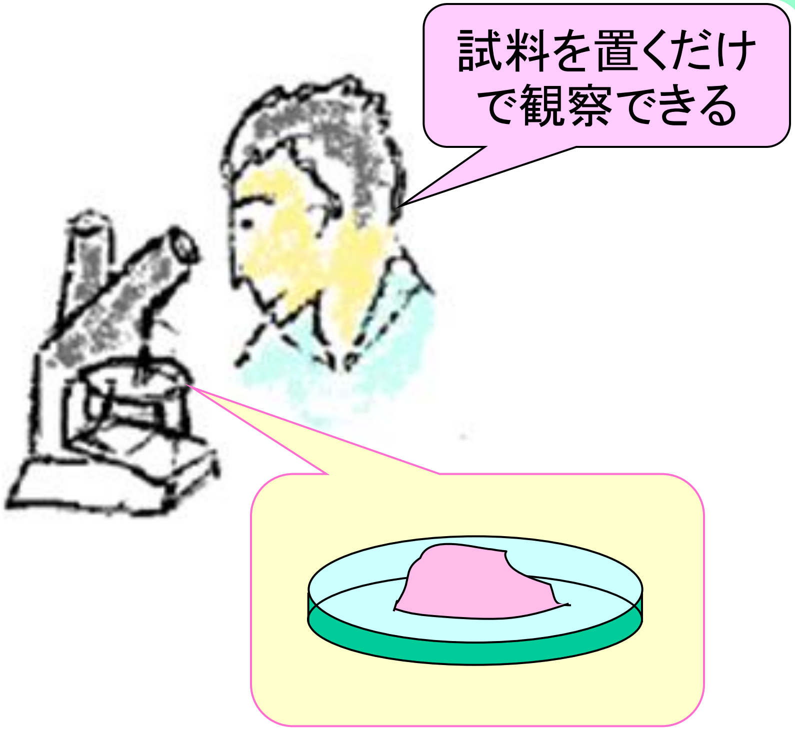
hozumi@icceed.tut.ac.jp



Scanning Acoustic Impedance Microscopy

音響インピーダンス顕微鏡開発の目的。



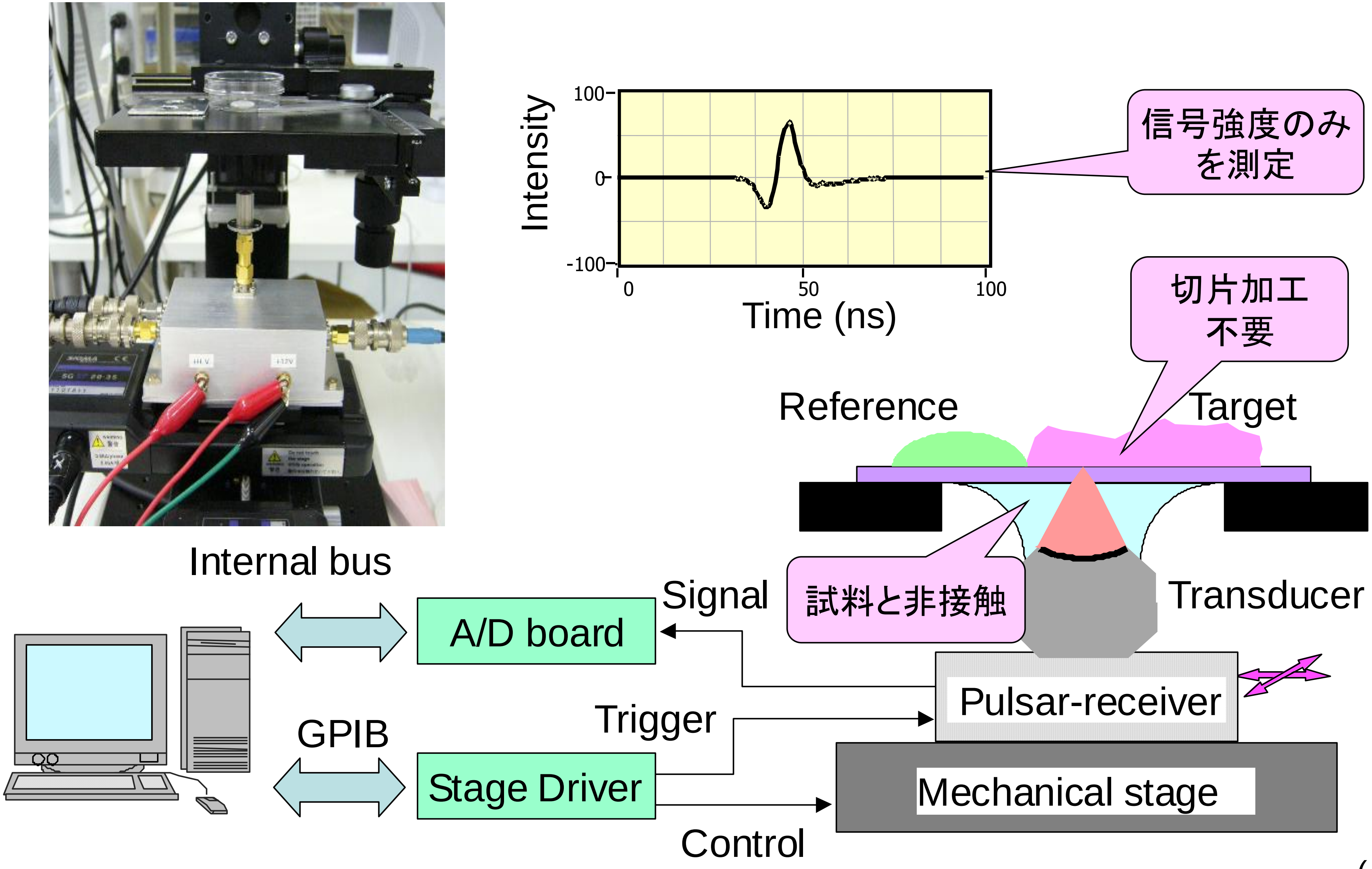
染色も切片作製も不要

顕微プローブ

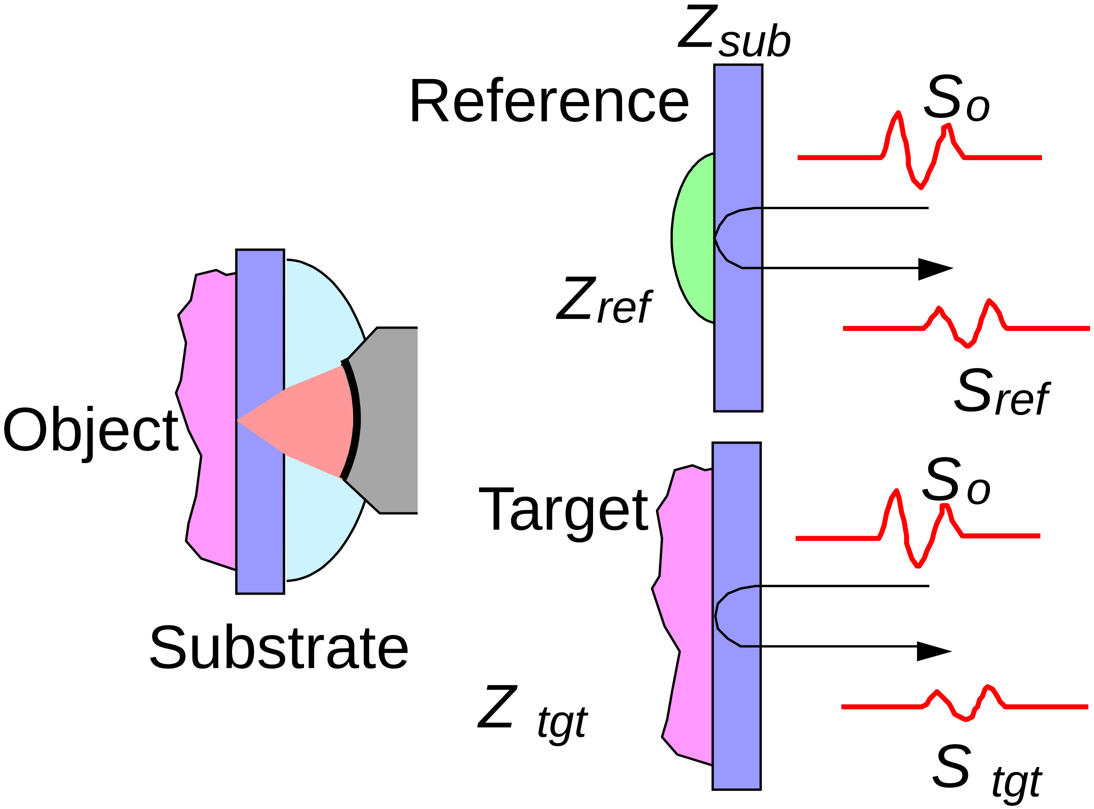
今進めている研究

将来像？

概念図


Intensity
100
0
-100
0
50
100
Time (ns)
信号強度のみを測定
切片加工不要
Reference
Target
試料と非接触
Transducer
Internal bus
Signal
A/D board
Pulsar-receiver
GPIB
Trigger
Stage Driver
Mechanical stage
Control

反射信号強度を音響インピーダンスに変換。



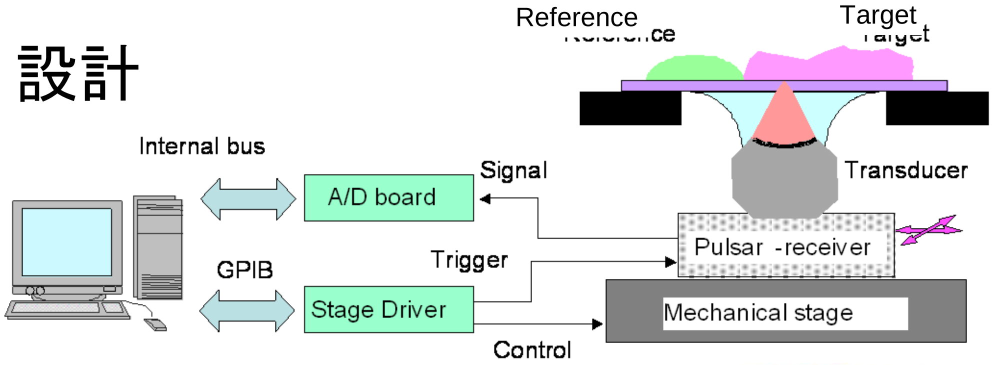
$$S_{ref} = \frac{Z_{ref} - Z_{sub}}{Z_{ref} + Z_{sub}} S_0$$

$$S_{tgt} = \frac{Z_{tgt} - Z_{sub}}{Z_{tgt} + Z_{sub}} S_0$$

$$Z_{tgt} = \frac{1 + \dfrac{S_{tgt}}{S_0}}{1 - \dfrac{S_{tgt}}{S_0}} Z_{sub} = \frac{1 - \dfrac{S_{tgt}}{S_{ref}} \cdot \dfrac{Z_{sub} - Z_{ref}}{Z_{sub} + Z_{ref}}}{1 + \dfrac{S_{tgt}}{S_{ref}} \cdot \dfrac{Z_{sub} - Z_{ref}}{Z_{sub} + Z_{ref}}} Z_{sub}$$

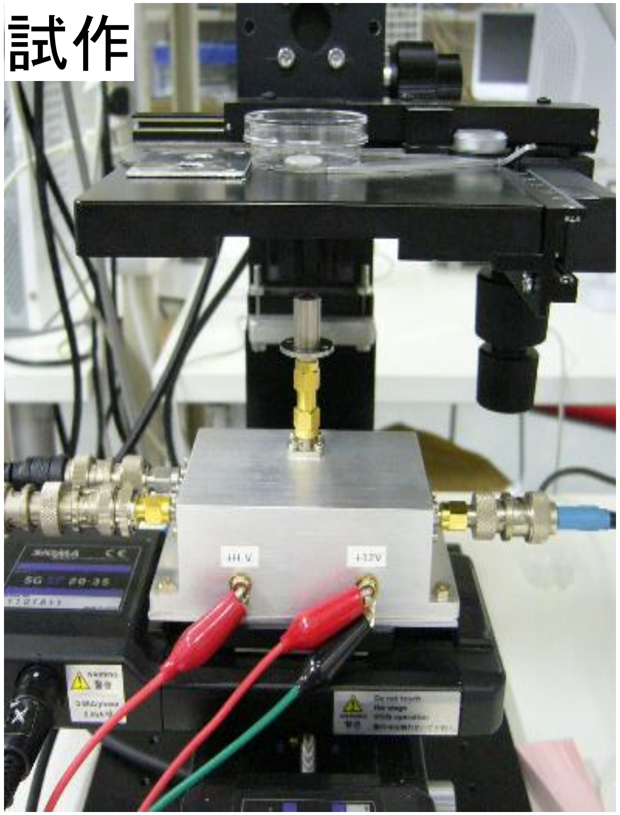
医学・生物学用超音波顕微鏡

設計

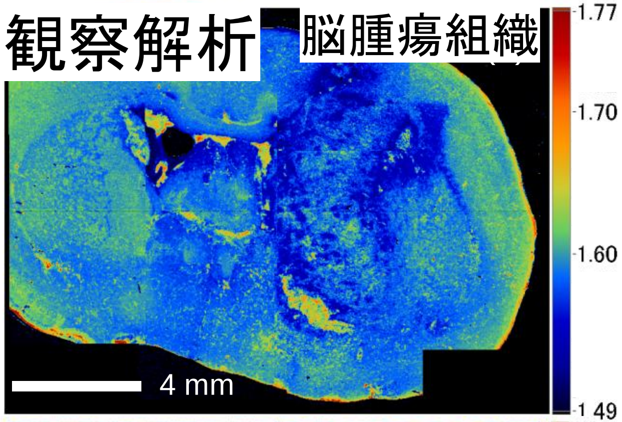


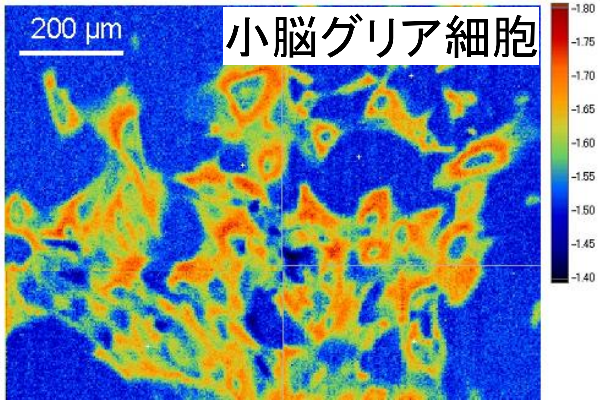
(1) 高分子基板の上に試料を接触させる。
(2) 集束超音波を走査。
(3) 参照材料(水)を使って、反射強度を硬さに関係する情報(音響インピーダンス)に変換し画像化。

試作



観察解析





実用機

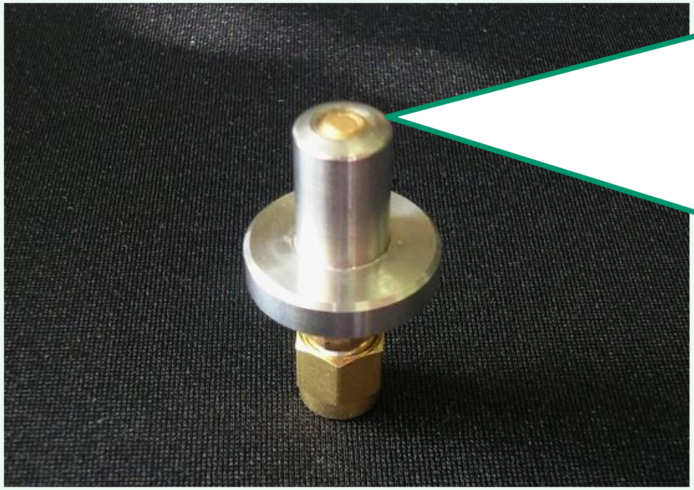
本多電子
AMS−50SI

浜松医科大・東北大学・
本多電子(㈱)との共同研究I

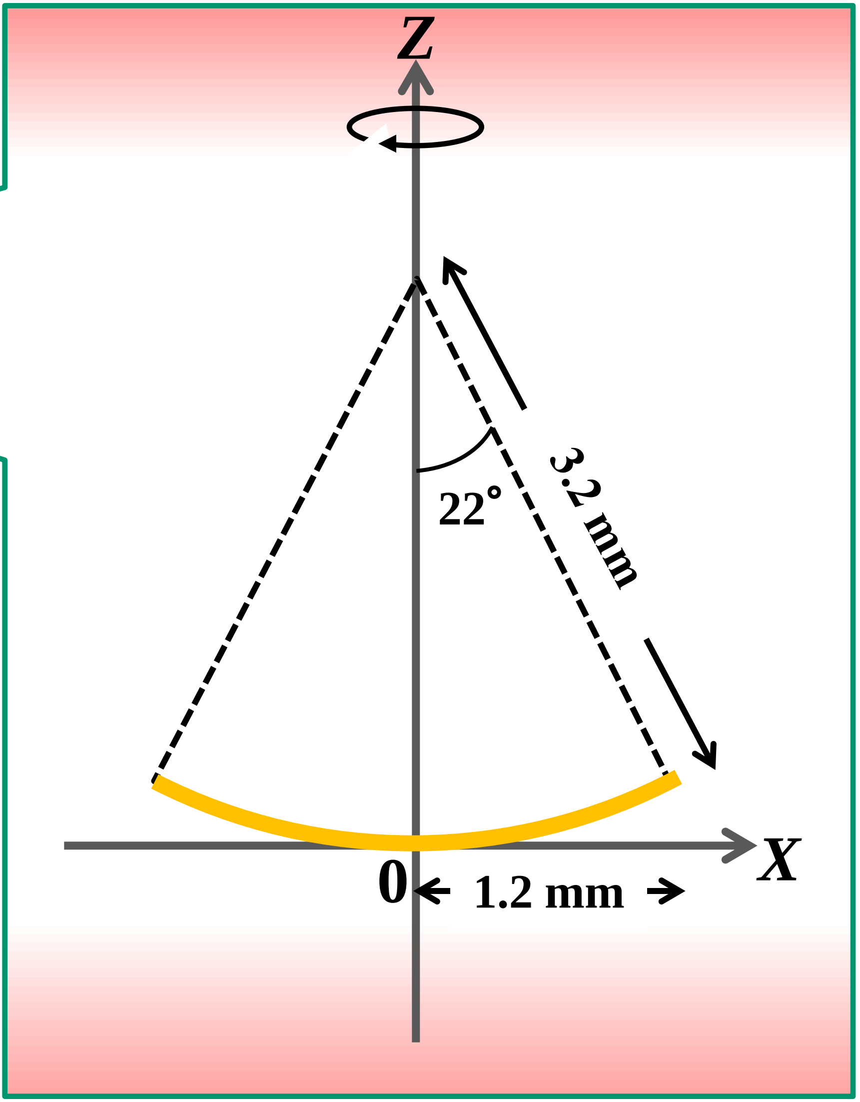
Improvement of accuracy

Shape of transducer

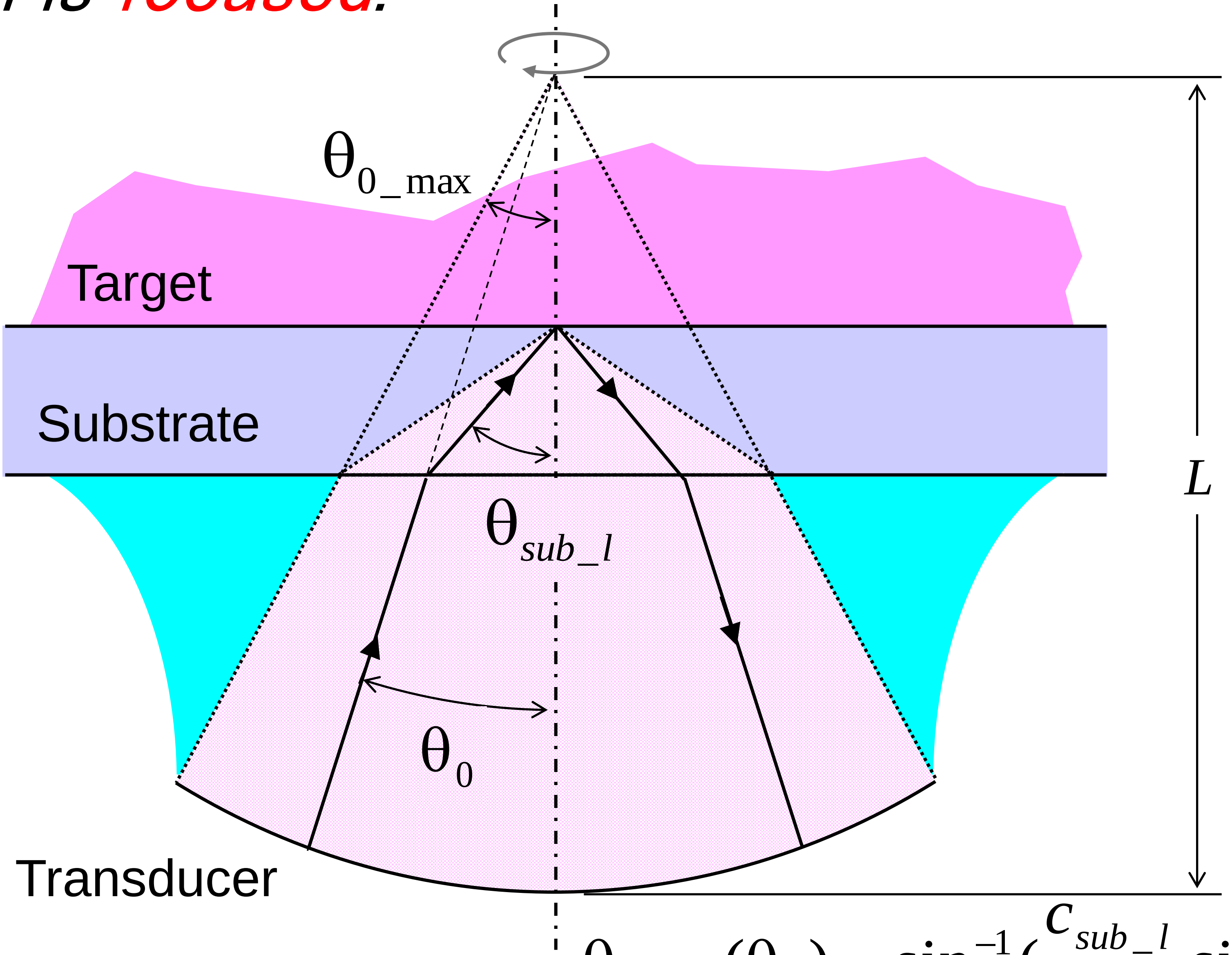
球面振動子



- 開口半径1.2mm
- 焦点距離3.2 mm
- 集束角22°
- 中心周波数80MHz

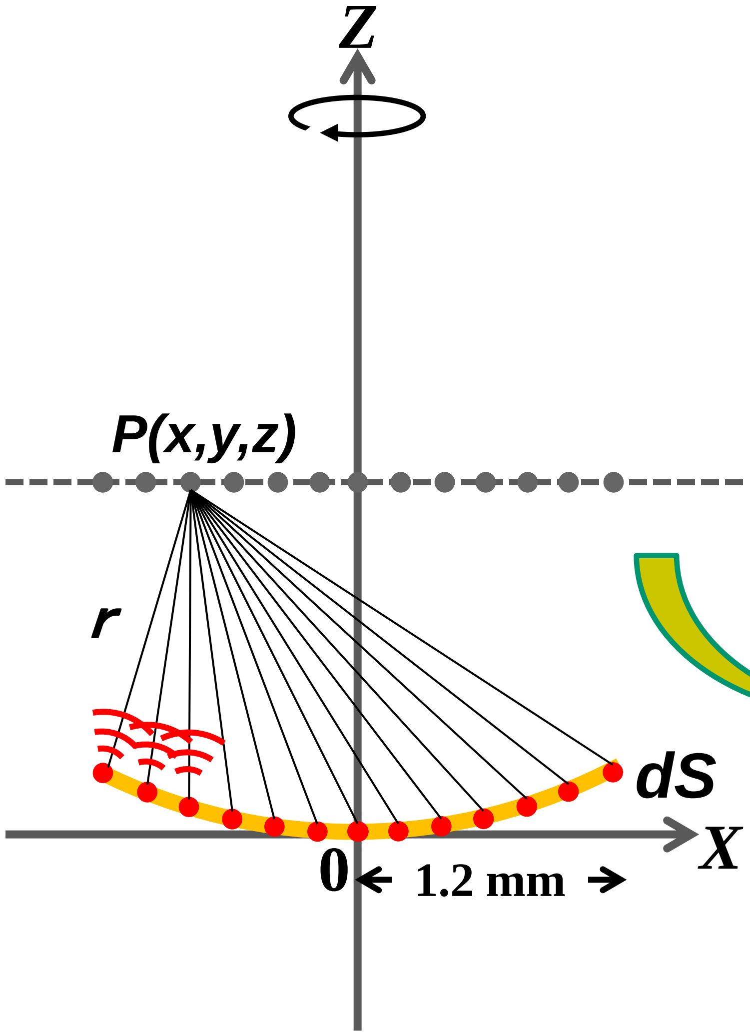


Beam is focused.



$$\theta_{sub\_l}(\theta_0) = \sin^{-1}\left(\frac{c_{sub\_l}}{c_0}\sin\theta_0\right)$$

Calculation of potential



$$\left[\, r=\sqrt{(x-x_0)^2+(y-y_0)^2+(z-z_0)^2}\, \right]$$

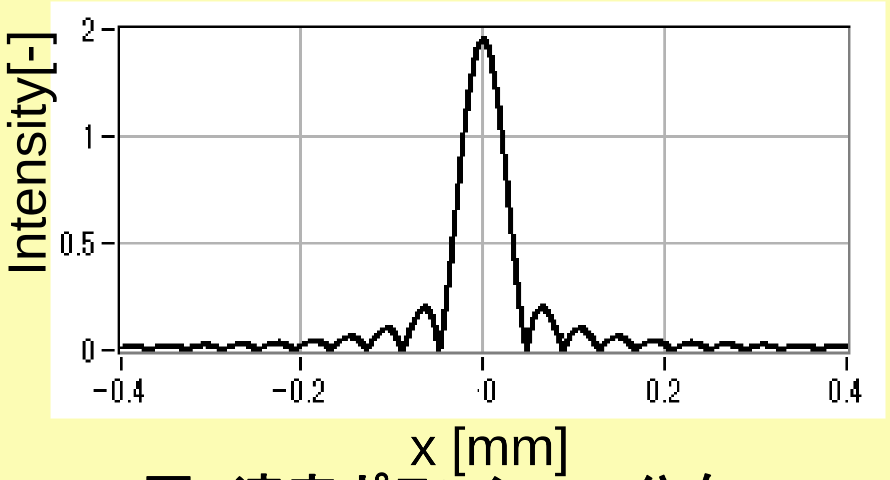


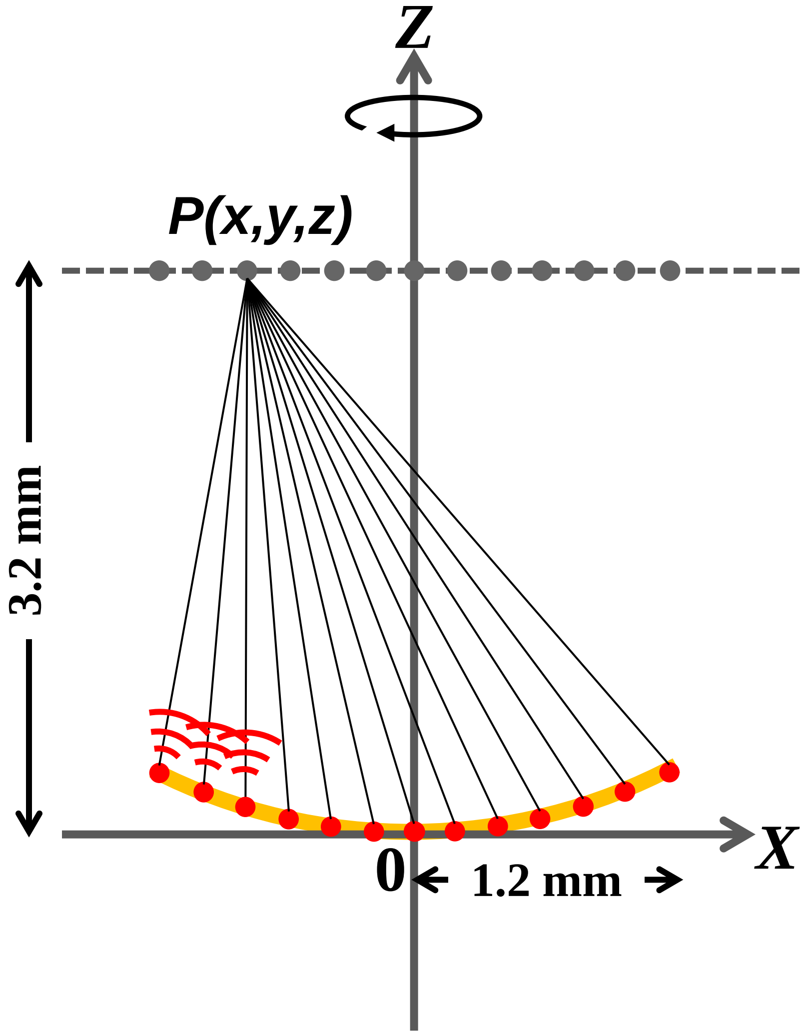
図　速度ポテンシャル分布

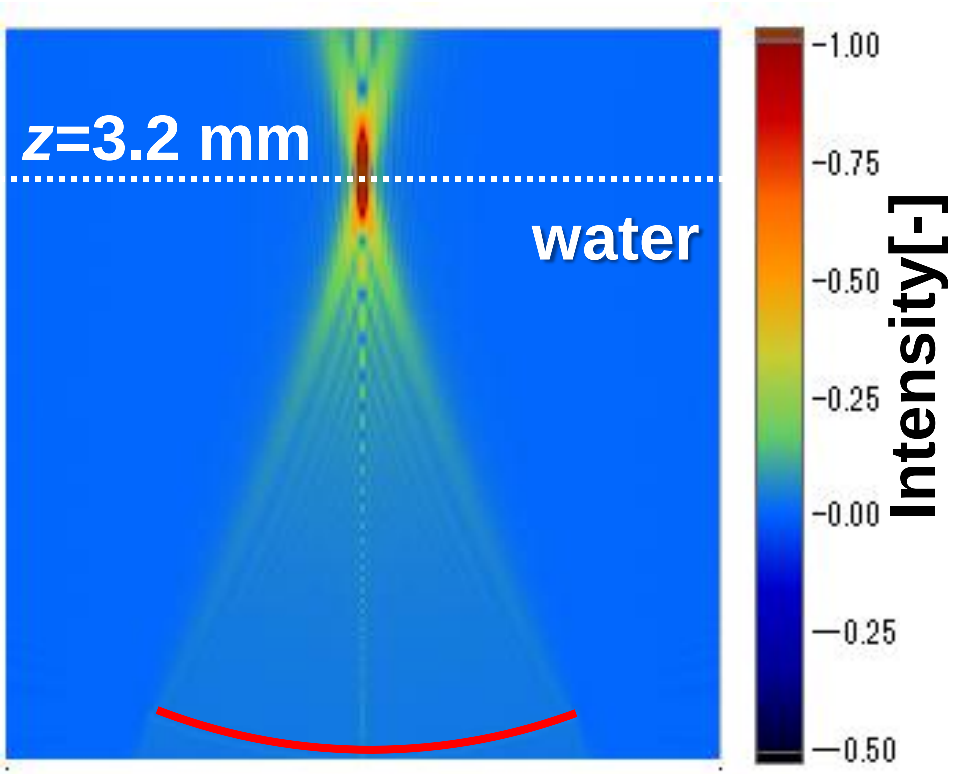
点(x,y,z)の速度ポテンシャル

$$P(x,y,z)=\int_{dS}\frac{A\exp(-jkr)}{r}dS$$

k:波数
r:音源からの距離
ds:音源の微小面積

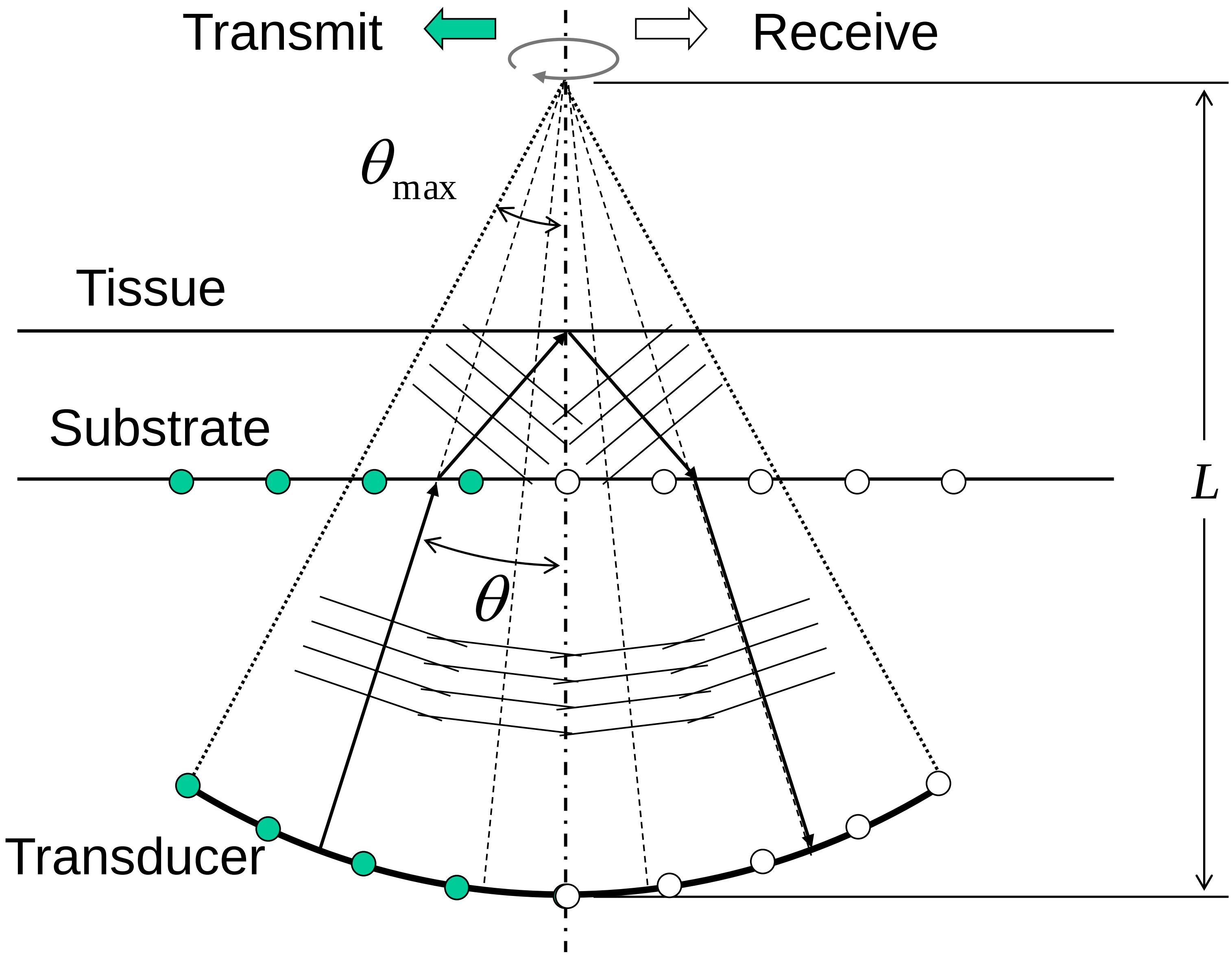
Potential distribution



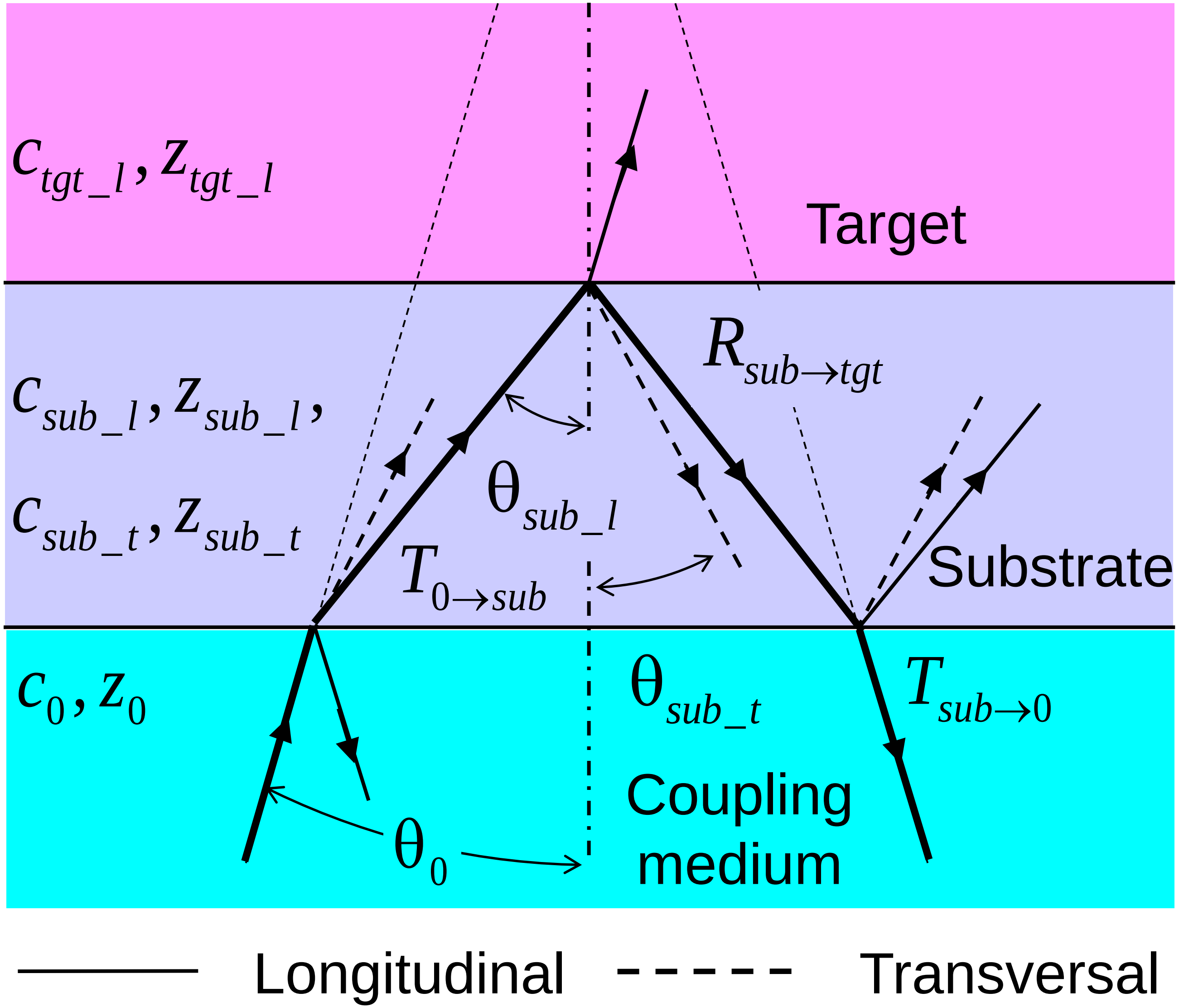


➤ 焦点距離3.2mmで強度最大。

Spherical transducer.



Wave propagation.

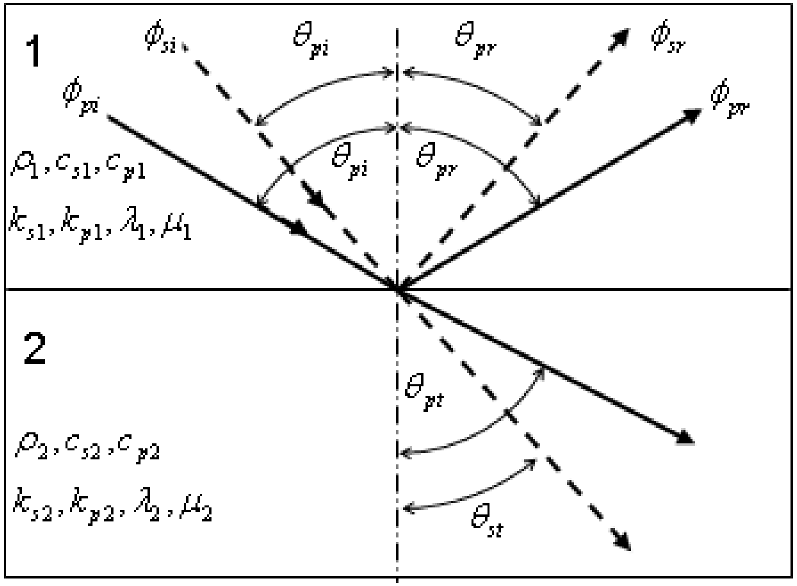


Wave propagation.

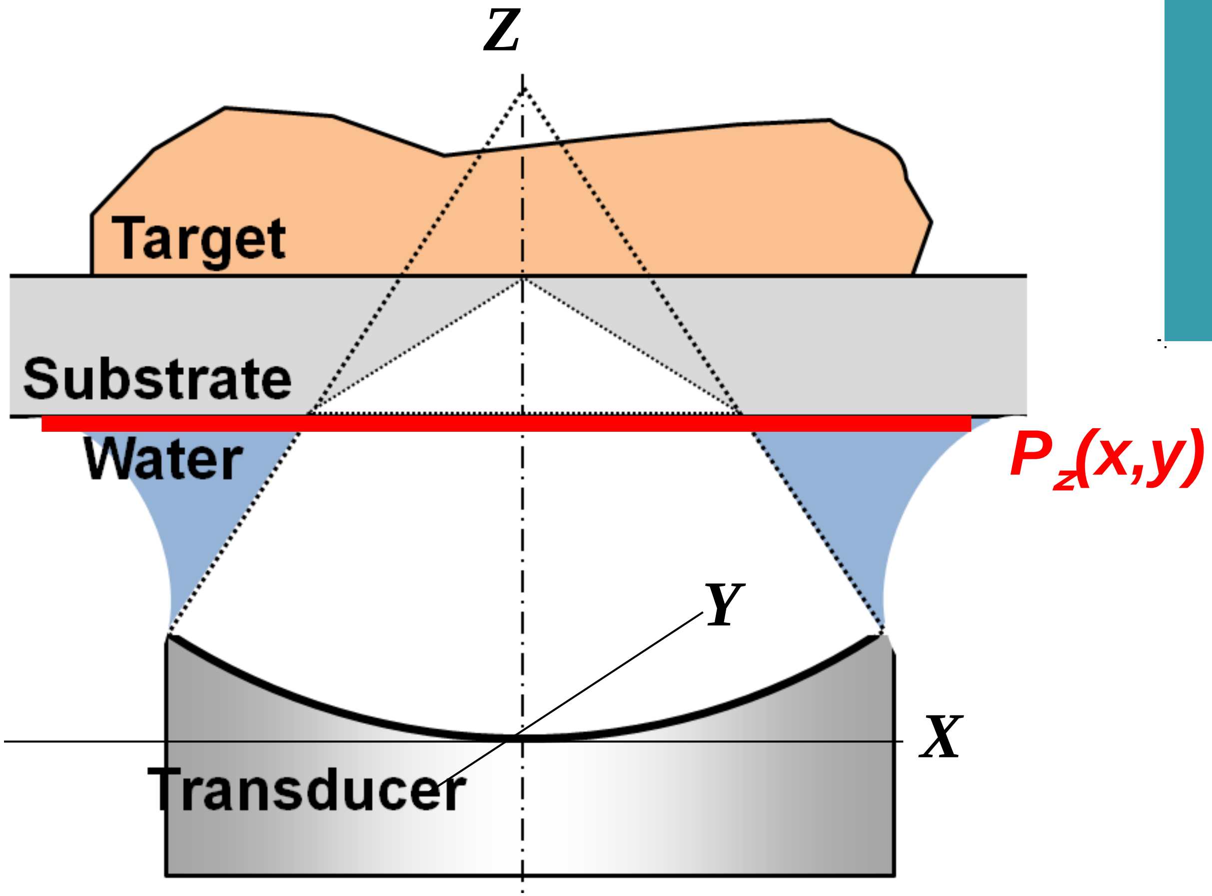
$$
\begin{pmatrix}
k_{s1} & k_{p1} & k_{s2} & -k_{p2} \\
-k_{s1} & k_{p1} & k_{s2} & k_{p2} \\
\rho_1 & -\rho_1 & \rho_2 & \rho_2 \\
-\rho_1 & -\dfrac{\mu_1\rho_1}{\lambda_1+2\mu_1} & \rho_2 & -\dfrac{\mu_2\rho_2}{\lambda_2+2\mu_2}
\end{pmatrix}
\cdot
\begin{pmatrix}
\cos\theta_{sr} & \sin\theta_{pr} & \cos\theta_{st} & \sin\theta_{pt} \\
\sin\theta_{sr} & \cos\theta_{pr} & \sin\theta_{st} & \cos\theta_{pt} \\
\sin 2\theta_{sr} & \cos 2\theta_{sr} & \sin 2\theta_{st} & \cos 2\theta_{st} \\
\cos 2\theta_{sr} & \sin 2\theta_{pr} & \cos 2\theta_{st} & \sin 2\theta_{pt}
\end{pmatrix}
\begin{pmatrix}
A_{sr} \\ A_{pr} \\ A_{st} \\ A_{pt}
\end{pmatrix}
$$

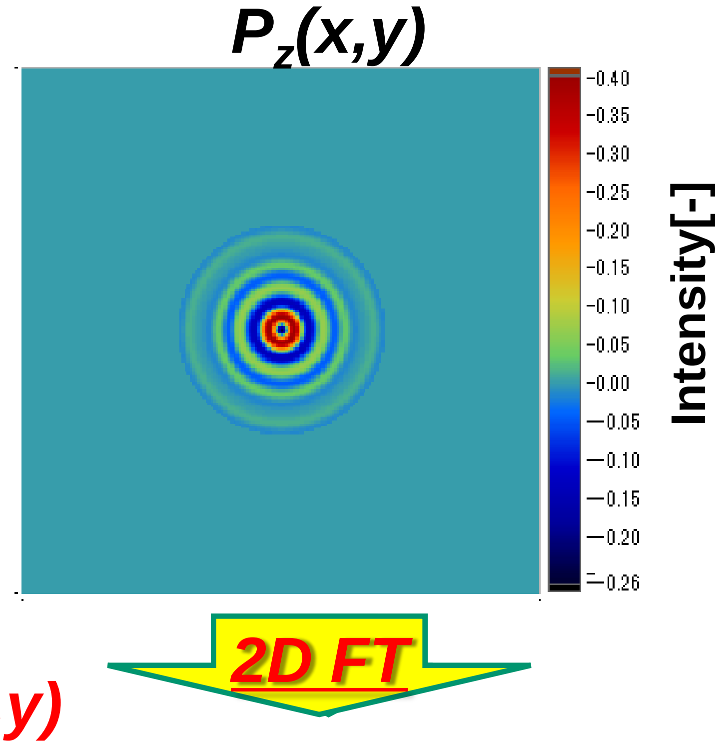
$$
=
\begin{pmatrix}
k_{s1}\cos\theta_{si} & -k_{p1}\sin\theta_{pi} \\
k_{s1}\sin\theta_{si} & k_{p1}\cos\theta_{pi} \\
\rho_1\sin 2\theta_{si} & \rho_1\cos 2\theta_{si} \\
\rho_1\cos 2\theta_{si} & -\dfrac{\mu_1\rho_1}{\lambda_1+2\mu_1}\sin 2\theta_{pi}
\end{pmatrix}
\begin{pmatrix}
A_{si} \\ A_{pi}
\end{pmatrix}
$$

$$
=
\begin{pmatrix}
k_{s1} & -k_{p1} \\
k_{s1} & k_{p1} \\
\rho_1 & \rho_1 \\
\rho_1 & -\dfrac{\mu_1\rho_1}{\lambda_1+2\mu_1}
\end{pmatrix}
\cdot
\begin{pmatrix}
\cos\theta_{si} & \sin\theta_{pi} \\
\sin\theta_{si} & \cos\theta_{pi} \\
\sin 2\theta_{si} & \cos 2\theta_{si} \\
\cos 2\theta_{si} & \sin 2\theta_{pi}
\end{pmatrix}
\begin{pmatrix}
A_{si} \\ A_{pi}
\end{pmatrix}
$$

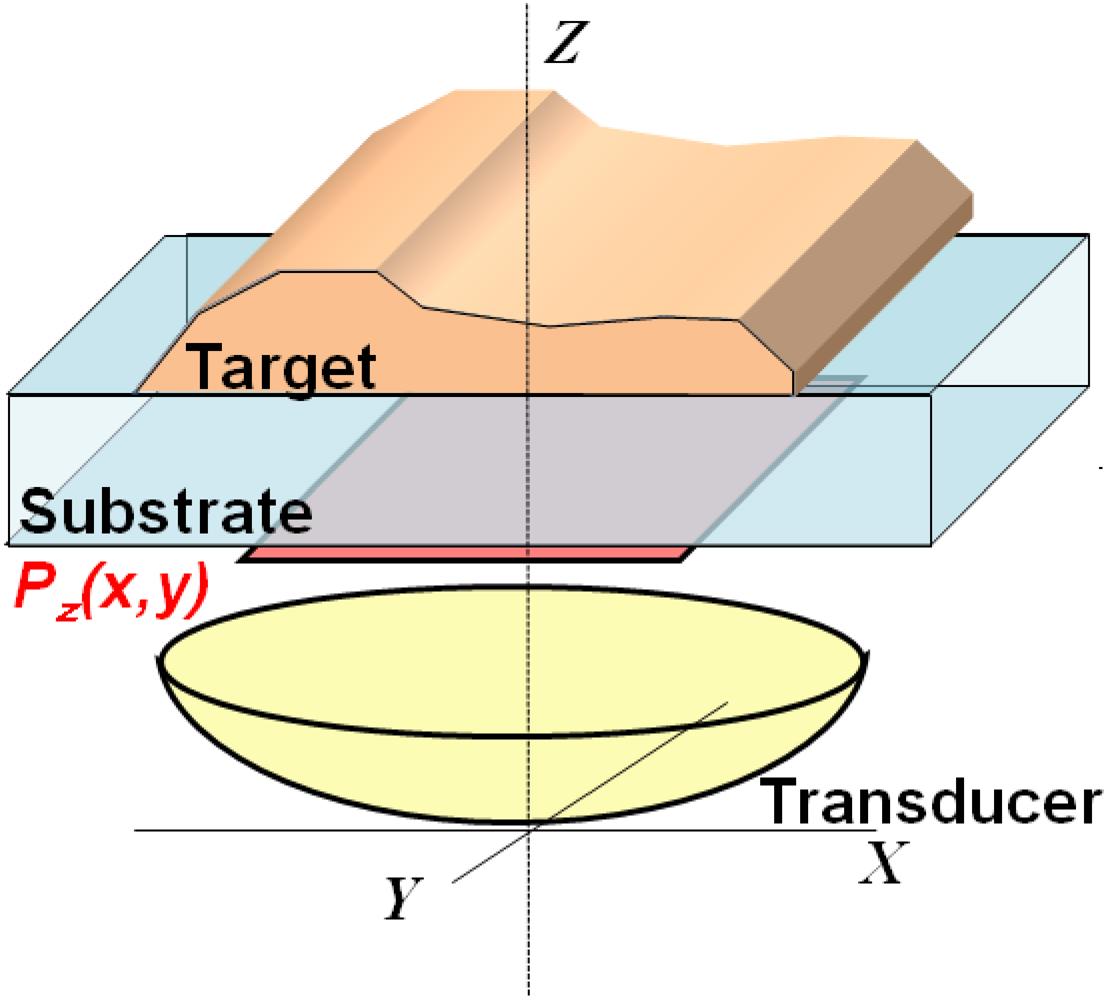


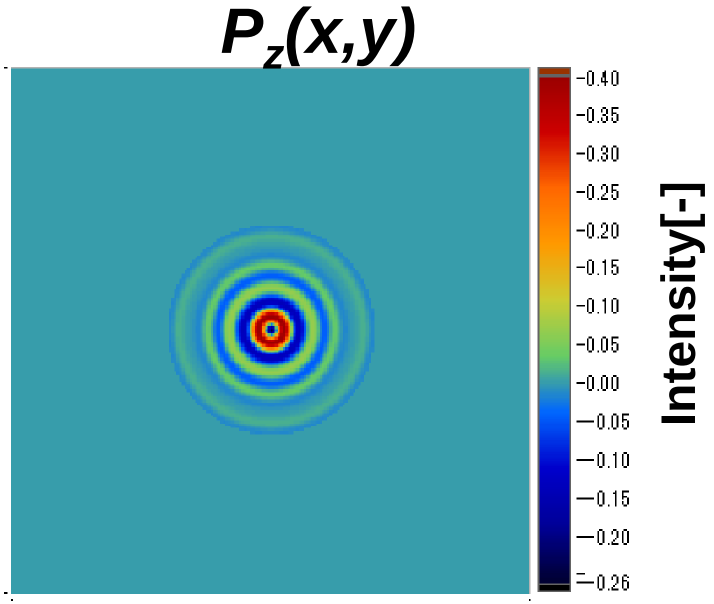
Fourier analysis





Fourier analysis





2D FT

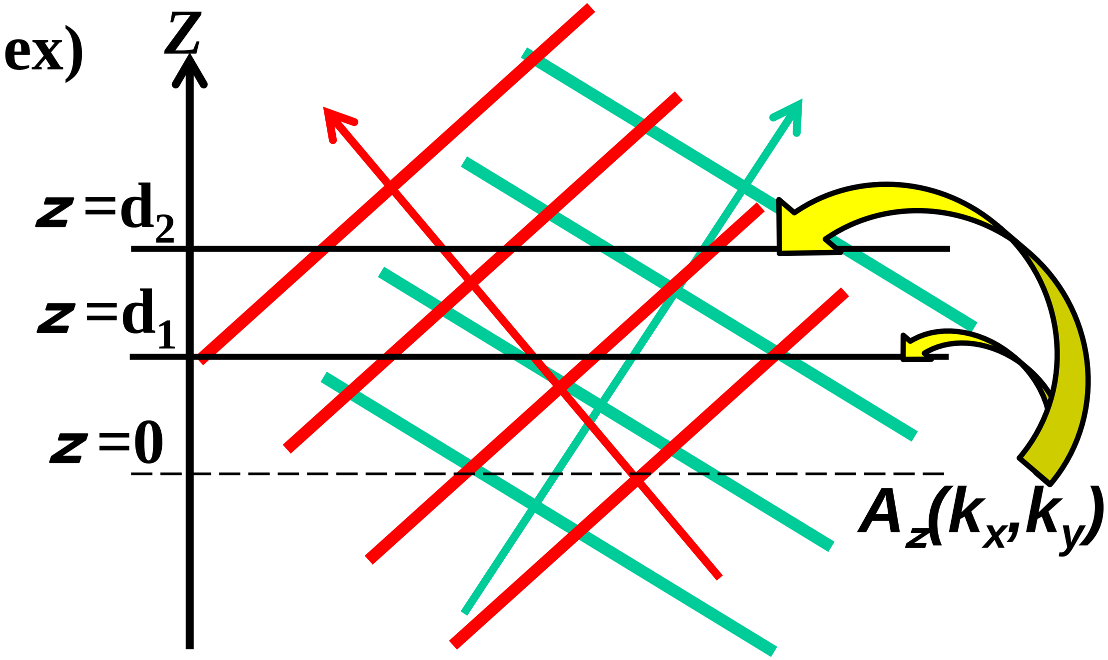
Fourier analysis

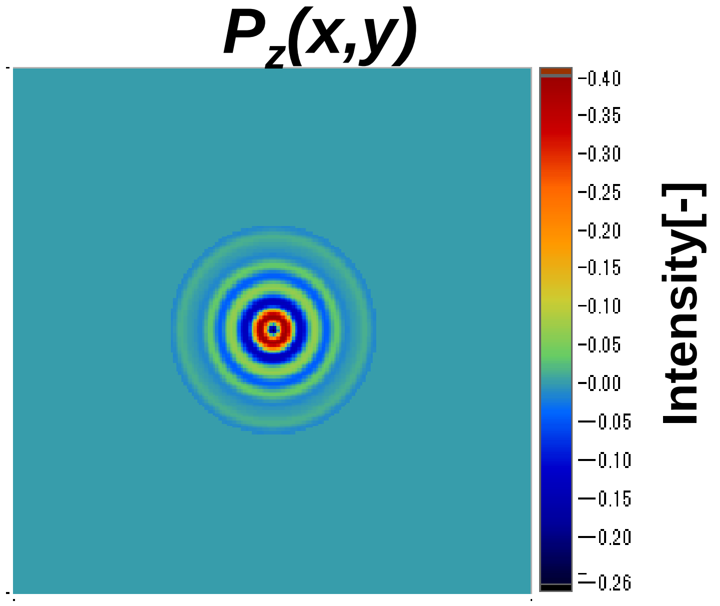
2D FT(2次元 フーリエ変換)

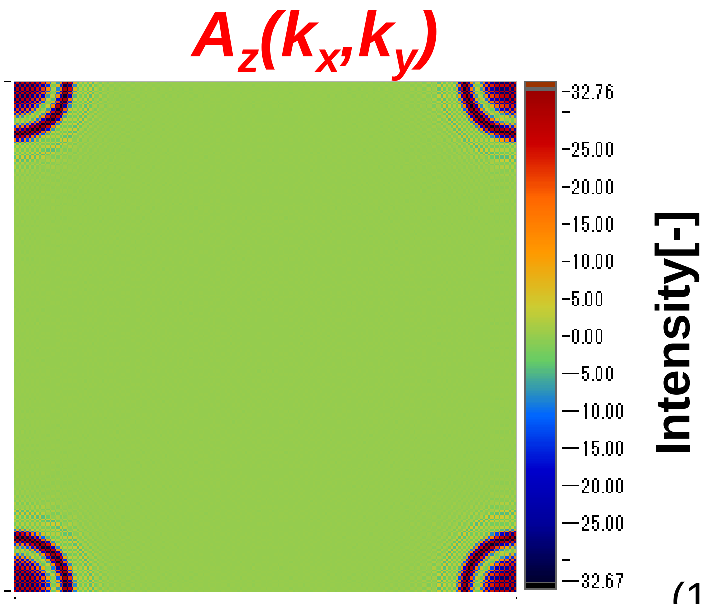
実空間→波数空間

$$A_z(k_x,k_y)=\int_{-\infty}^{\infty}\int_{-\infty}^{\infty}P_z(x,y)\exp(jk_x x+jk_y y)dxdy$$

ex)



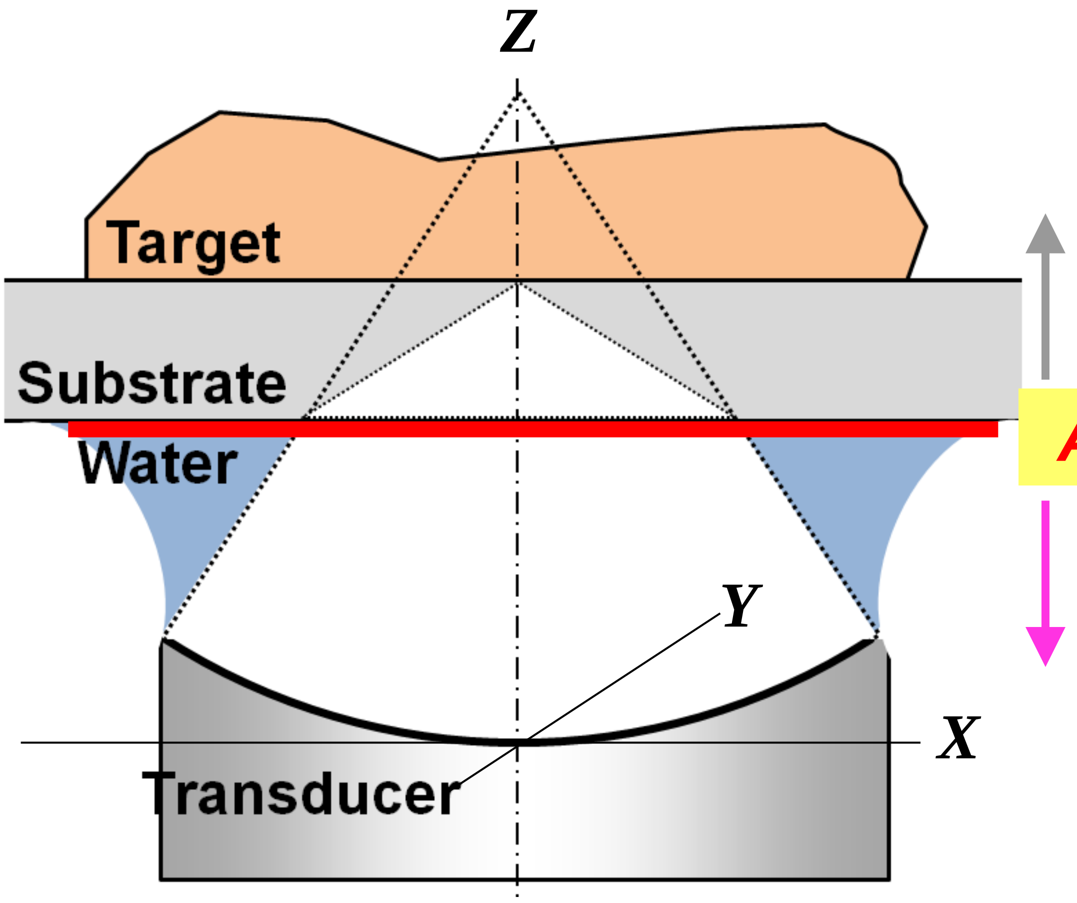




Az(kx,ky)が求まれば、

任意の場所のポテンシャルの計算可能

Fourier analysis



$$k_{z\_sub} = \frac{2\pi f}{c_{sub}}$$

$$\exp\left(jk_{z\_sub}z\right)$$

(基板)

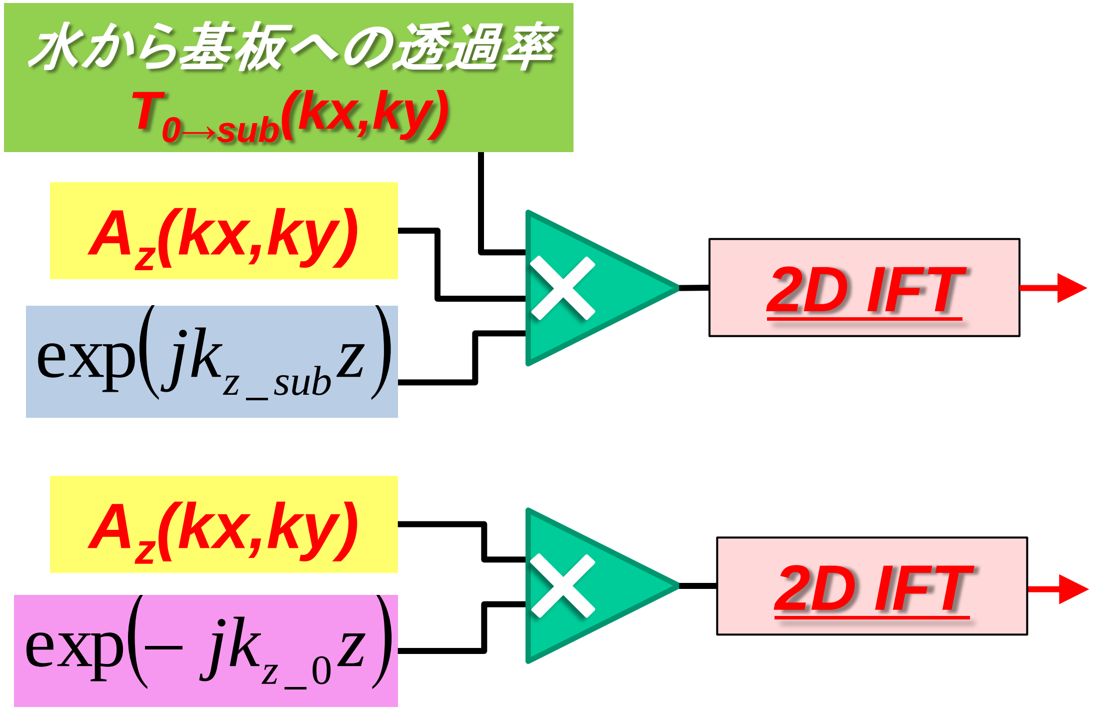
$A_z(kx,ky)$

$$\exp\left(-jk_{z\_0}z\right)$$

(水)

$$k_{z\_0} = \frac{2\pi f}{c_0}$$

Result



水から基板への透過率 $T_{0\rightarrow sub}(kx,ky)$

$A_z(kx,ky)$

$\exp\left(jk_{z\_sub}z\right)$

×

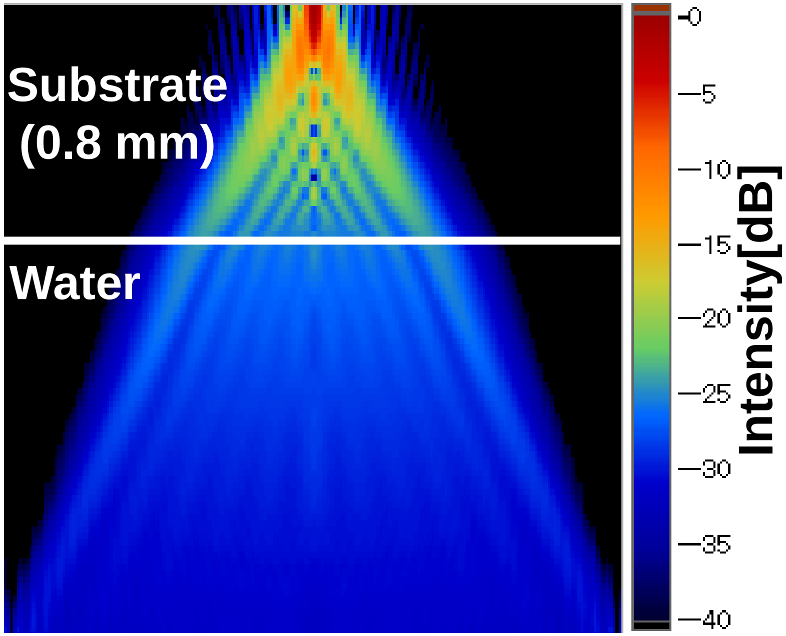
2D IFT

$A_z(kx,ky)$

$\exp\left(-jk_{z\_0}z\right)$

×

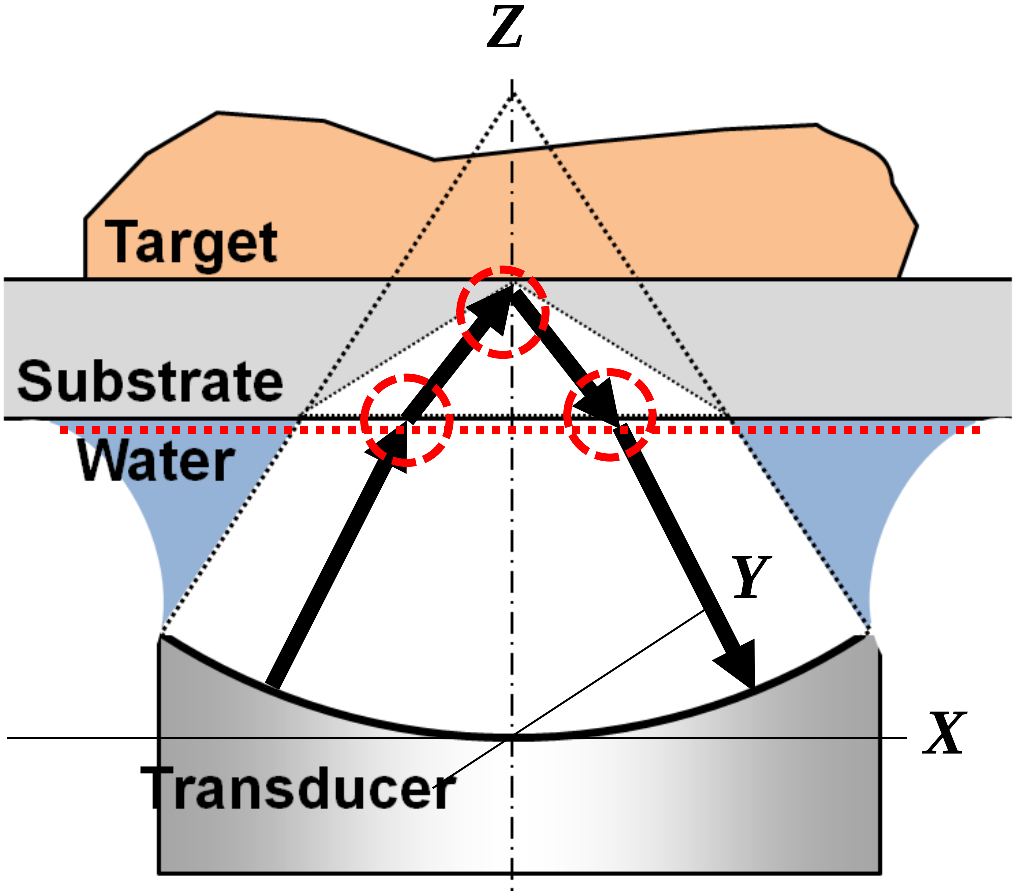
2D IFT

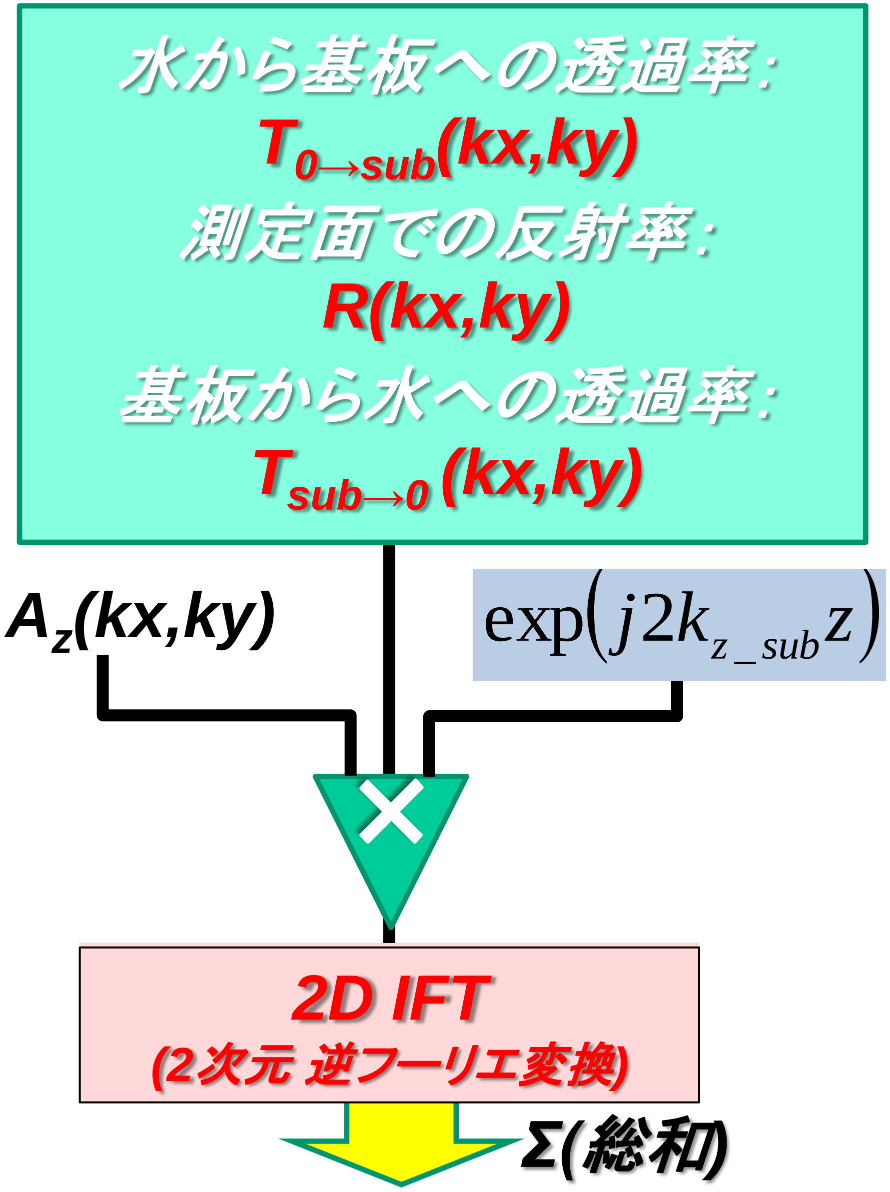


2D IFT(2次元 逆フーリエ変換)

$$P_z(x,y)=\int_{-\infty}^{\infty}\int_{-\infty}^{\infty}\left\{A_z(k_x,k_y)\exp(-jk_z z)\right\}\exp(-jk_x x-jk_y y)dk_x dk_y$$

Calculation of acoustic intensity





水から基板への透過率:
$T_{0\rightarrow sub}(kx,ky)$

測定面での反射率:
$R(kx,ky)$

基板から水への透過率:
$T_{sub\rightarrow 0}(kx,ky)$

$A_z(kx,ky)$

$\exp(j2k_{z\_sub}z)$

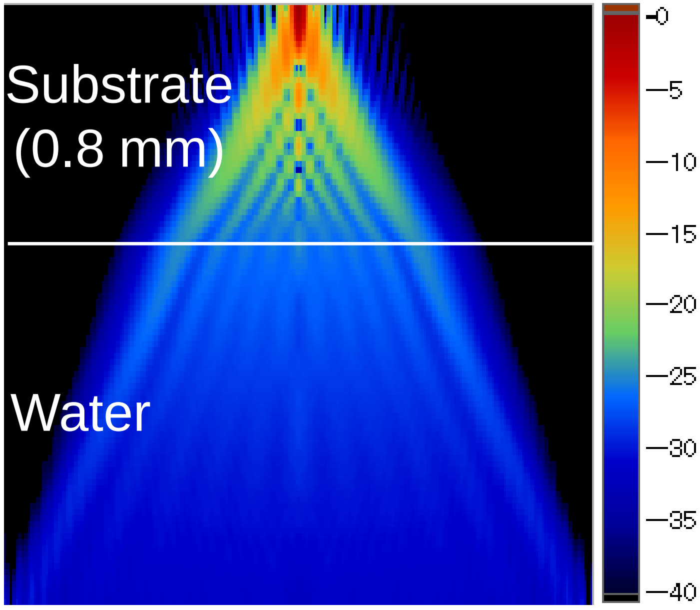
×

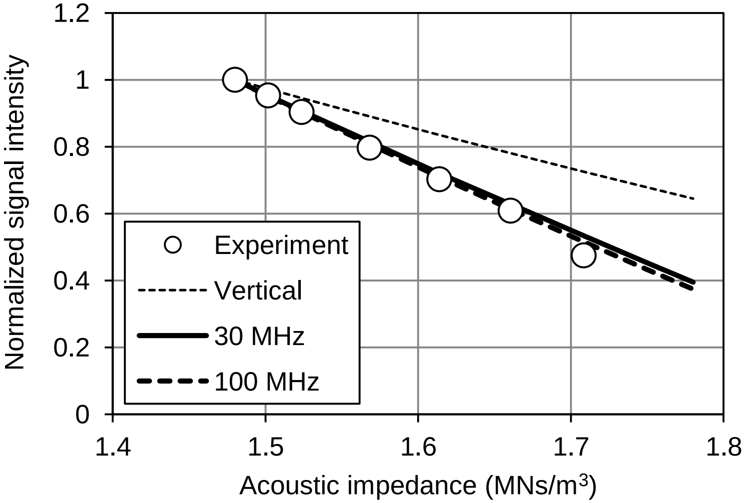
2D IFT
(2次元 逆フーリエ変換)

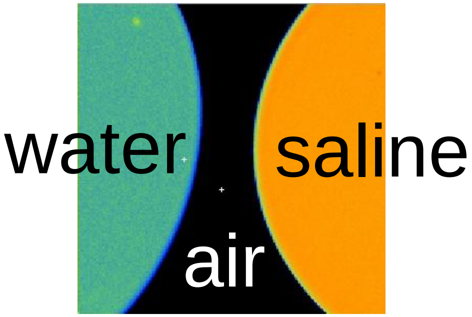
Σ(総和)

反射強度(計算値)

Spherical transducer. (80 MHz)







Analysis result

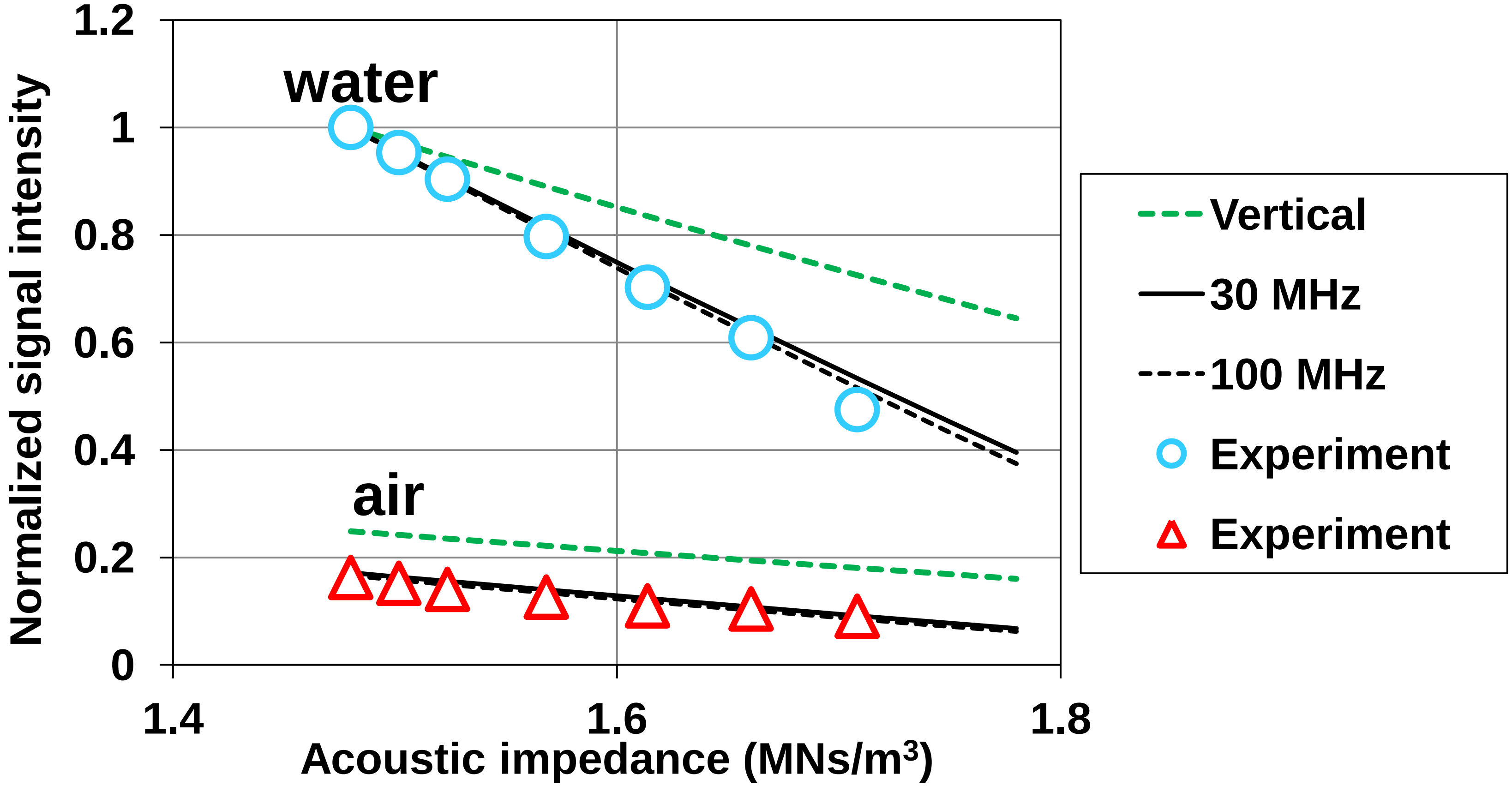
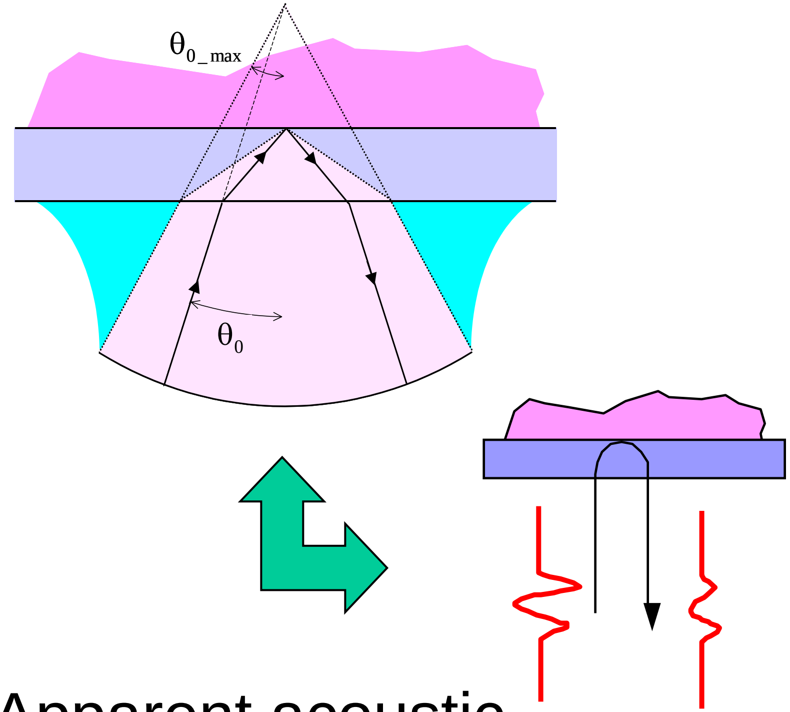


図　水の信号強度で規格化した結果

- 計算値と実験結果はよく一致。
- 音響インピーダンスの大きいところで乖離がやや大きくなる
  →濃度の高い食塩水からの水の蒸発が要因

Apparent acoustic impedance of the target assuming vertical incidence.



Apparent reflection constant

target:

$$S_{tgt}(\underline{Z_{tgt}, c_{tgt}}, \theta_{0\_\max}) / S_0 =$$

$$\int_0^{\theta_{0\_\max}} 2\pi L^2 \sin\theta_0 R_{sub\to tgt}(\theta_0) T'_{0\to sub}(\theta_0) d\theta_0$$

reference:

$$S_{ref}(Z_{ref}, c_{ref}, \theta_{0\_\max}) / S_0 =$$

$$\int_0^{\theta_{0\_\max}} 2\pi L^2 \sin\theta_0 R_{sub\to ref}(\theta_0) T'_{0\to sub}(\theta_0) d\theta_0$$

Apparent acoustic impedance of the target:

$$\underline{Z_{tgt\_app}} = \frac{1 + \dfrac{S_{tgt}(\underline{Z_{tgt}}, c_{tgt}, \theta_{0\_\max})}{S_{ref}(Z_{ref}, c_{ref}, \theta_{0\_\max})} \cdot \dfrac{Z_{ref} - Z_{sub\_l}}{Z_{ref} + Z_{sub\_l}}}{1 - \dfrac{S_{tgt}(\underline{Z_{tgt}}, c_{tgt}, \theta_{0\_\max})}{S_{ref}(Z_{ref}, c_{ref}, \theta_{0\_\max})} \cdot \dfrac{Z_{ref} - Z_{sub\_l}}{Z_{ref} + Z_{sub\_l}}} \cdot Z_{sub\_l}$$

Effect of compensation.

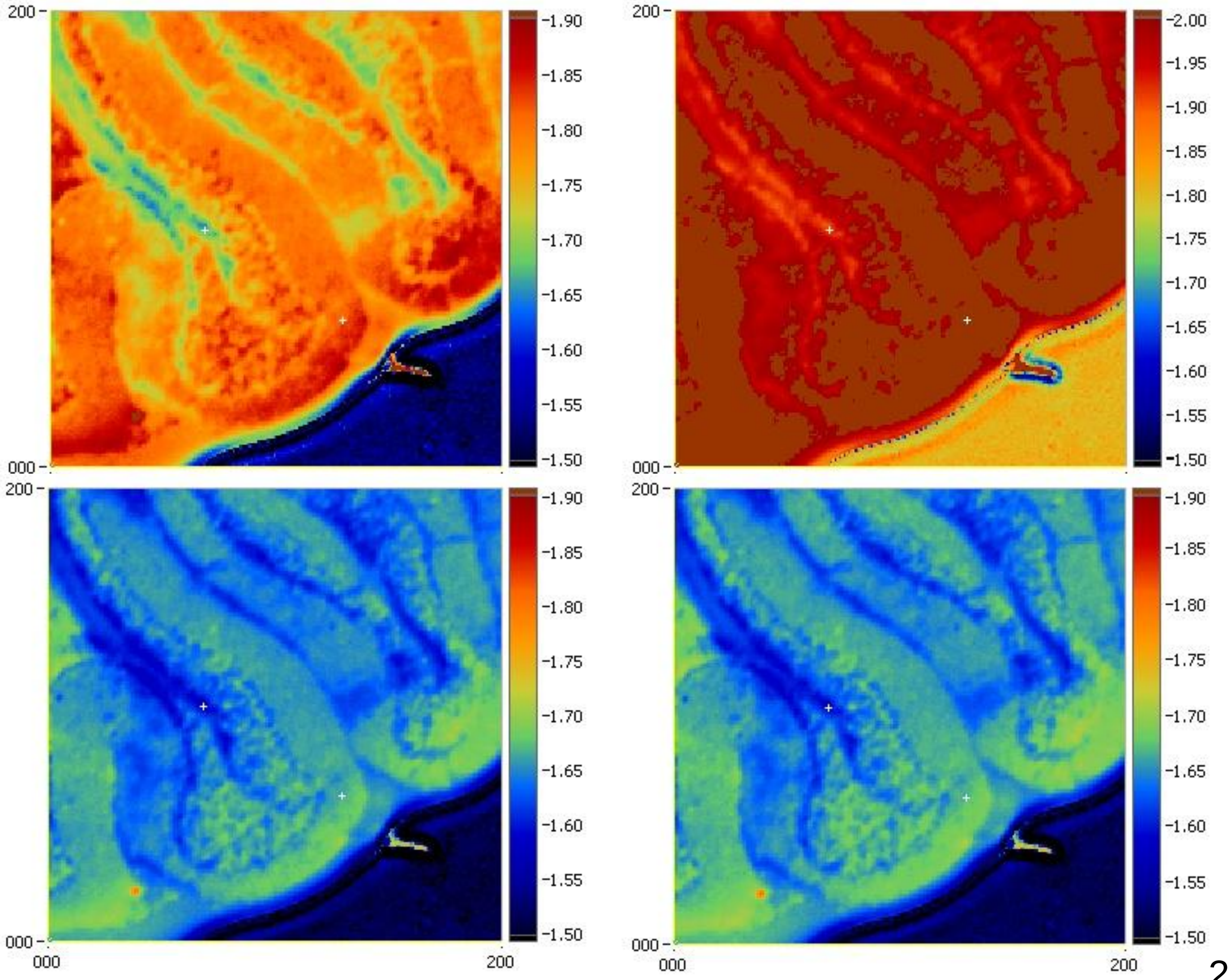
Ref: water

Ref: air

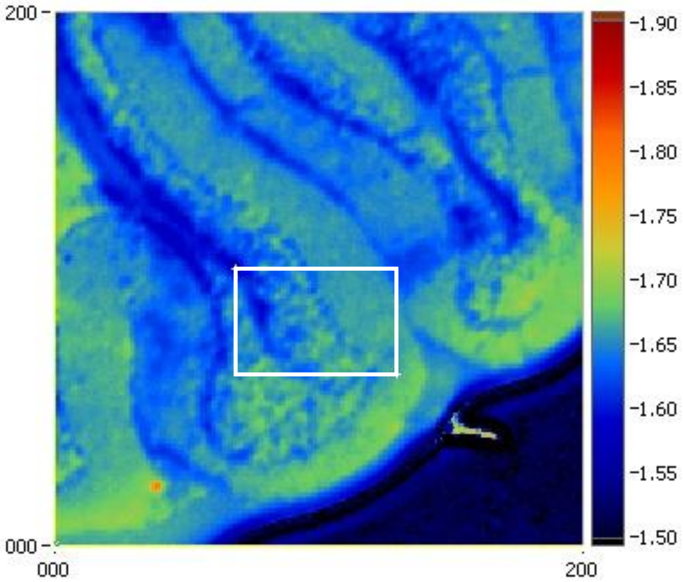
Before compensation

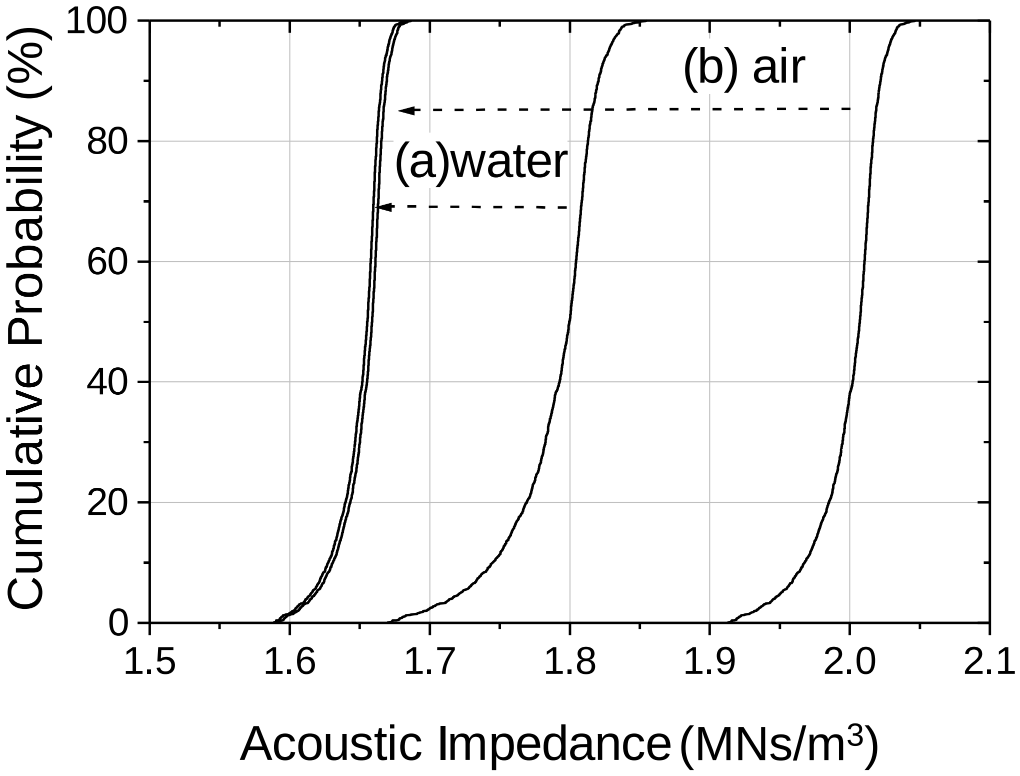
vertical incidence assumed

After compensation

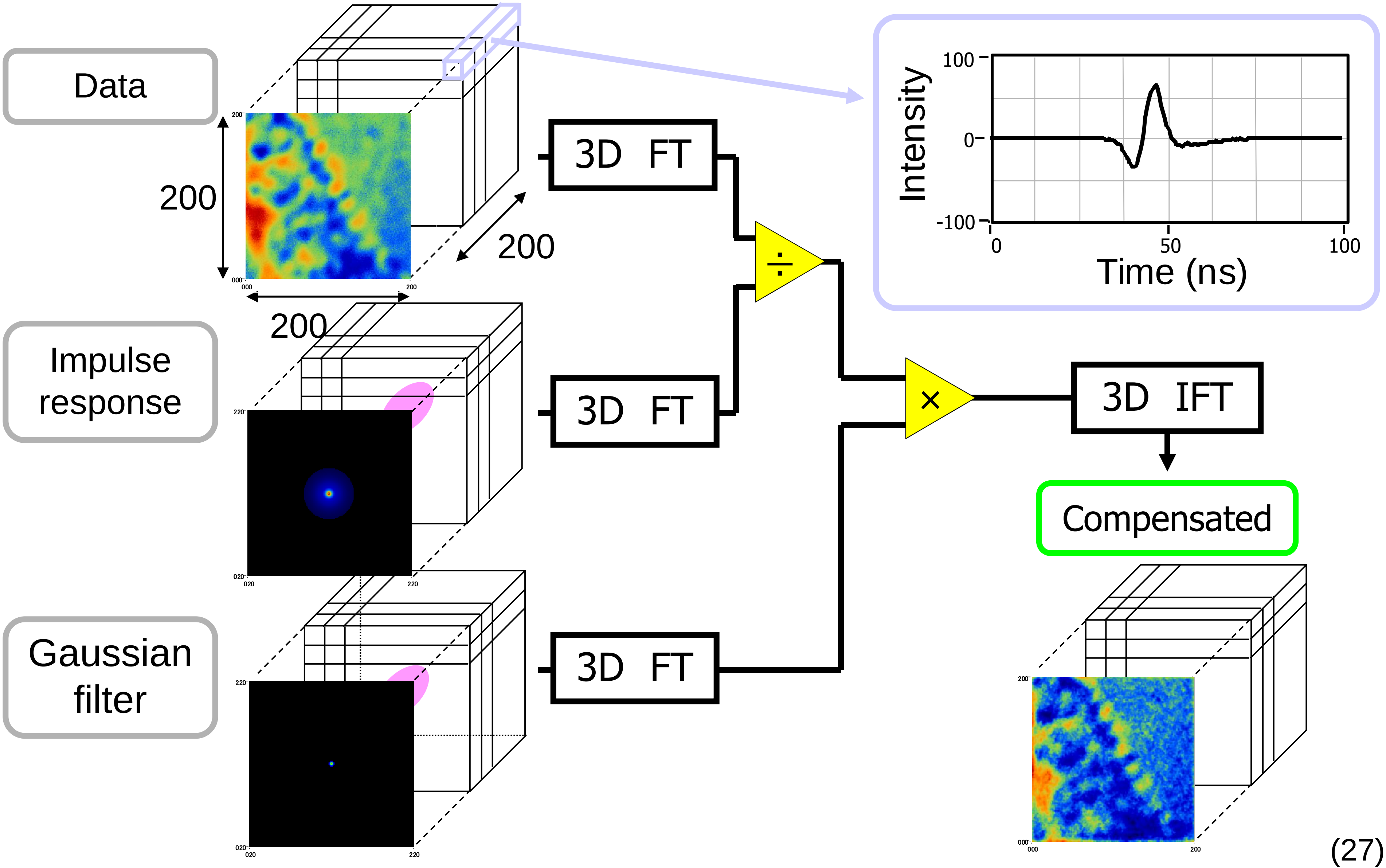


Distribution of the acoustic impedance.





3D deconvolution processing



Data

Impulse response

Gaussian filter

3D FT

3D FT

3D FT

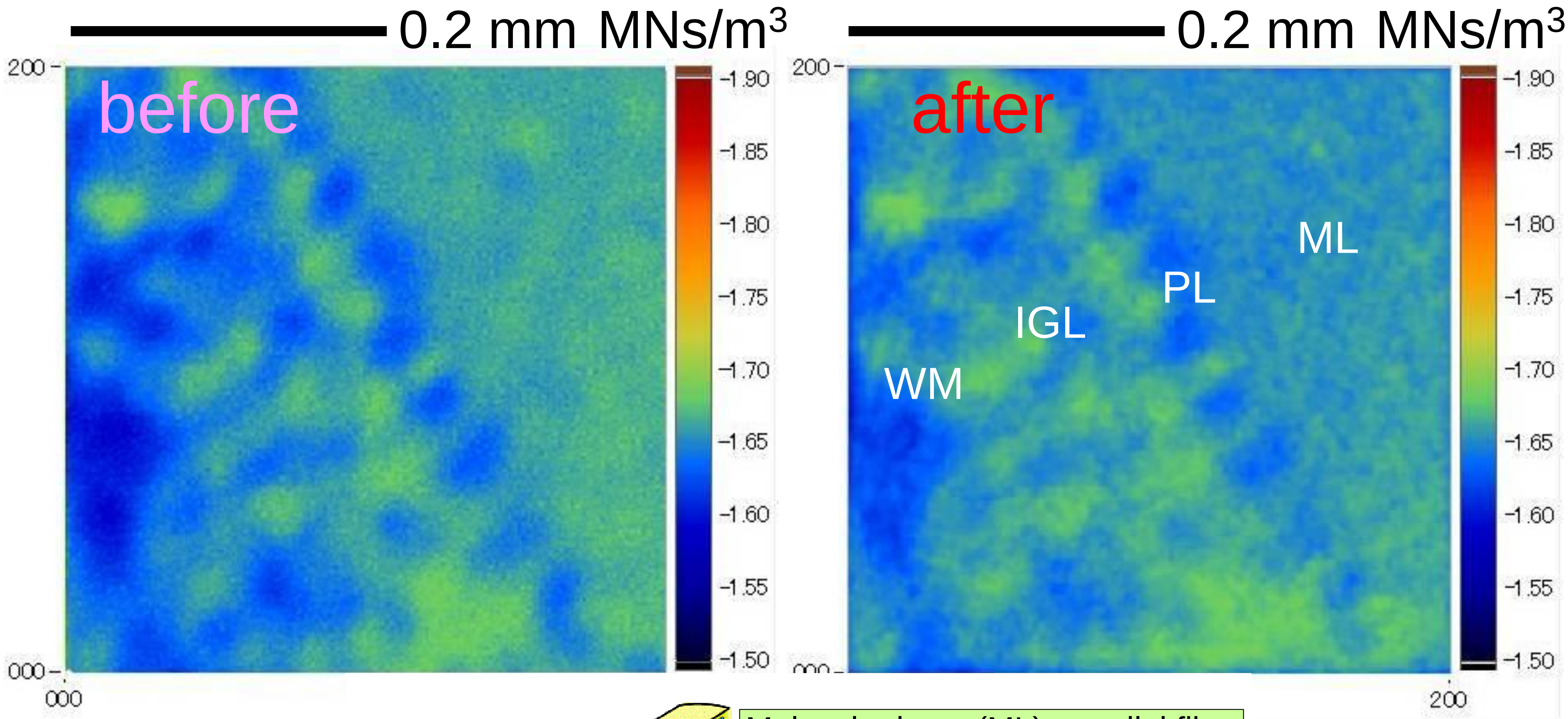
÷

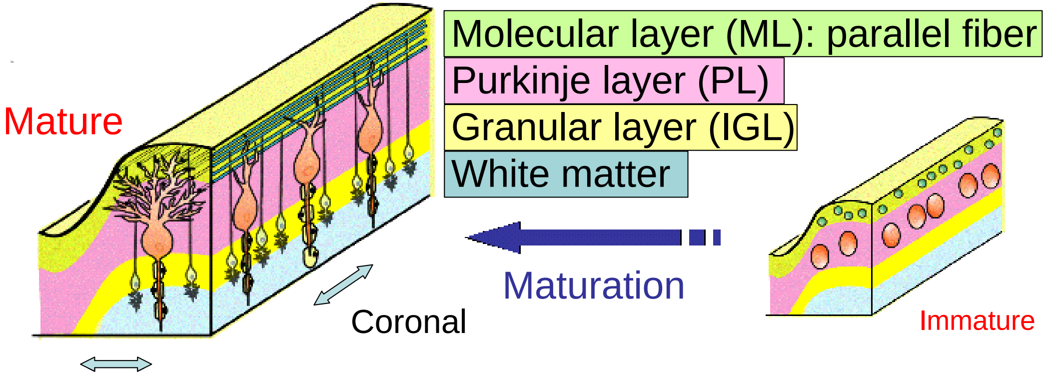
×

3D IFT

Compensated

Acoustic impedance images





Molecular layer (ML): parallel fiber

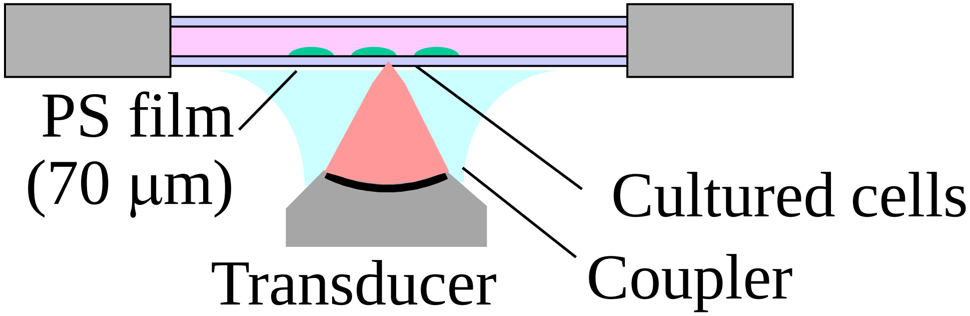
Purkinje layer (PL)

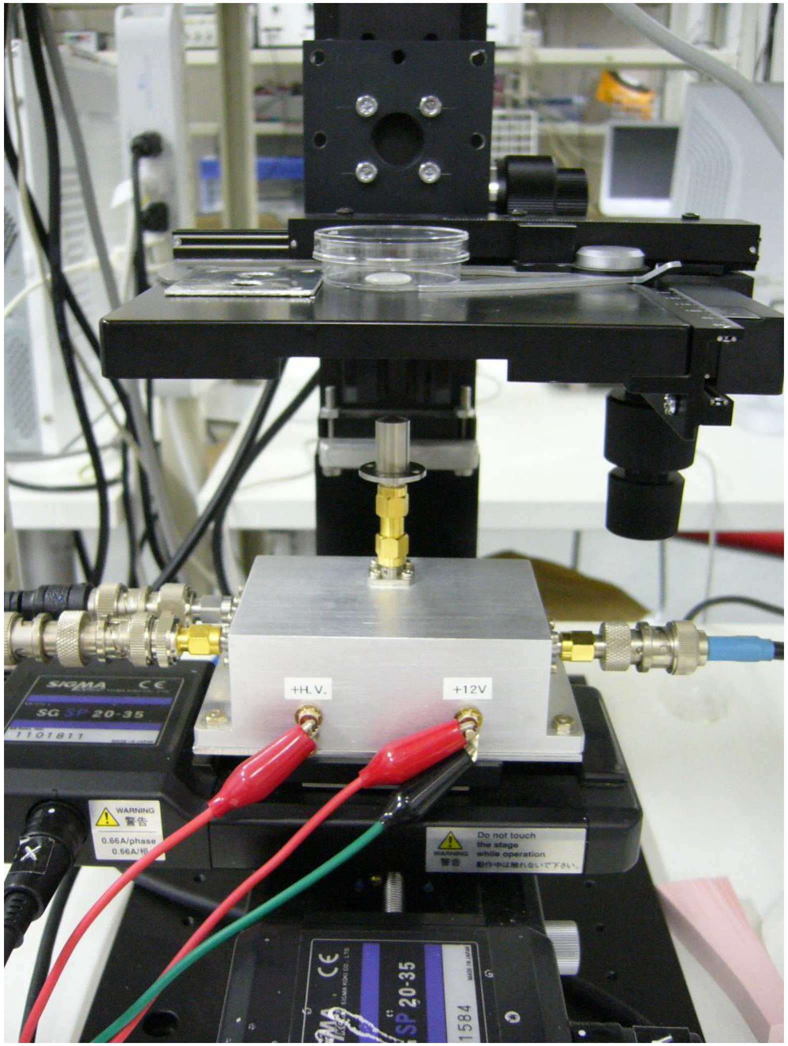
Granular layer (IGL)

White matter

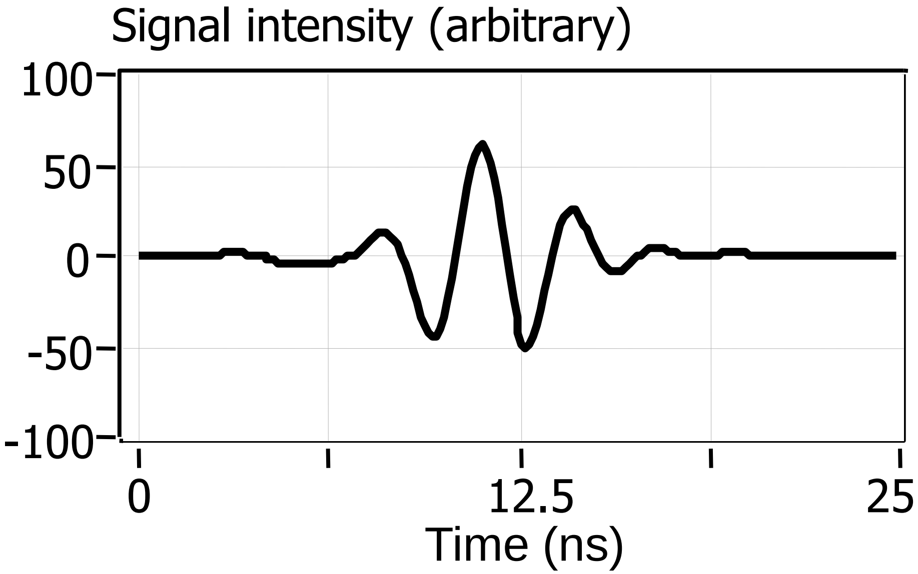
Cell size observation

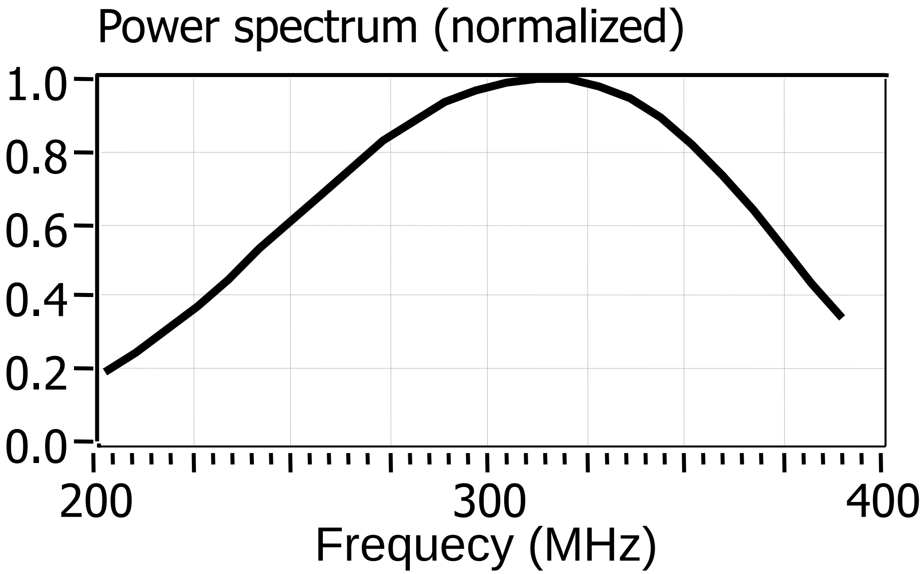
Observation system for cultured cells.





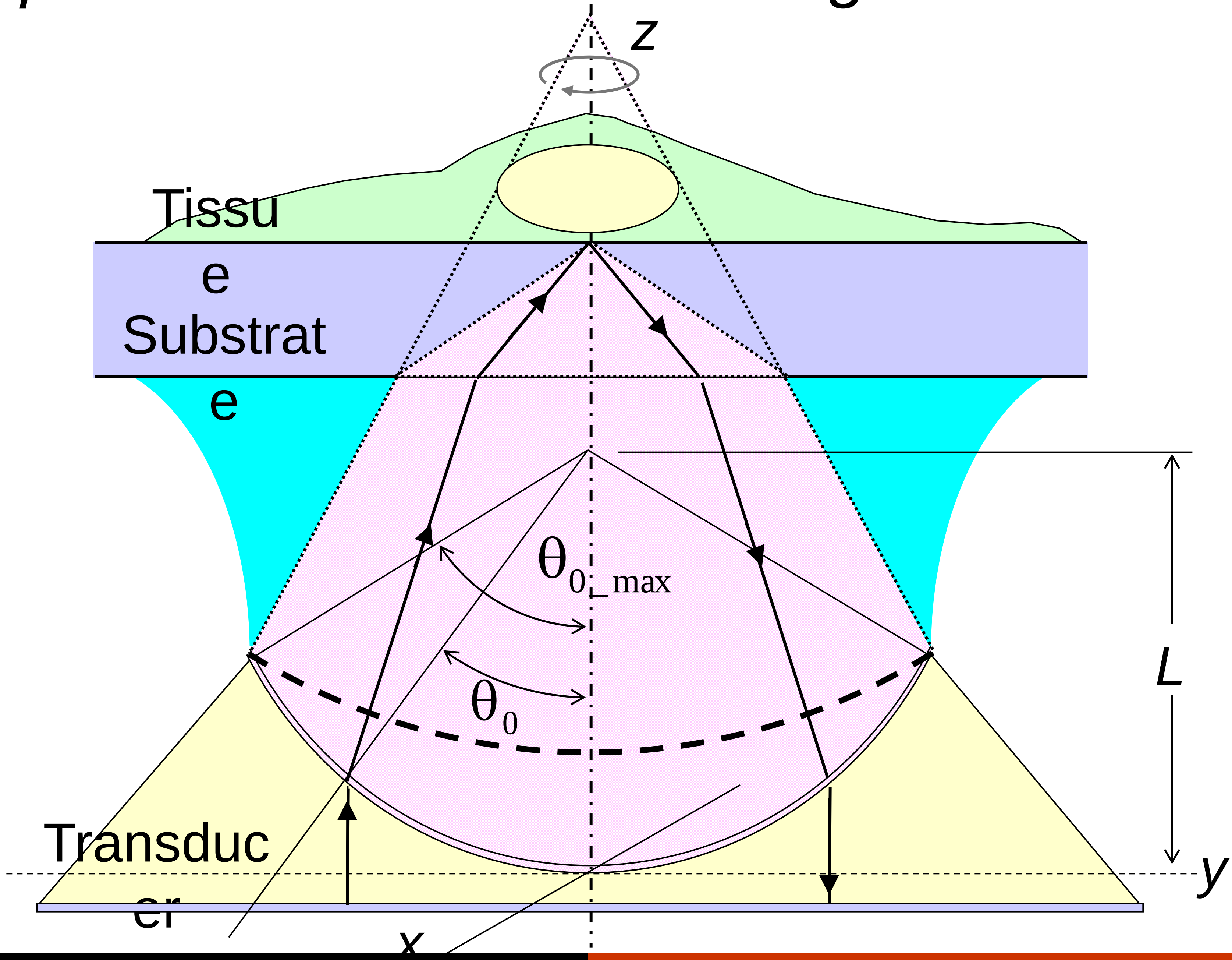
Waveform and spectrum.



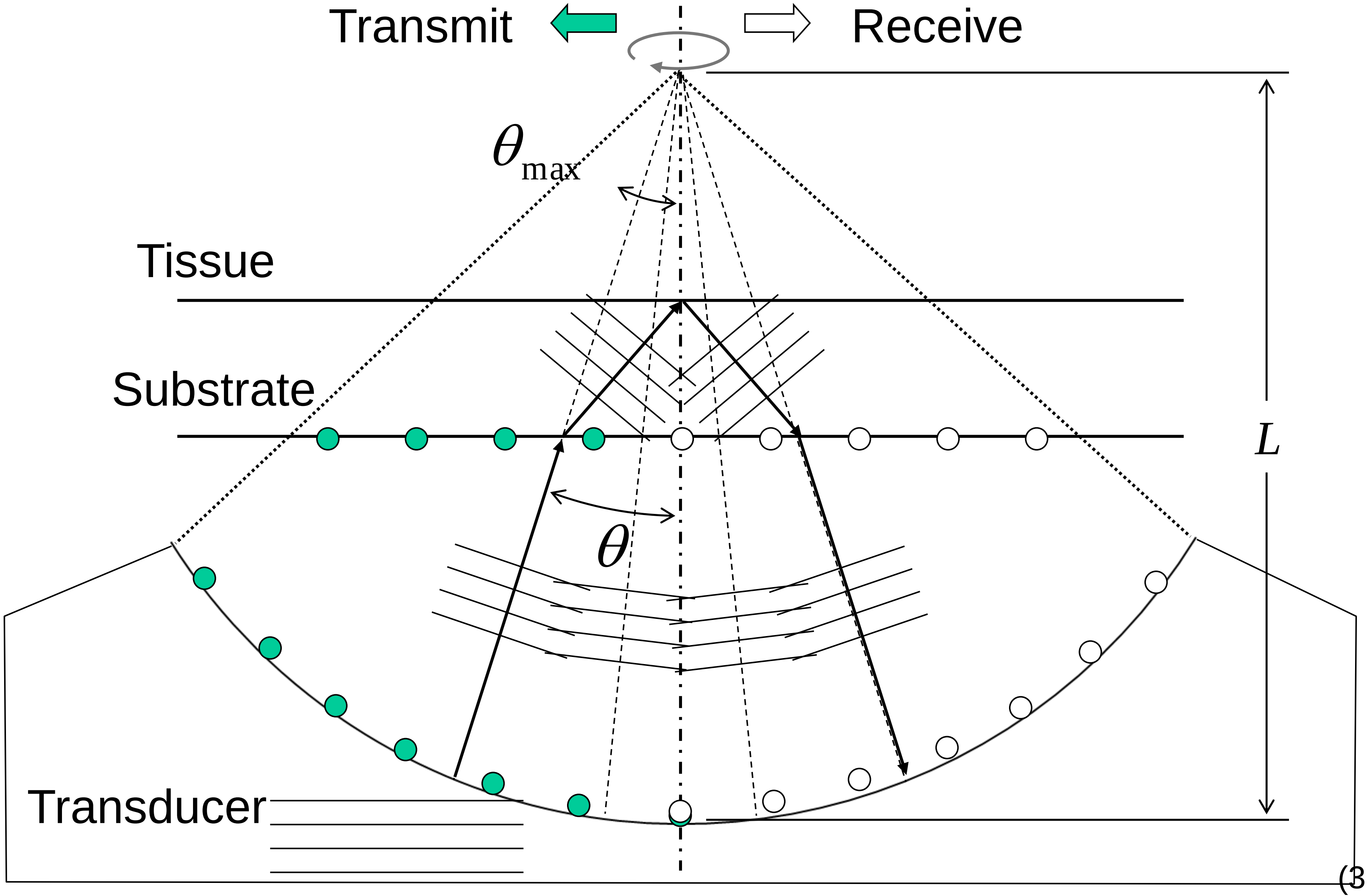


200～400 MHz
range was used.

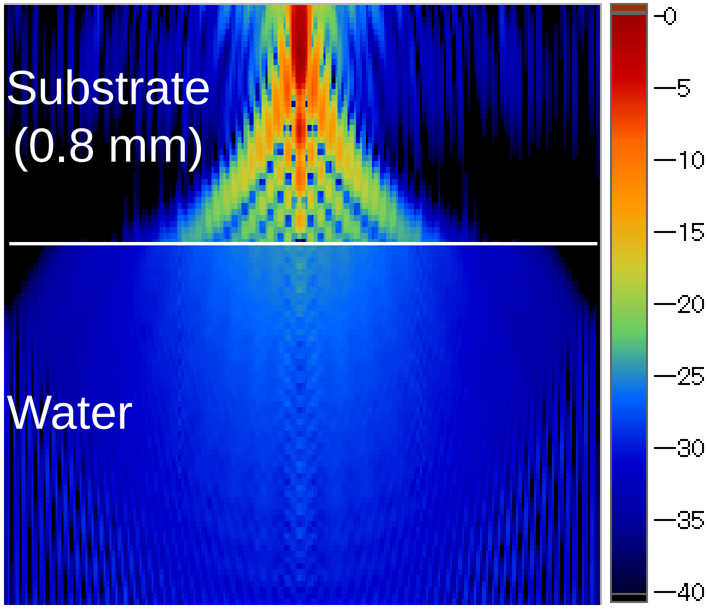
Sapphire rod transducer for high resolution.

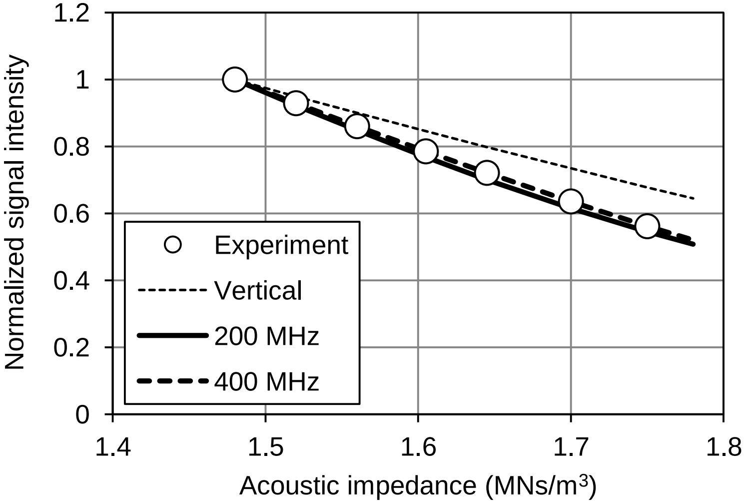


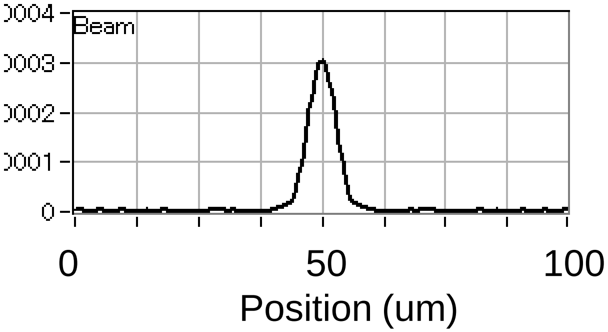
Flat transducer with a lens.

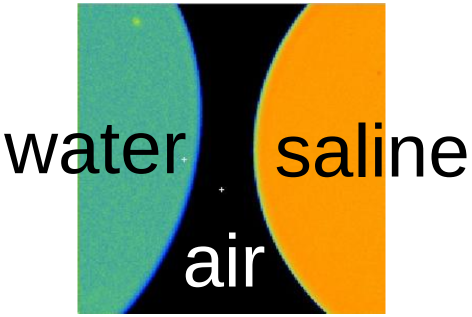


Flat transducer with a lens for high freq. (300 MHz)

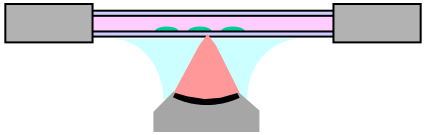


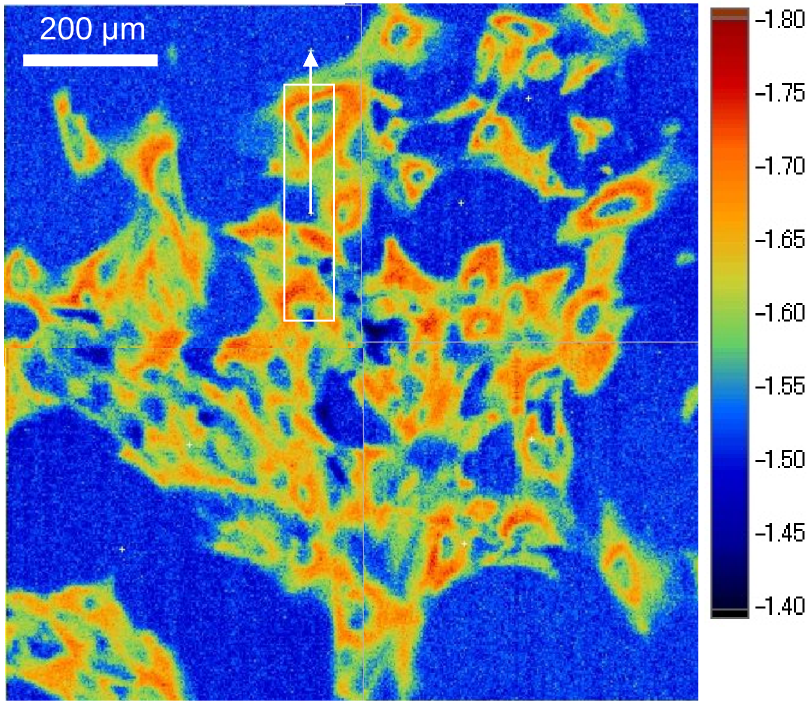




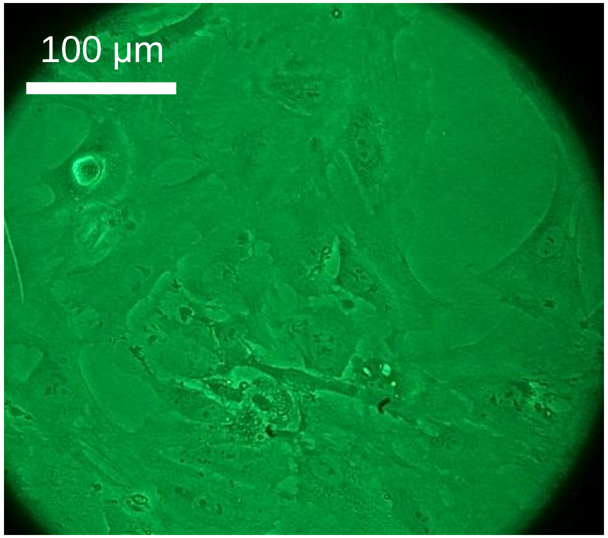


Cultured glial cells, rat.

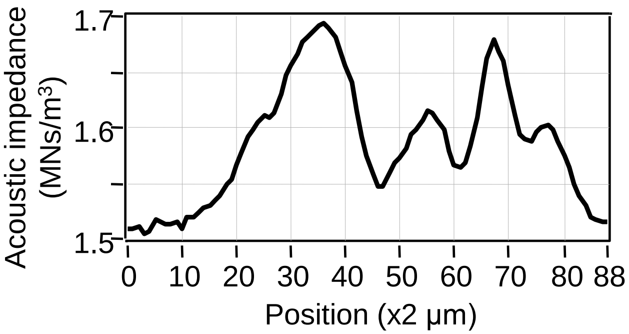




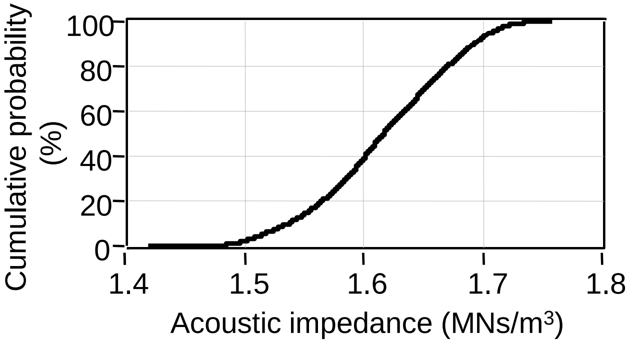
Acoustic impedance



Optical

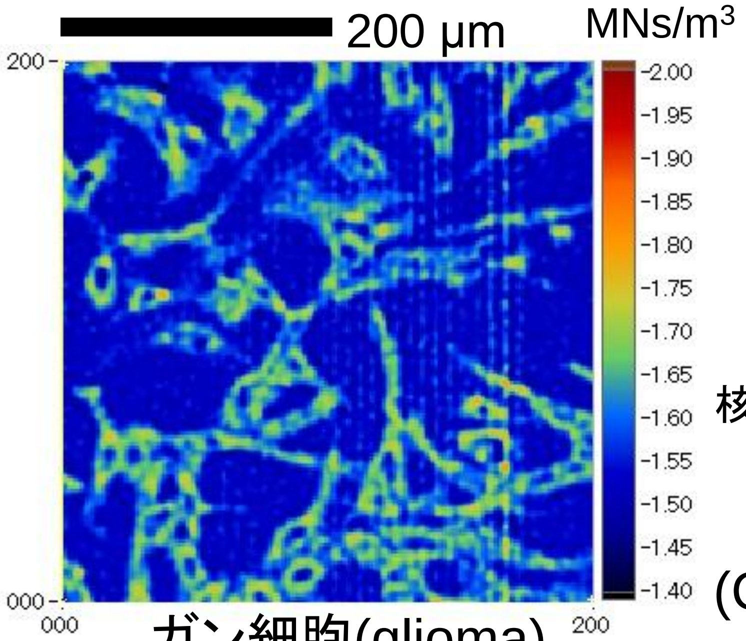


Trace along the white arrow

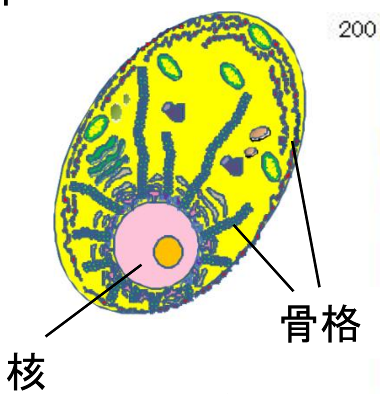


Distribution in the ROI

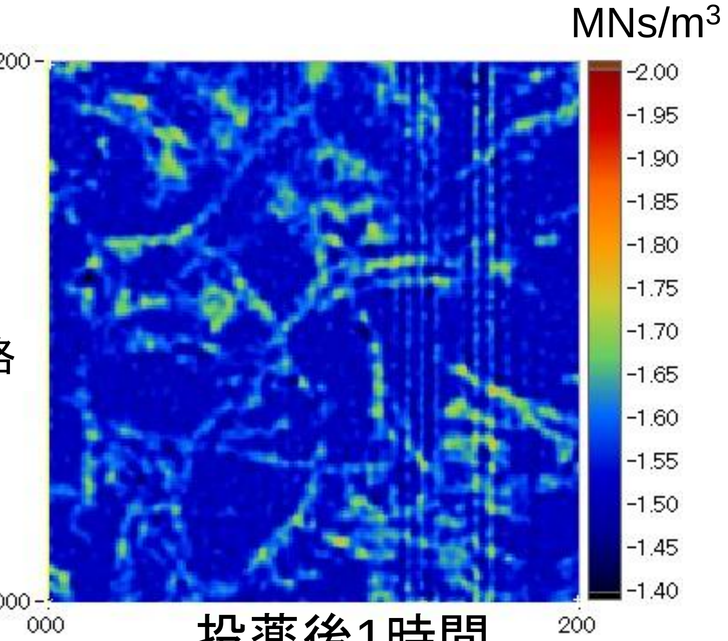
細胞に対する投薬効果を生きたまま観察



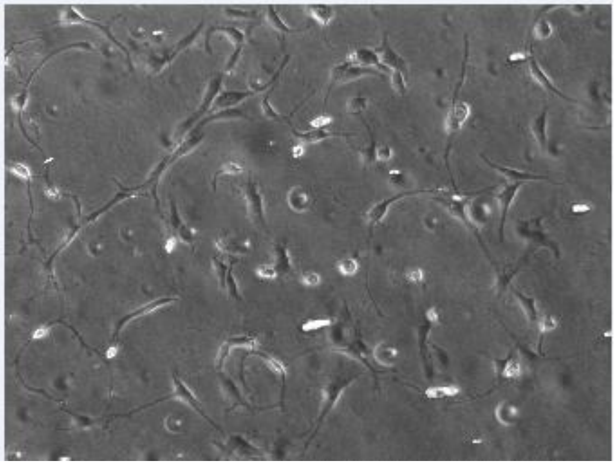
ガン細胞(glioma)
明るい環の部分が細胞骨格



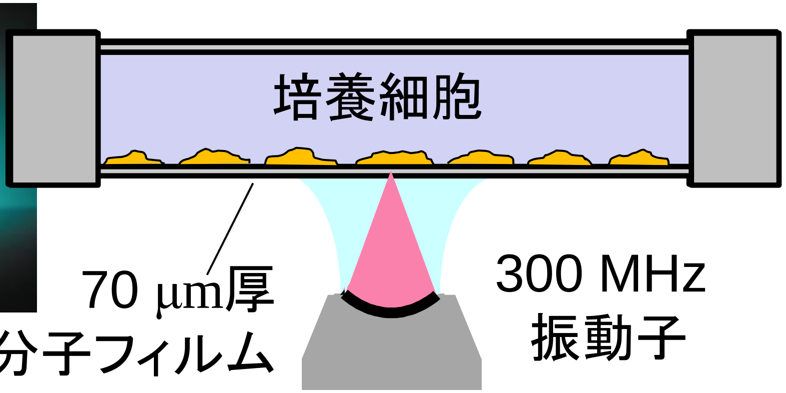
投薬
(Cytochalasin)



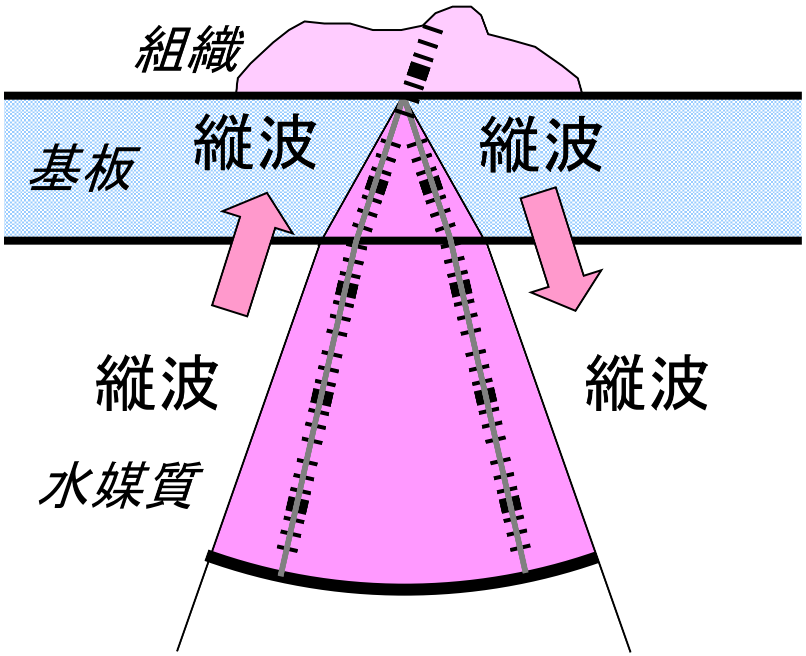
投薬後1時間
細胞骨格が崩れている



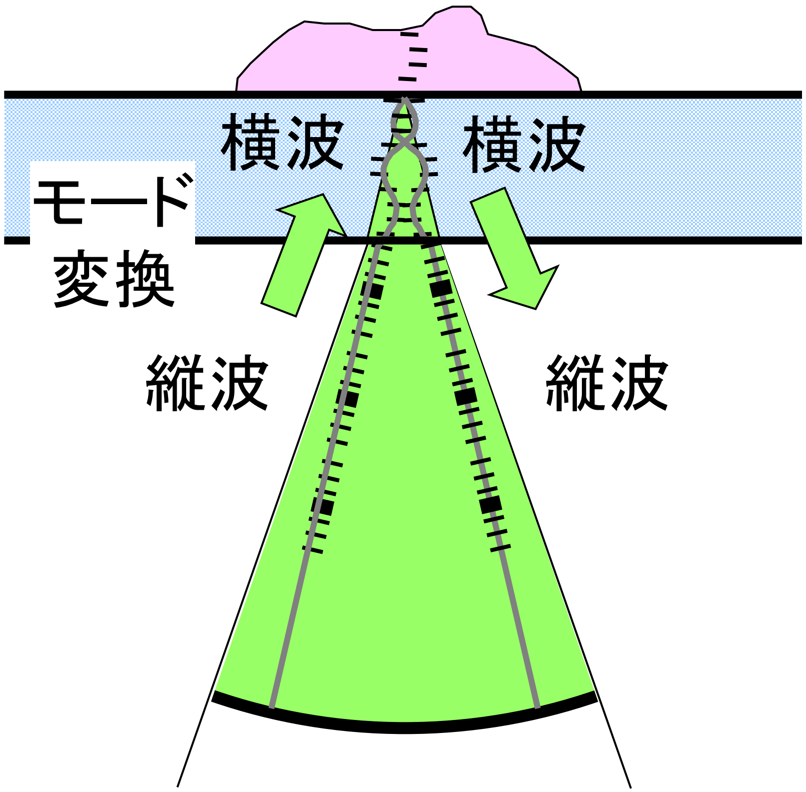
光学顕微鏡では内部構造が見えない



縦波と横波の出し方。



縦波



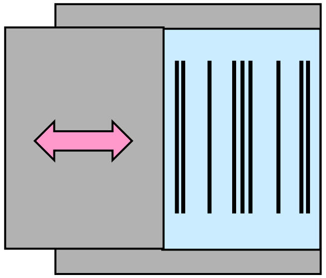
縦波

生体軟組織の縦波物性と横波物性。

縦波特性は体積弾性率*K*で決まる。

$$c_p = \sqrt{(K + \frac{4}{3}G) / \rho},$$

$$Z_p = \rho c_p \qquad K >> G$$



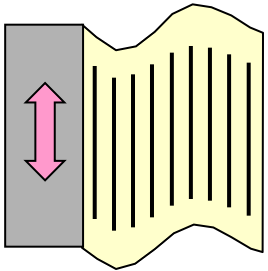
気体・液体
・固体

横波特性はずり弾性率*G*で決まる。

$$c_s = \sqrt{G / \rho},$$

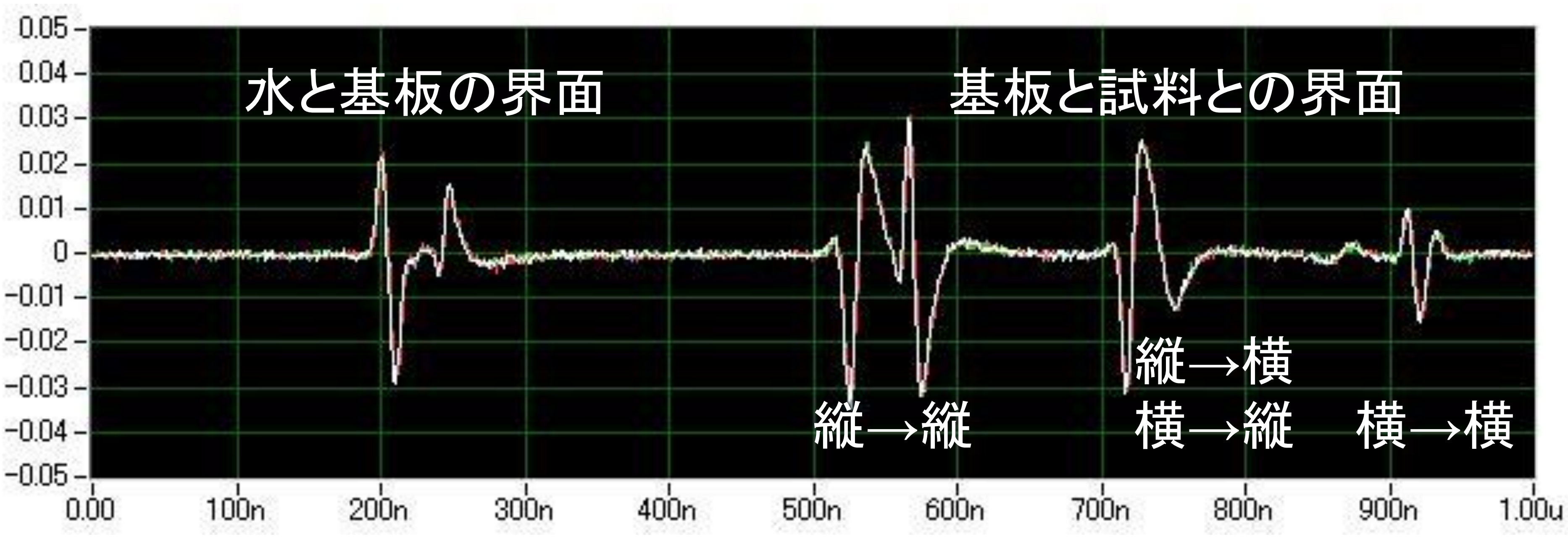
$$Z_s = \rho c_s$$

Z: 特性音響インピーダンス
c: 音速 *ρ*: 密度
p: 縦波(pressure wave)
s: 横波(shear wave)



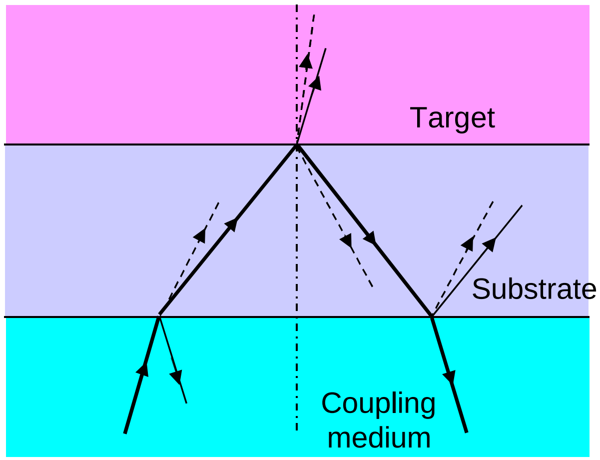
固体のみ

多くの反射波から横→横の反射を取出す。

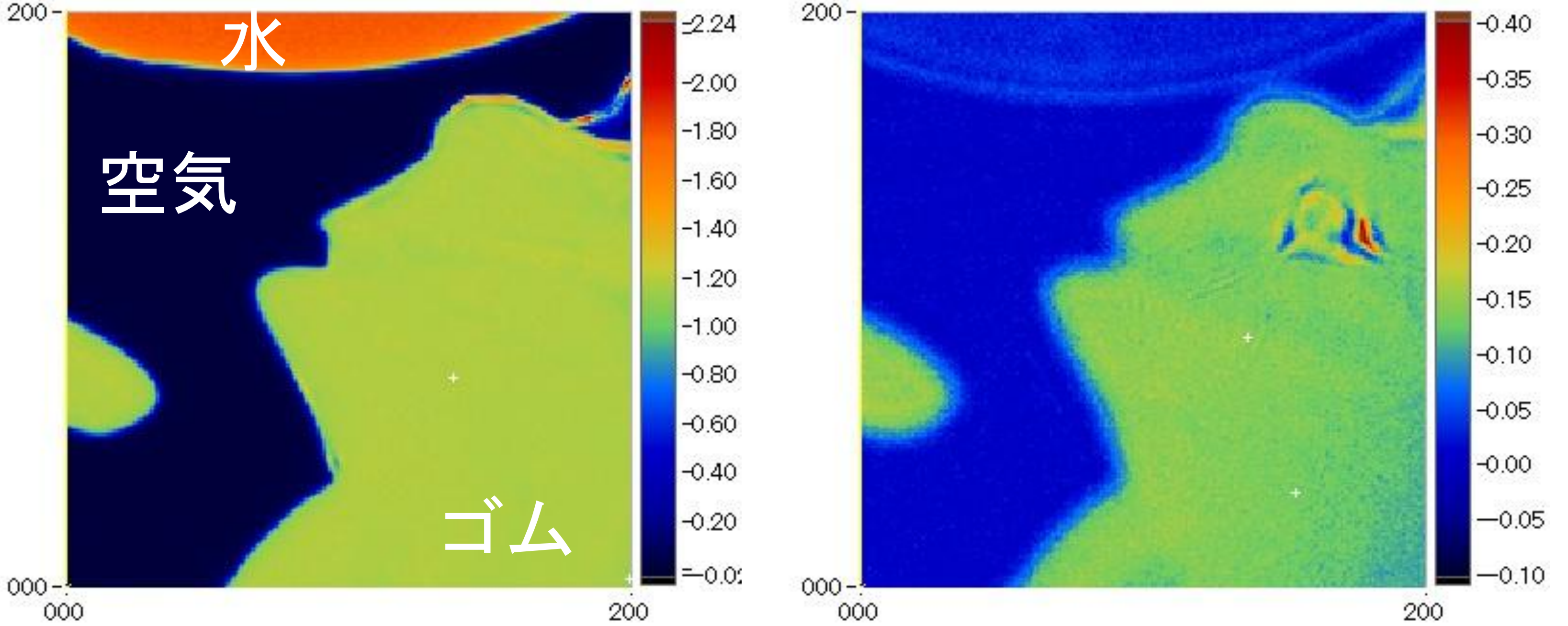


縦波入射→縦波反射と
横波入射→横波反射のモードが使える。

縦波入射→横波反射と
横波入射→縦波反射は集束しない。



空気とゴムと水を見た結果(音響インピーダンス)



縦波　横波

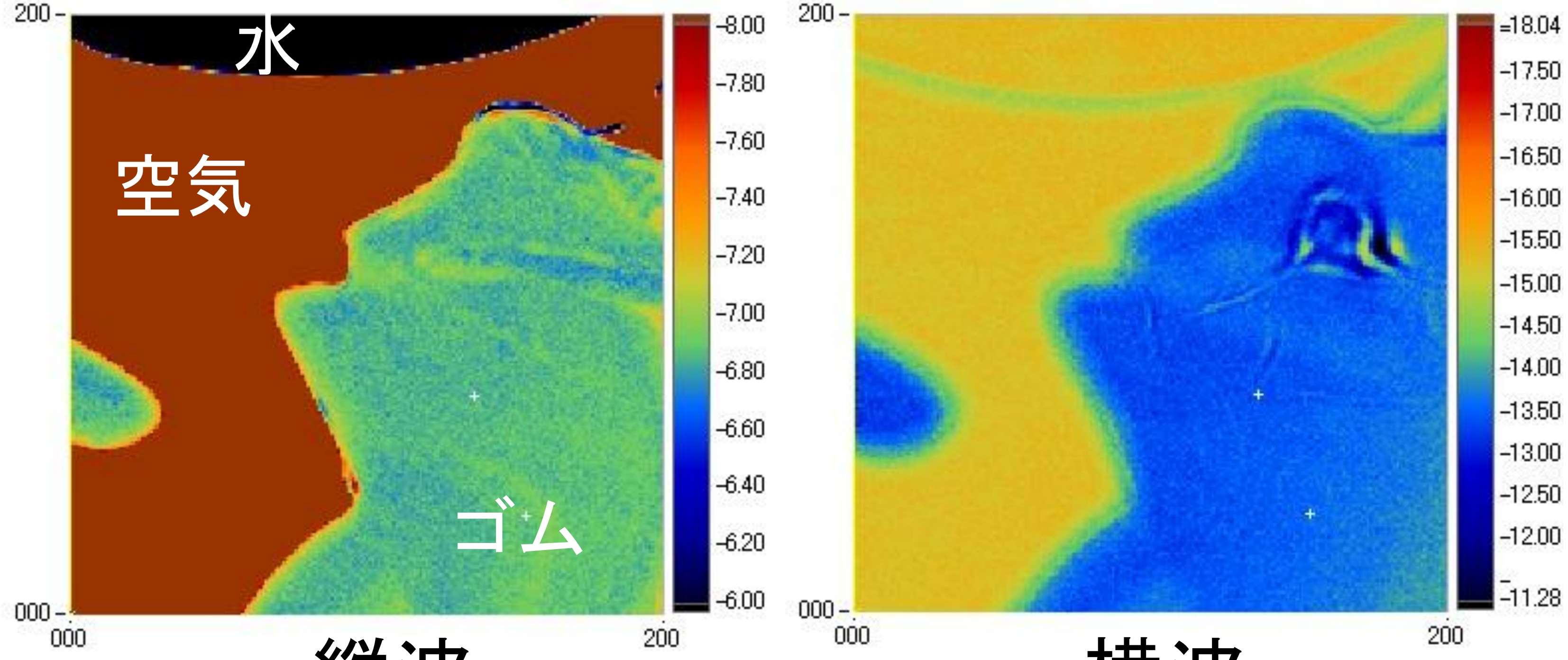
2 mm × 2 mm

音響インピーダンスと音速

縦波: 空気＜ゴム＜水　横波: 空気＝水＜ゴム

横波で見ると、ゴムが最も硬くて水と空気は同じ程度。

空気とゴムと水を見た結果(反射強度像)。



縦波　　横波

2 mm × 2 mm

反射強度

縦波: 空気＞ゴム＞水　横波: 空気＝水＞ゴム

音響インピーダンスと音速

縦波: 空気＜ゴム＜水　横波: 空気＝水＜ゴム

横波で見ると、ゴムが最も硬くて水と空気は同じ程度。

まとめ

- 超音波顕微鏡の2種類の振動子
  - 球面型
  - レンズ付
- フーリエ解析により音場を計算
- 音響インピーダンスに変換

Thank you for your attention.