

生醫訊號分析理論與實務研習營

Detection and Quantification of Early Hepatic Fibrosis from Ultrasonography

工業技術研究院
Industrial Technology
Research Institute

台大醫院
NTUH

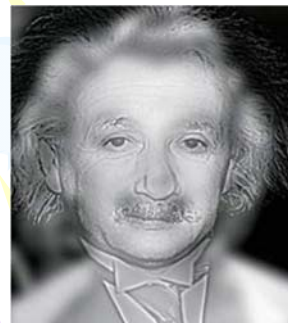


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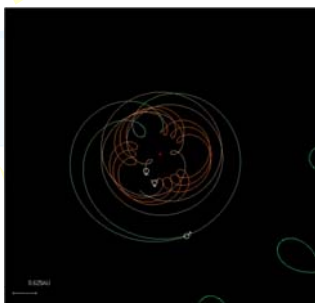
itri960484@itri.org.tw

因為觀點不同，結果就不同。

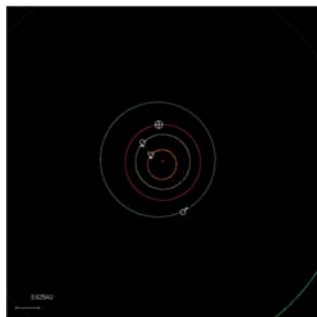
如果資料不付予物理意義，那僅是資料處理，不能稱為資料分析。



沒有那個錯誤，就不會有新的機會！



我們看到的天體運動



科學裡的天體運動

• 策略：

從頻率觀點分解(FFT)

從振幅觀點分解(HHT, PCA)

• 限制：

取樣的限制（取樣率、取樣時間、取樣間距）

基底的限制

物理的限制(非週期、非線性、非穩態)

硬體的限制（頻寬）



- 巴比倫數學家最早引入週期觀念來計算行星軌道 (BC3500)。



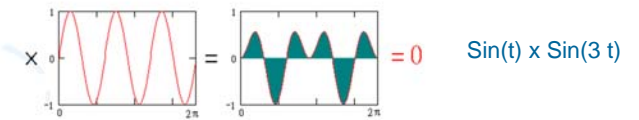
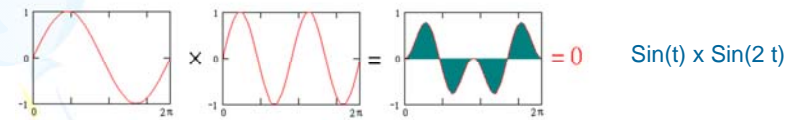
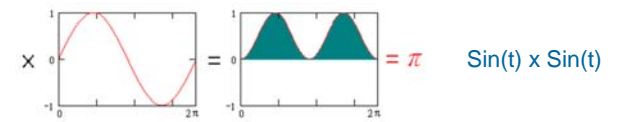
- 1754 Alexis Clairaut 運用離散傅立葉轉換分析行軌道。

- 1770 Lagrange 發展傅立葉分析的概念。

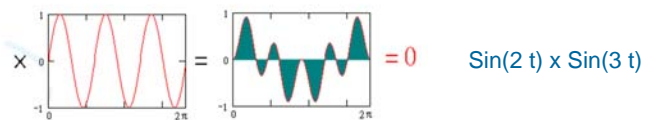
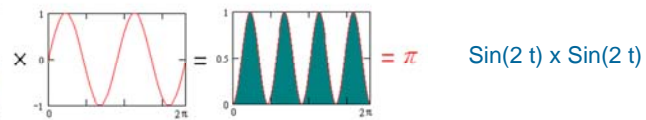
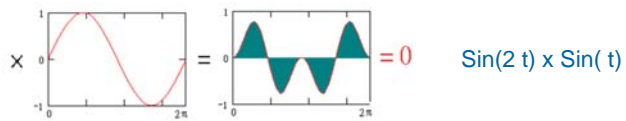
- 1807 Fourier 建立完整的傅立葉分析數學基礎。



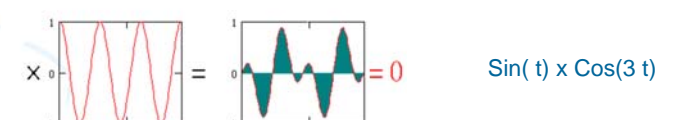
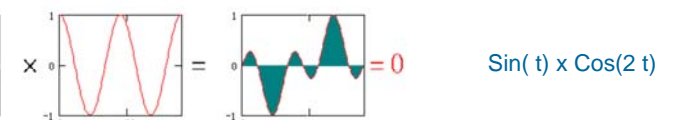
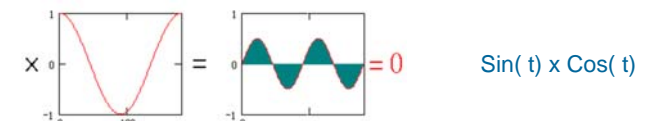
傅立葉轉換 – 正交性質 1



傅立葉轉換 – 正交性質 2



傅立葉轉換 – 正交性質 3



數學表示

$$F(\omega) = \frac{2}{T} \cdot \int_0^T [s(t) \cdot \cos(\omega \cdot t) - s(t) \cdot \sin(\omega \cdot t)] \cdot dt$$

$$= \frac{2}{T} \cdot \int_0^T s(t) \cdot e^{-i\omega \cdot t} dt = \frac{2}{T} \cdot \int_0^T s(t) \cdot e^{-i2\pi f \cdot t} dt$$

$$f(t) = \int_0^T [F(\omega) \cdot \cos(\omega \cdot t) + F(\omega) \cdot \sin(\omega \cdot t)] d\omega$$

$$= \int_0^T F(\omega) \cdot e^{i\omega \cdot t} d\omega$$

傅立葉轉換

$$f(t) = C_1 \cdot \sin(t) + C_2 \cdot \sin(2t) + C_3 \cdot \sin(3t) + \dots + D_1 \cdot \cos(t) + D_2 \cdot \cos(2t) + D_3 \cdot \cos(3t) + \dots$$

如何取得 C_1, C_2, C_3, \dots 與 D_1, D_2, D_3, \dots

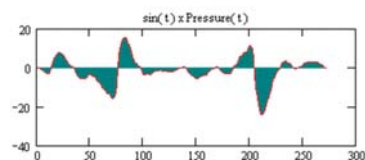
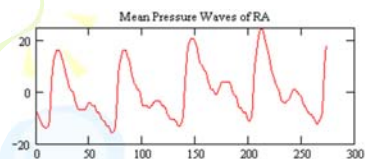
$f(t) \cdot \sin(t)$ 的面積 = $C_1 \cdot \pi$

$f(t) \cdot \sin(2t)$ 的面積 = $C_2 \cdot \pi$

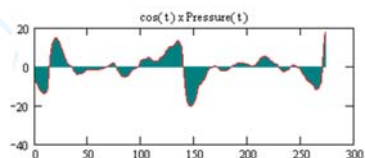
$f(t) \cdot \sin(3t)$ 的面積 = $C_3 \cdot \pi$

$f(t) \cdot \cos(t)$ 的面積 = $D_1 \cdot \pi$

範例 1

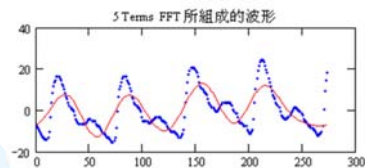


= -3.04 x π

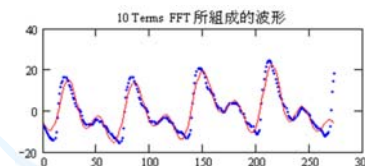


= -1.59 x π

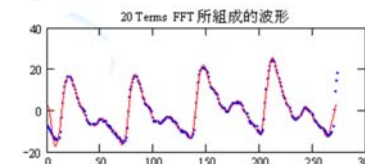
$$f(t) = C_1 \cdot \sin(t) + C_2 \cdot \sin(2t) + C_3 \cdot \sin(3t) + \dots + D_1 \cdot \cos(t) + D_2 \cdot \cos(2t) + D_3 \cdot \cos(3t) + \dots$$



5 個 sin 與 cos 所組成

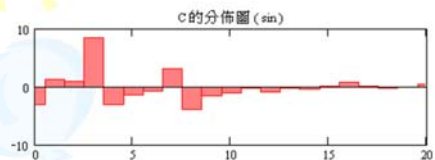


10 個 sin 與 cos 所組成

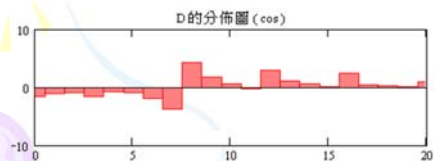


20 個 sin 與 cos 所組成

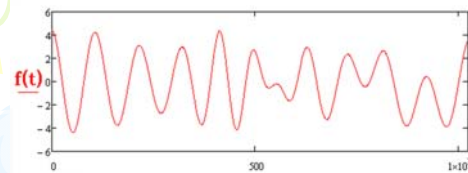
傅立葉分析 的物理意義



振盪 3~4 次的正弦波能量最多。
其次為振盪 7~8 次的正弦波與餘弦波。



範例 2

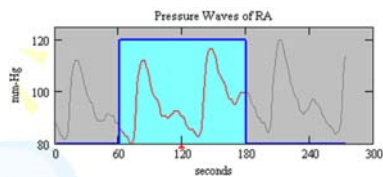


	0		0
0	0	0	-4.771
1	1.814	1	-5.14
2	5.422	2	-4.099
3	7.75	3	1.19
4	3.567	4	7.015
5	-3.995	5	4.713
6	-4.253	6	-3.234
7	-0.538	7	-1.155
8	-6.352	8	9.549
9	-6.126	9	9.502
10	11.121	10	42.001
11	4.227	11	0.915
12	-8.056	12	-1.808
13	11.116	13	6.036
14	-5.986	14	-4.587
15	...	15	...

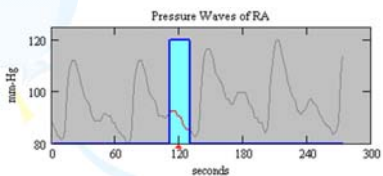
$$f(t) = 0 \cdot \sin(t) + 1.814 \cdot \sin(2t) + 5.422 \cdot \sin(3t) + \dots +$$

$$- 4.771 \cdot \cos(t) - 5.14 \cdot \cos(2t) - 4.099 \cdot \cos(3t) + \dots$$

加入窗戶 (window) 的傅立葉轉換



可獲得 120sec 時刻的頻譜(不過時間解析度很差)。

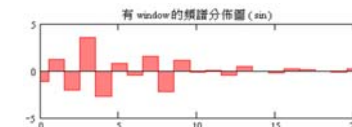
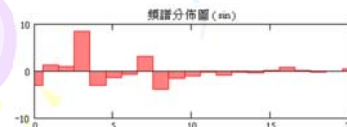
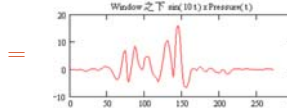
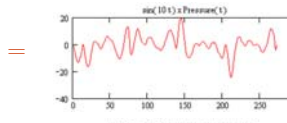
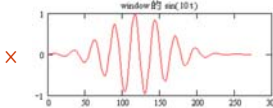
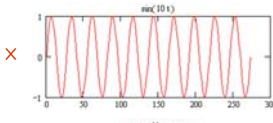
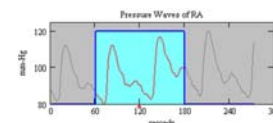


現在 120sec 時刻的時間解析度提高了(不過頻譜解析度卻很差)。

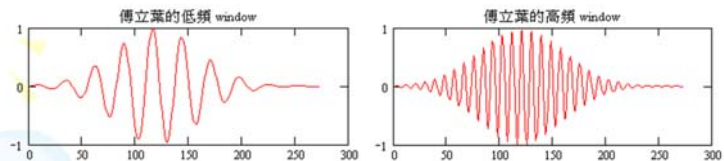
測不準原理！

通常window不會使用方波, 會使用 高斯分佈

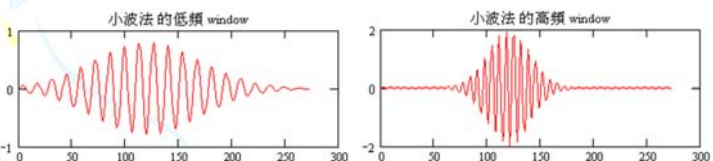
加入window 的傅立葉轉換



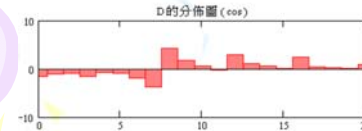
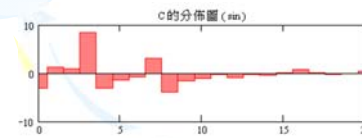
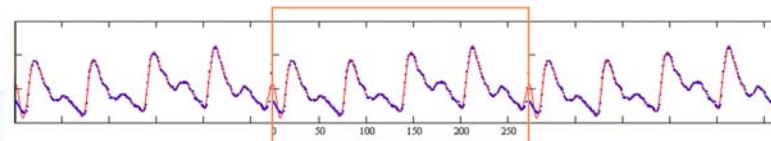
為什麼使用 小波變換？



傅立葉轉換使用的 window 都是相同的時間解析度



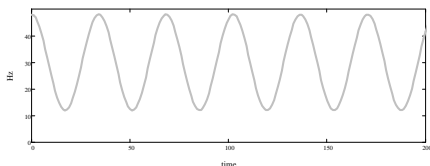
小波轉換使用的 window，在低頻擷取較佳的頻譜解析度，在高頻擷取較佳的時間解析度



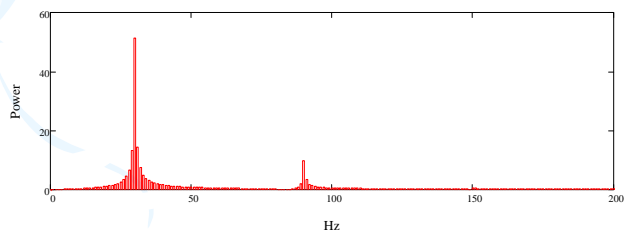
如果紅色區域的 FFT 頻譜要正確：

- (1) 我們必需假設分析的資料是具重複性的。
- (2) 資料必須等間距的。

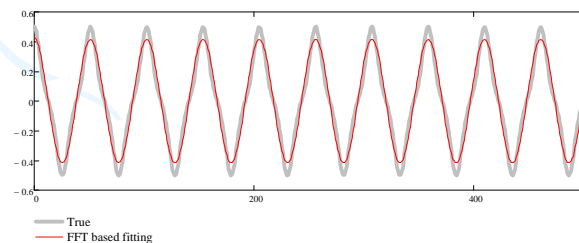
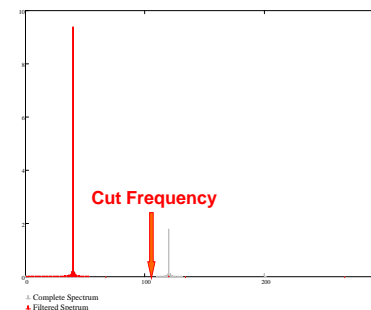
FFT對於頻率的誤解



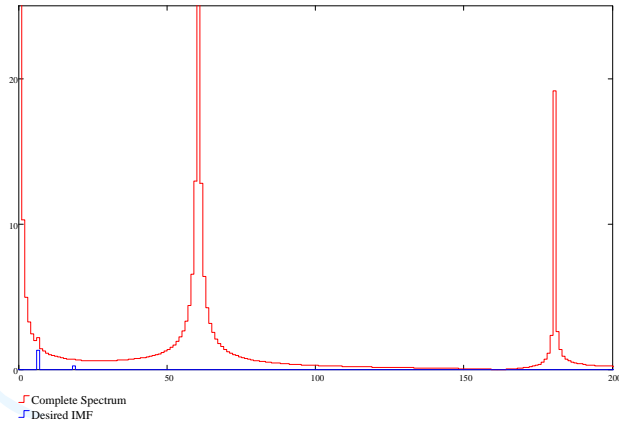
The **true frequency** of $y(t)$ altered from 12Hz to 48Hz with time.



In Fourier spectrum, you found 30Hz, 90Hz and 150Hz with few nearby tails. They are **mathematical solution** rather than **physical solution**.



HHT vs. FFT Filter



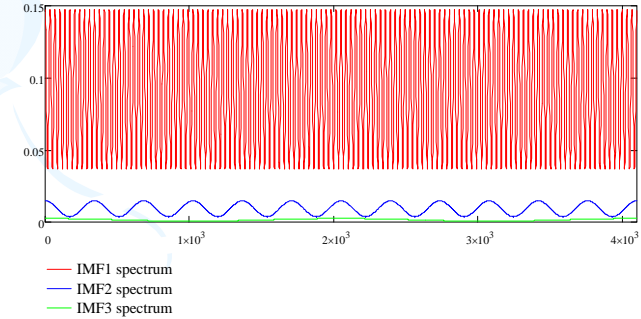
$$y(t) = 5.5 \cos[0.092t + 0.3 \sin(0.184t)] \cdot e^{-0.0002t} + 0.05 \cos[0.0092t + 0.3 \sin(0.0184t)] + 5 \sin(0.00015t - \pi/2)$$

$$= \text{IMF1} + \text{IMF2} + \text{IMF3}$$

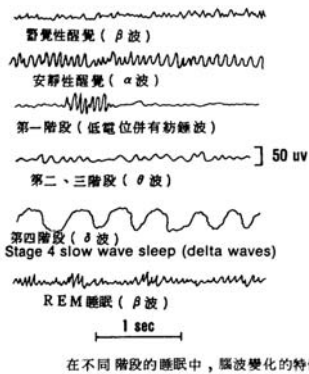
How to extract desired **IMF2(blue)** out of complete spectrum by Filter ?

It is almost impossible to extract the desired mode (blue) out of complete spectrum because of the **overlapped spectrum**.

Because the real spectrum of IMFs are actually **independent**, IMF2 is adaptively decomposed by EMD shown on the next page.



Real EEG signals



EEG 波的特性：

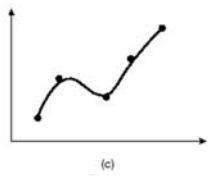
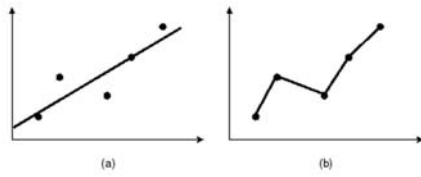
- (1) 間歇性、極微弱
有週期，但不連續
- (2) 非穩態
有週期，但不重複
- (3) 不一定有週期
沒有週期，但有意義
- (4) 瞬時頻譜
週期劇烈變化，但連續

α Wave	8-12 Hz	正常人清醒在安靜、休息的大腦活動狀態
β Wave	≥ 13 Hz	在睡眠之淺睡期，第一及第二期會增加
θ Wave	4-7 Hz	情緒壓力時，失望和挫折。在許多腦疾患者可記錄到。
δ Wave	≤ 3 Hz	深度睡眠、嬰兒和嚴重器官性腦疾病，不具節律性。

FFT 的其它詮釋方法

- Linear Curve Fitting
：線性代數 方法

Linear Curve Fitting



Real Data Point $x_i, y_i (i=1..n)$
 Model $\hat{y}_i = a \cdot x_i + b$
 Error $E^2 = \sum_{k=1}^n (y_k - \hat{y}_k)^2 = \sum_{k=1}^n (y_k - a \cdot x_k - b)^2$

The left unknowns are only a and b.
 How to determine a and b?

$$\frac{\partial E^2}{\partial a} = 0 \text{ ----- (1)}$$

$$\frac{\partial E^2}{\partial b} = 0 \text{ ----- (2)}$$

Real Data Points $t_i, y_i (i=1..n)$

$$\hat{y}(t_i) = C_1 \cdot \sin(t_i) + C_2 \cdot \sin(2t_i) + C_3 \cdot \sin(3t_i) + \dots + D_1 \cdot \cos(t_i) + D_2 \cdot \cos(2t_i) + D_3 \cdot \cos(3t_i) + \dots$$

$$E^2 = \sum_{k=1}^n [y_k - \hat{y}(t_k)]^2$$

$$\frac{\partial E^2}{\partial C_1} = 0 \quad \frac{\partial E^2}{\partial C_2} = 0 \quad \frac{\partial E^2}{\partial C_3} = 0 \quad \frac{\partial E^2}{\partial C_4} = 0 \dots\dots$$

$$\frac{\partial E^2}{\partial D_1} = 0 \quad \frac{\partial E^2}{\partial D_2} = 0 \quad \frac{\partial E^2}{\partial D_3} = 0 \quad \frac{\partial E^2}{\partial D_4} = 0 \dots\dots$$

FFT 的基礎架構可以看成一種線性回歸計算的 近似。

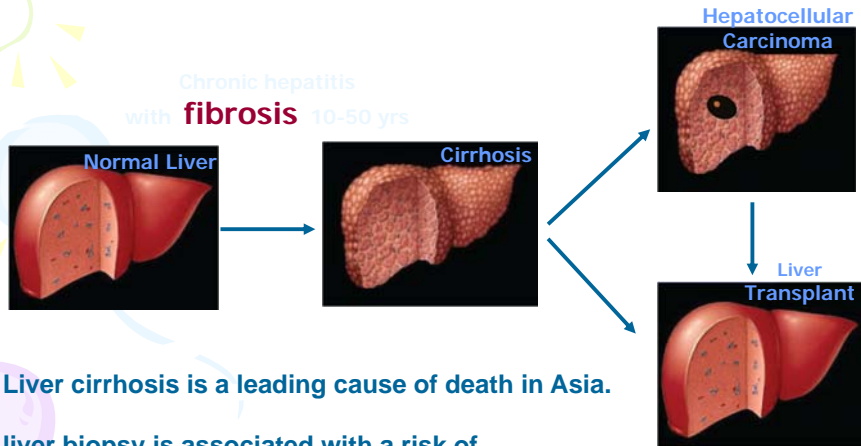
Conclusion

- 資料的前世今生 → FFT → 相信嗎？
- FFT 可以多維度計算？

Medical Application

Needs

- Natural History of Chronic Liver Disease



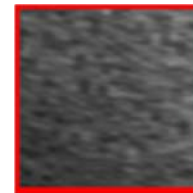
Liver cirrhosis is a leading cause of death in Asia.

liver biopsy is associated with a risk of complications, patient discomfort and high cost.

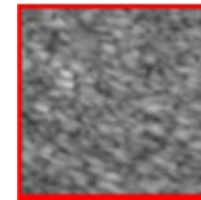
Texture Analysis

- Texture Coarseness Quantification

Normal liver



Cirrhotic liver



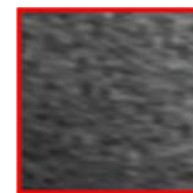
Cirrhotic Liver creates more heterogeneous texture in ultrasound imaging.

Empirically, our naked eye can differentiate them, however, we need more objective quantification.

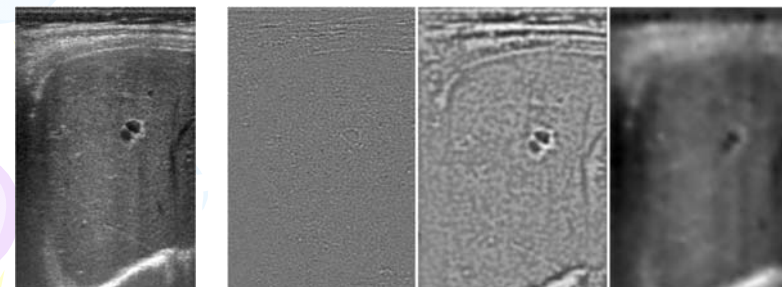
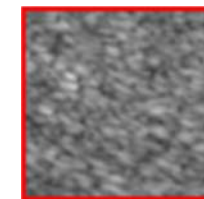
What kind of spatial scale we are interested in ?

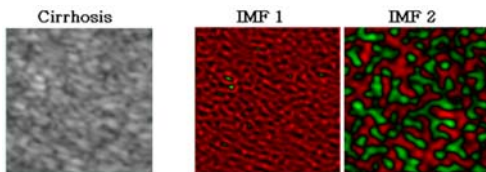
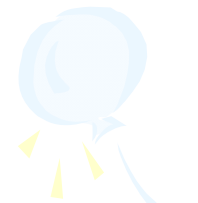
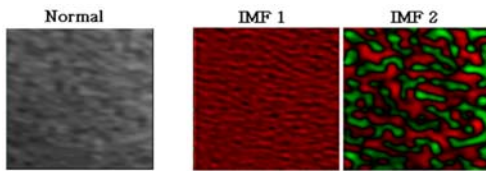


Normal liver



Cirrhotic liver

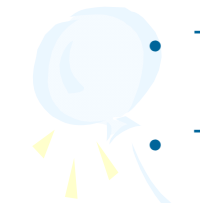




Cirrhosis Liver contains more contrast in fine structure and more fragile in coarse structure.



Why not FFT and Wavelet ?



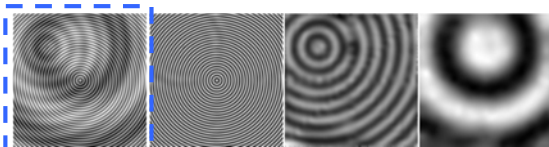
- They are prior bases based.
- They are not truly 2D analyzer.
- They are not adaptive.



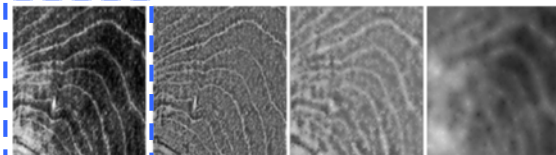
What is EMD ?

- **Bi-dimension Empirical Mode Decomposition**

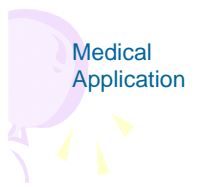
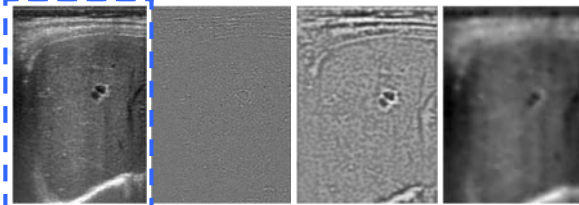
Artificial Testing



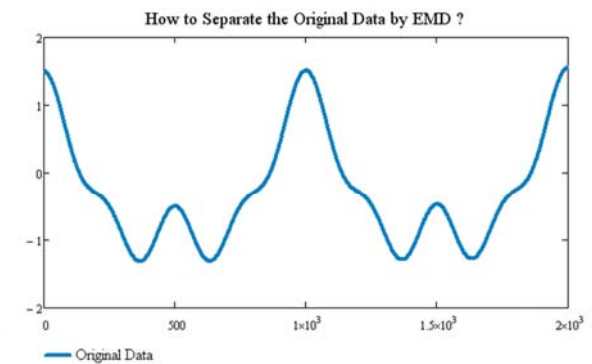
Real Testing



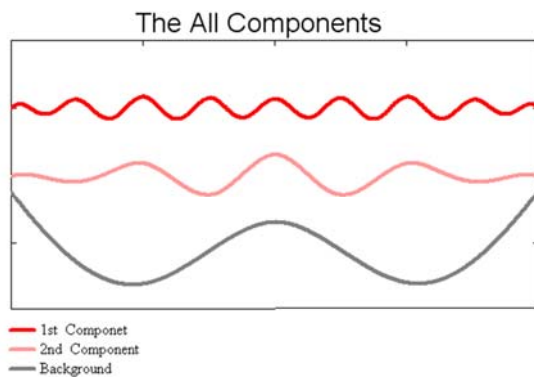
Medical Application



How to Process EMD ?

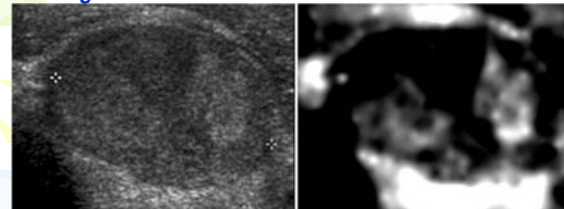


How to Find the 2nd Component ?

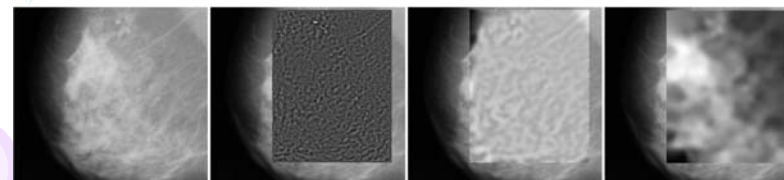


Tumor Calcification

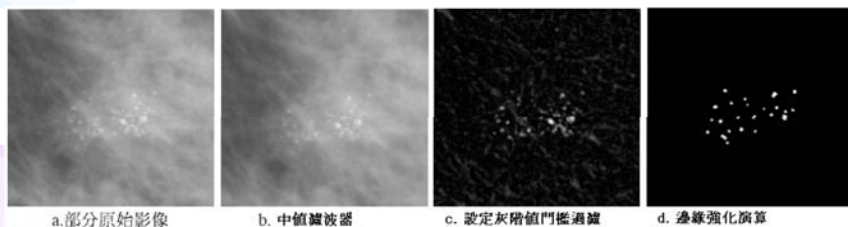
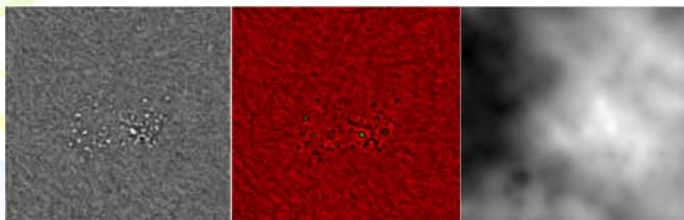
Heterogeneous Tissue with microcalcification



X-Ray Calcification of Breast Cancer



Detailed Comparison

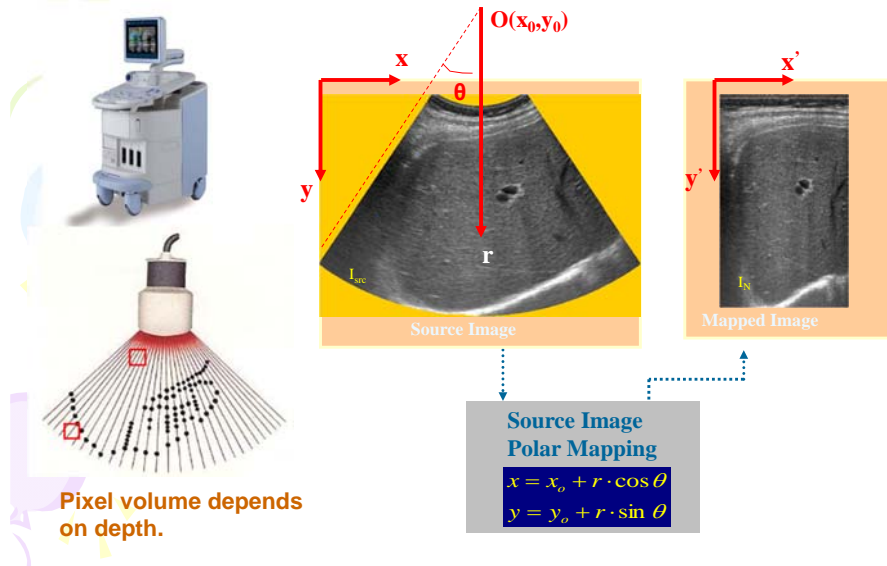


Clinical Database

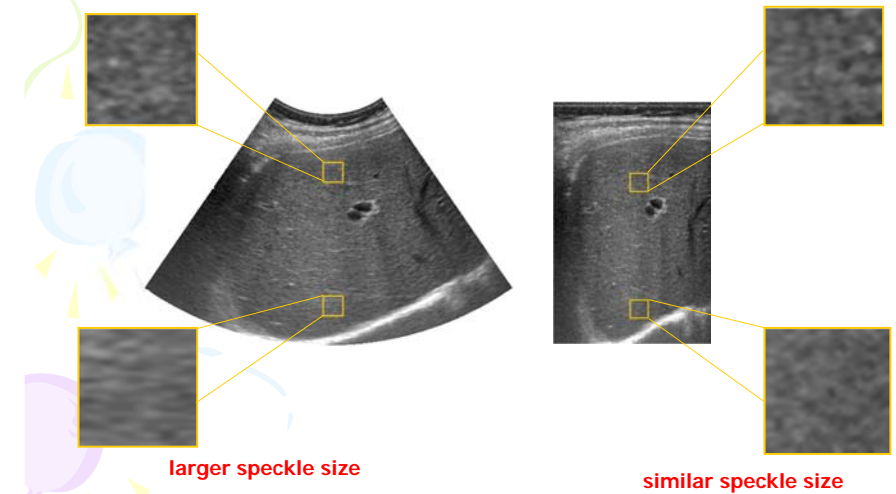
- Patients with chronic liver disease (n = 63)
 - Age : 49 ± 11 yrs
 - Males: 42 (67%)
 - Diagnosis
 - chronic hepatitis B: 30 (48%)
 - chronic hepatitis C: 30 (48%)
 - chronic hepatitis B+C: 3 (4%)
 - Metavir Score
 - F0: 7 (11%)
 - F1: 22 (35%)
 - F2: 17 (27%)
 - F3 + F4: 18 (27%)



Spatial Resolution Alignment



Spatial Resolution Alignment

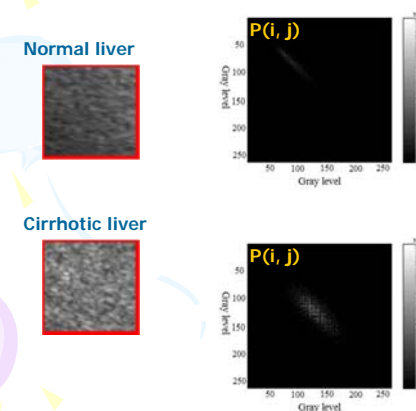


Other System Setting

- Scanning Frequency(3.5MHz)
High Frequency enhance resolution
- Scanning Depth(10cm)
Deeper scanning decrease resolution
- Time Gain Control (TGC)
TGC create incomparable echo
- Without Persistence
Persistence makes speckle more smooth
- Frame Rate (15 fps)
Fast fps decrease the resolution

Texture Analysis after EMD

- Texture Coarseness Quantification



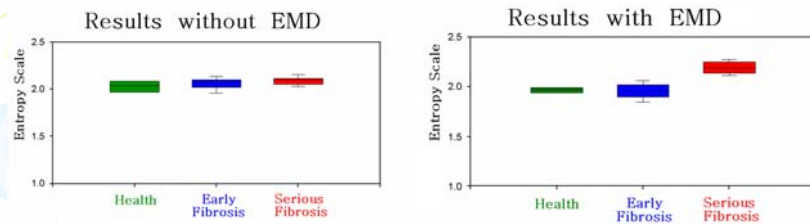
$$Entropy = \sum_k P_{sum}(k) \cdot \log[P_{sum}(k)]$$

where:

$$P_{sum}(k) = \sum_i \sum_j P(i, j) \text{ with } i + j = k$$

Heterogeneous texture has greater entropy

Results



Health and Early Fibrosis are not easily distinguished.

(Serious Fibrosis) is significantly different from (Early Fibrosis), $df=63$, $P < 10^{-10}$ (too small)

Conclusion

Acting only before careful consideration:

- Spatial resolution should be well controlled. Probe frequency, Frame rate, TGC, Scanned Depth
- Suitable separation is a better tool than contrast or Gamma correction in imaging analysis.

Thank You for
Your Attention