Introduction to

Physiological Variability

Dr. G. D. Jindal
Prof & Head, Bio-Medical Engineering,
MGM College of Engineering & Technology
Navi Mumbai.
Ex. Head, Bio-Medical Instru. Section, BARC
PhD Guide, University of Mumbai.
gd.jindal@gmail.com

What is Variability?

Unused faculty leads to malfunction…

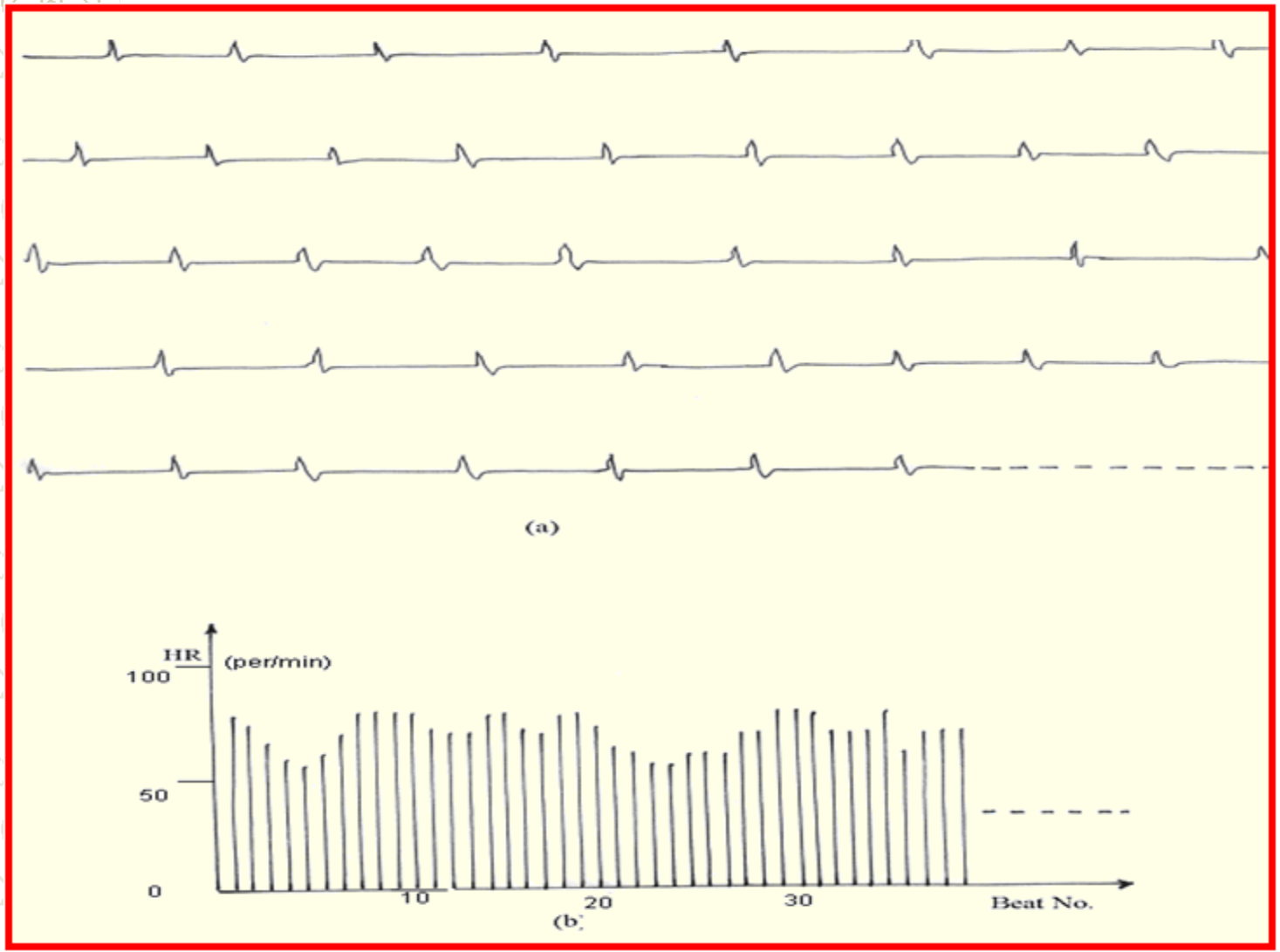
1. Machinery
2. Man Made Material
3. Professionals
4. Tools/Appliances
5. Unused house
6. Vaccination
7. Vehicle
8. Weapons

Physiological Parameter

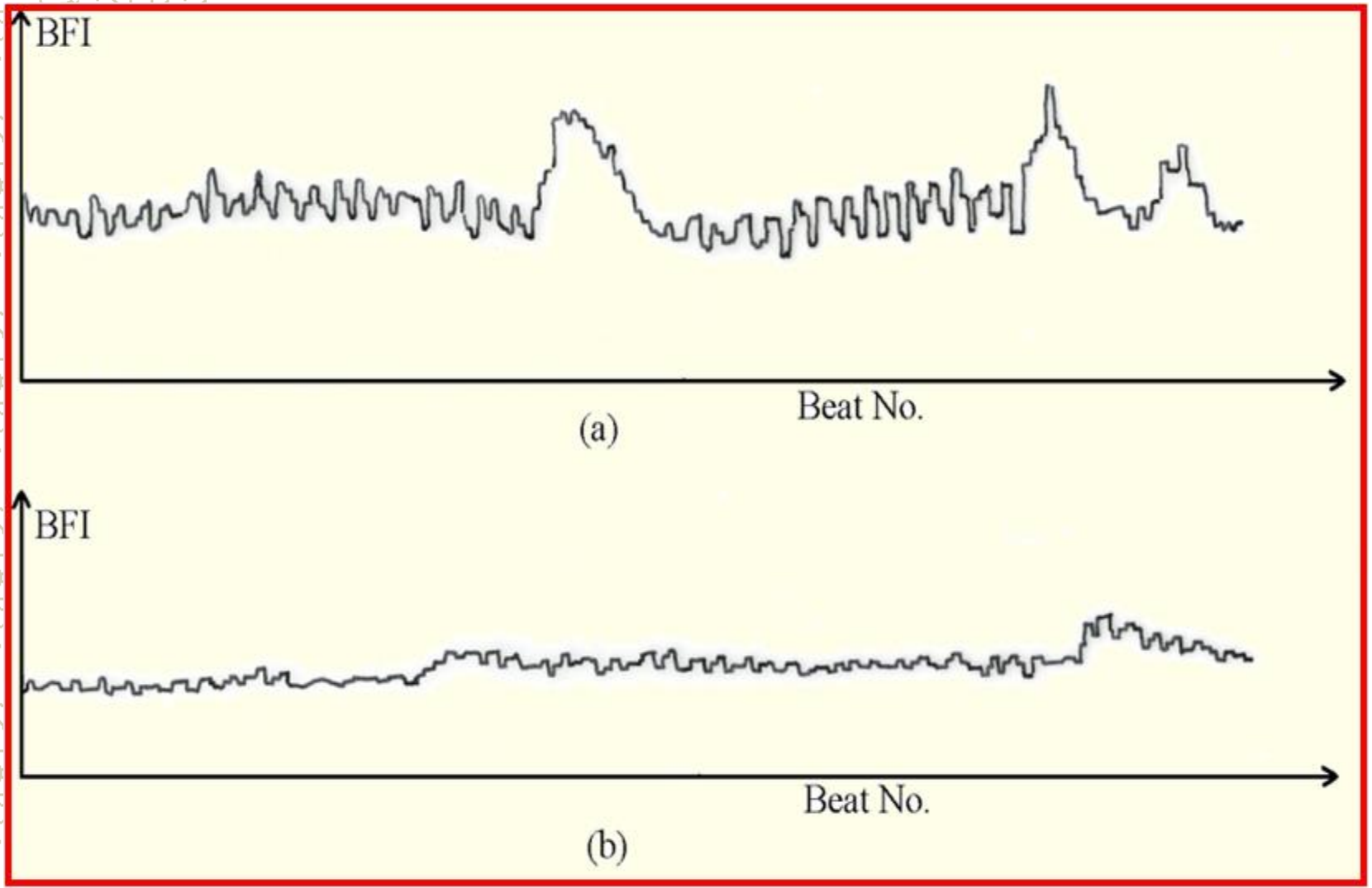
1. Functioning of the living body is better described with the help of physiological parameters.
2. These parameters can be measured either non-invasively or by invasive means.
3. Some of the most common examples are Heart Rate, Body Temperature, Blood Pressure and Respiration Rate.
4. Other physiological parameters are stroke output, peripheral blood flow, peristalsis, secretion of endocrinal and salivary glands, glycogen-glucose conversion, motility of large and small intestines, secretion of urine and so on.
5. Some of these like heart rate, respiration rate and blood pressure can be easily measured for long time interval without causing any harm or discomfort to the patient.

Indian Medical System took cognizance…

Variability in Physiological Parameter



Variations in Blood Flow



Time Domain Analysis

$$\mu = \left(\frac{1}{N}\right)\sum_{i=1}^{i=N} RR_i$$

$$SDNN = \sqrt{\left(\frac{1}{N}\right)\sum_{i=1}^{i=N} (RR_i - \mu)^2}$$

$$\text{Total Power} = \text{Variance} = \left(\frac{1}{N}\right)\sum_{i=1}^{i=N} (RR_i - \mu)^2$$

$$Total\ Power = \frac{Variance}{\mu} = \frac{\sigma^2}{\mu}$$

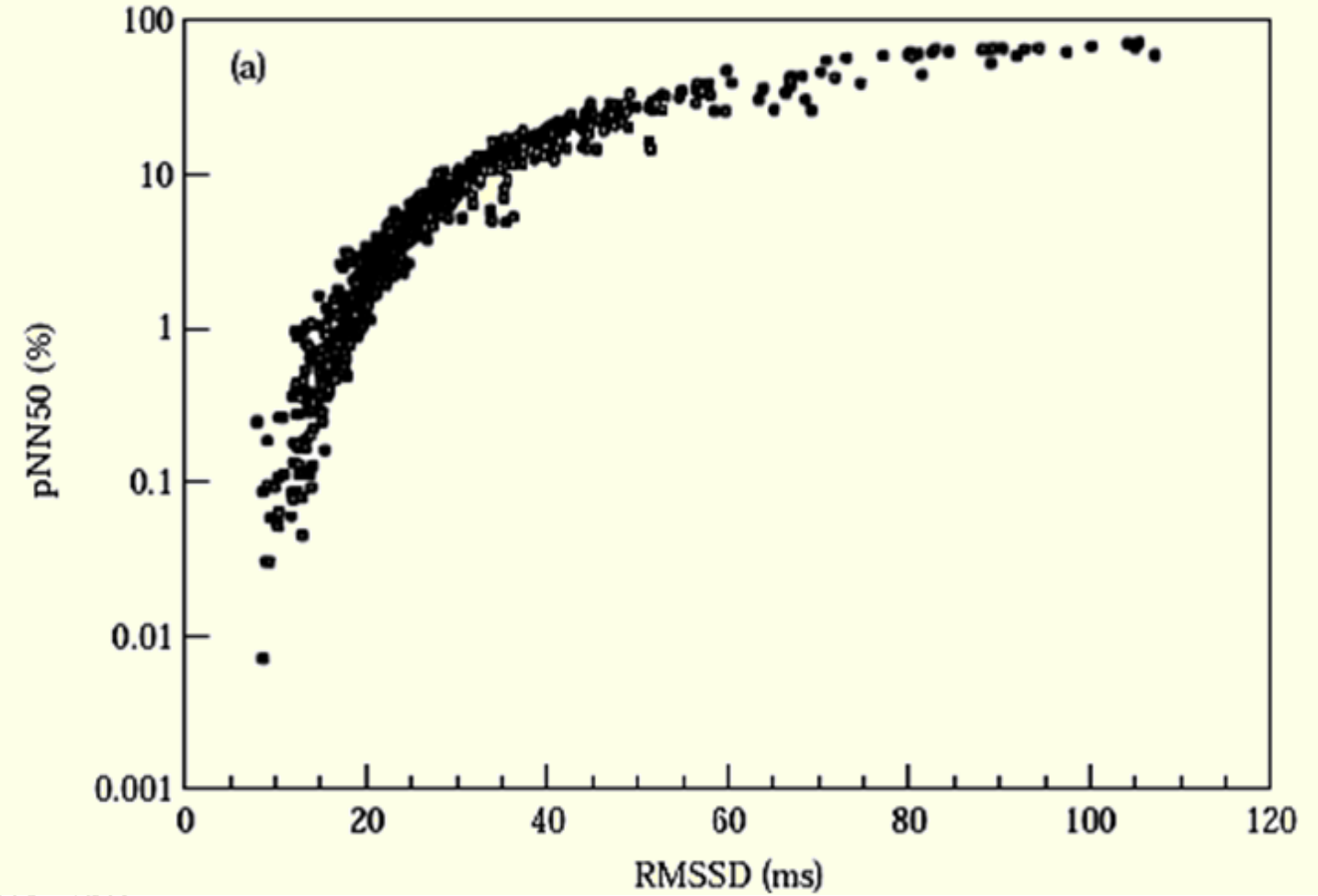
Time Domain Analysis

$$\mathrm{SDANN} = \sqrt{\left(\frac{1}{N}\right)\sum_{j=1}^{j=N}(RR^{j} - \mu)^{2}}$$

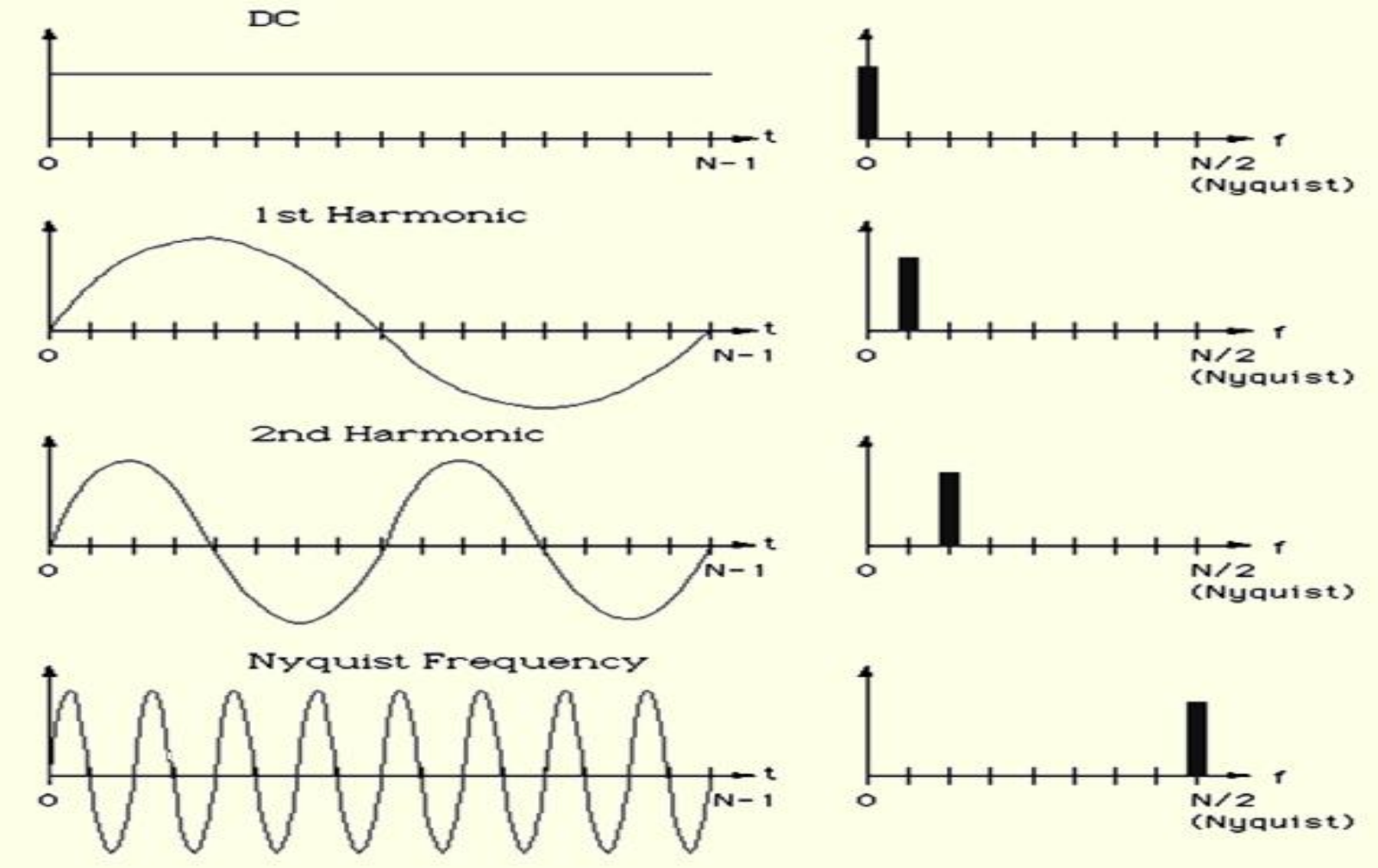
$$SDNN\ Index = \left(\frac{1}{N}\right)\sum_{j=1}^{j=N}\mathrm{SDNN}^{j}$$

$$\mathrm{RMSSD} = \sqrt{\left(\frac{1}{N}\right)\sum_{i=1}^{i=N}(RR_{i+1} - RR_{i})^{2}}$$

Time Domain Analysis



Frequency Domain Analysis

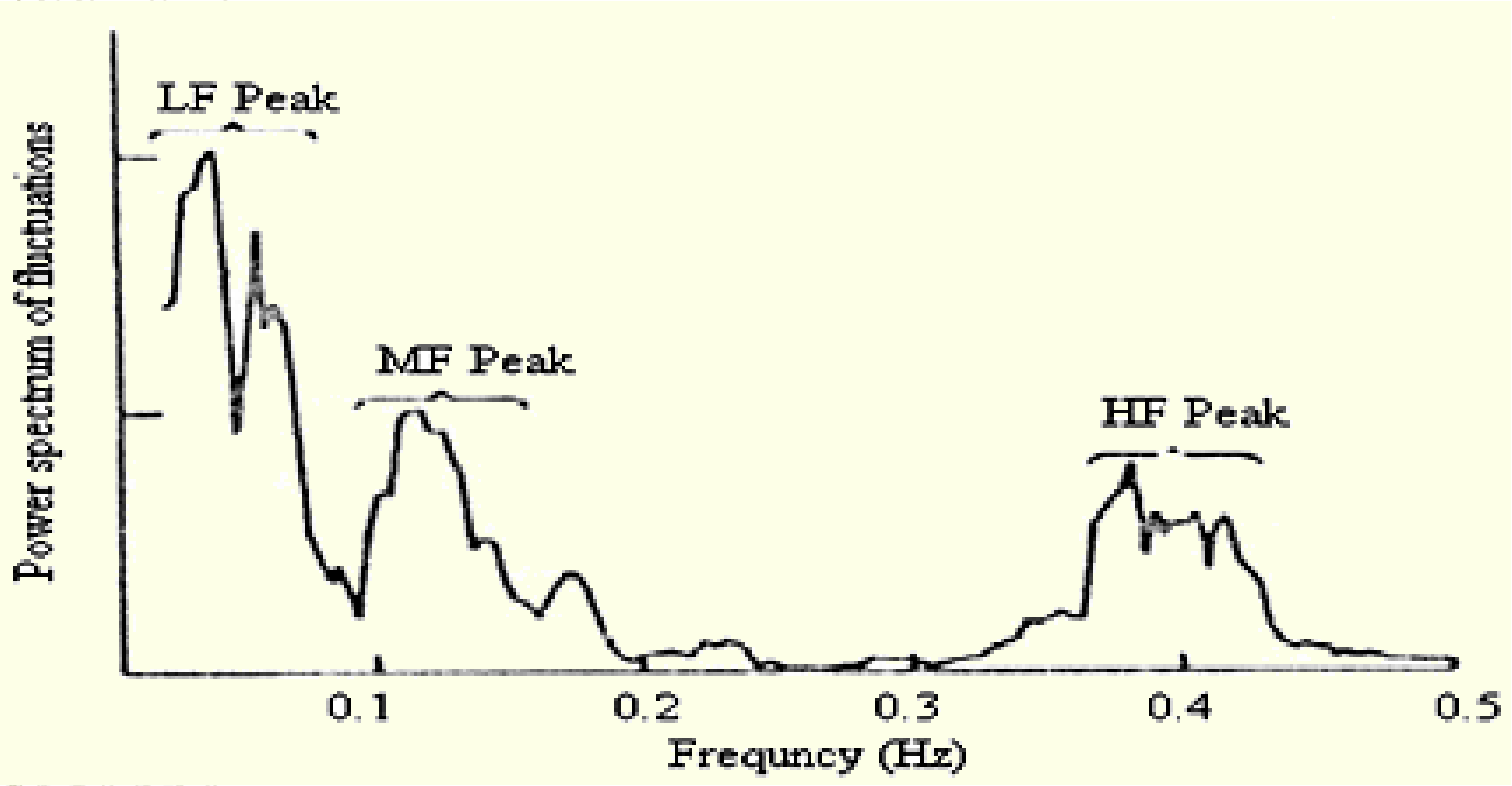


Frequency Domain Analysis

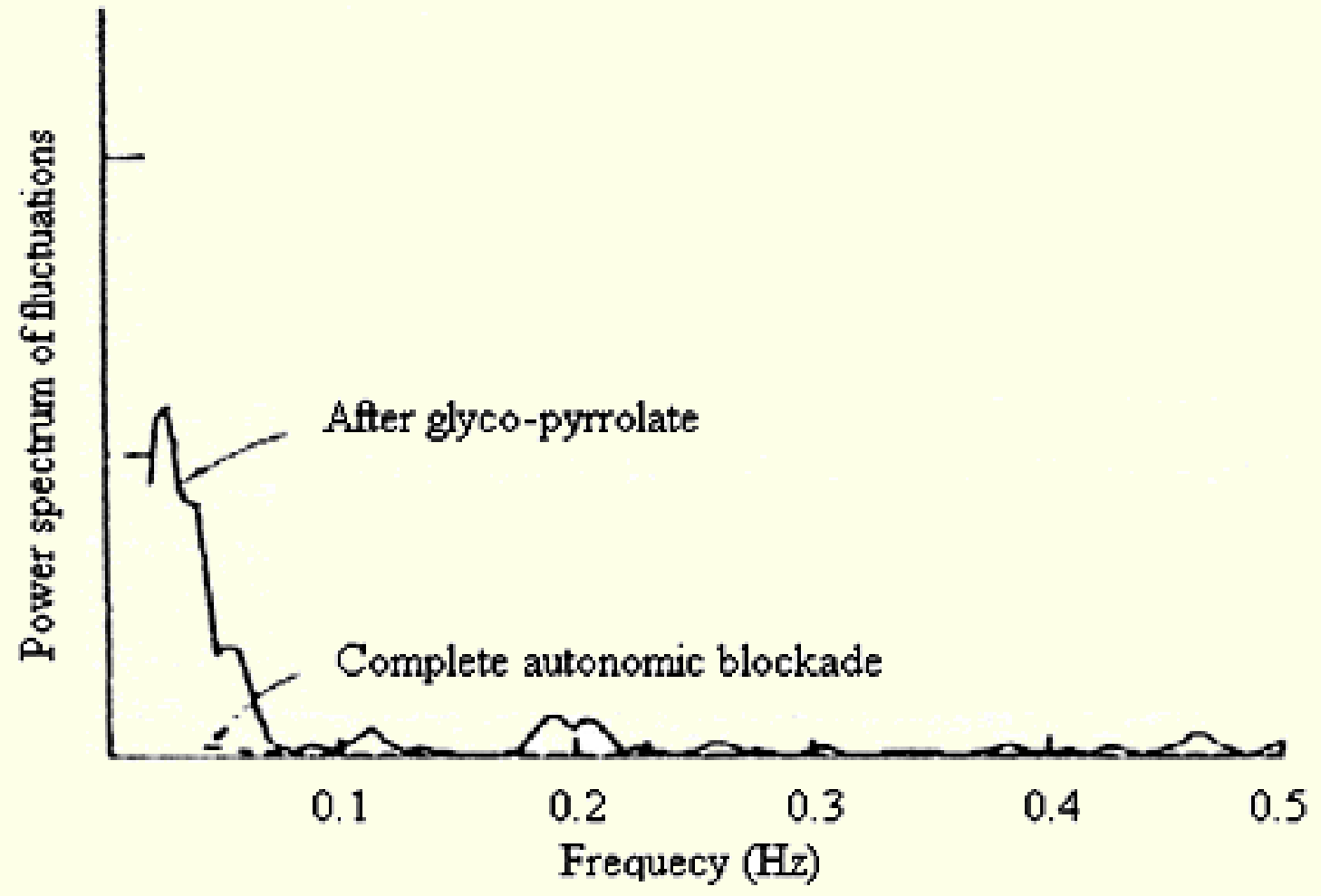
$$X_k = \sum_{n=0}^{N-1} x_n e^{-\frac{2\pi i}{N} kn} \qquad k = 0, \ldots, N-1$$

$$x_n = \frac{1}{N} \sum_{k=0}^{N-1} X_k e^{\frac{2\pi i}{N} kn} \qquad n = 0, \ldots, N-1$$

Frequency Domain Analysis



Frequency Domain Analysis



Fast Fourier Transform

For N=8 and W= $e^{(-i2\pi/N)}$ the equations are written as

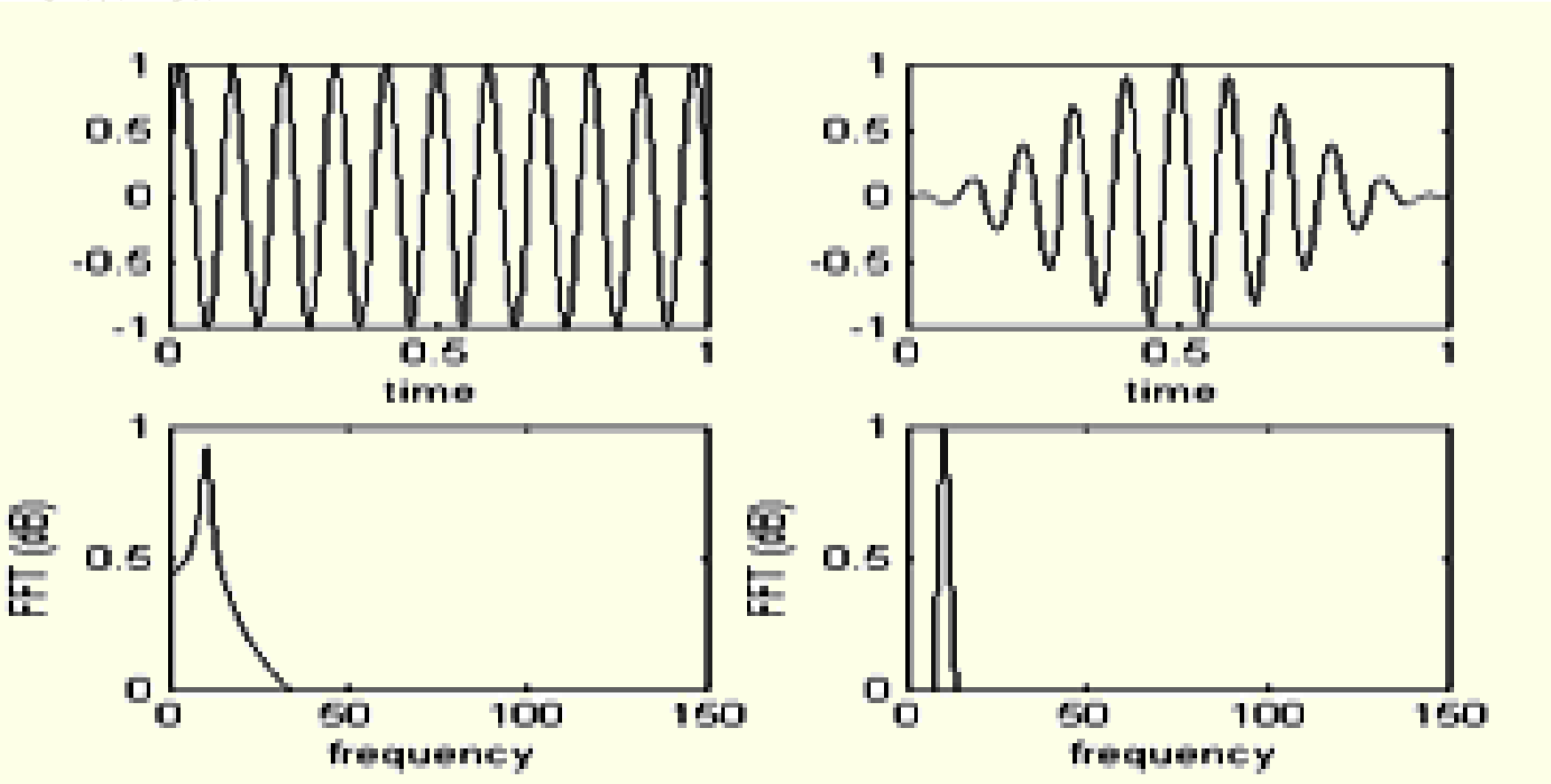
$$X_0=x_0W^0+x_1W^0+x_2W^0+-------+x_7W^0$$
$$X_1=x_0W^0+x_1W^1+x_2W^2+-------+x_7W^7$$
$$X_2=x_0W^0+x_1W^2+x_2W^4+-------+x_7W^{14}$$
$$-$$
$$-$$
$$-$$
$$X_7=x_0W^0+x_1W^7+x_2W^{14}+-------+x_7W^{49}$$

Since $W^{(N+i)} = W^i$ due to periodic properties of W, The Equation can be rewritten as

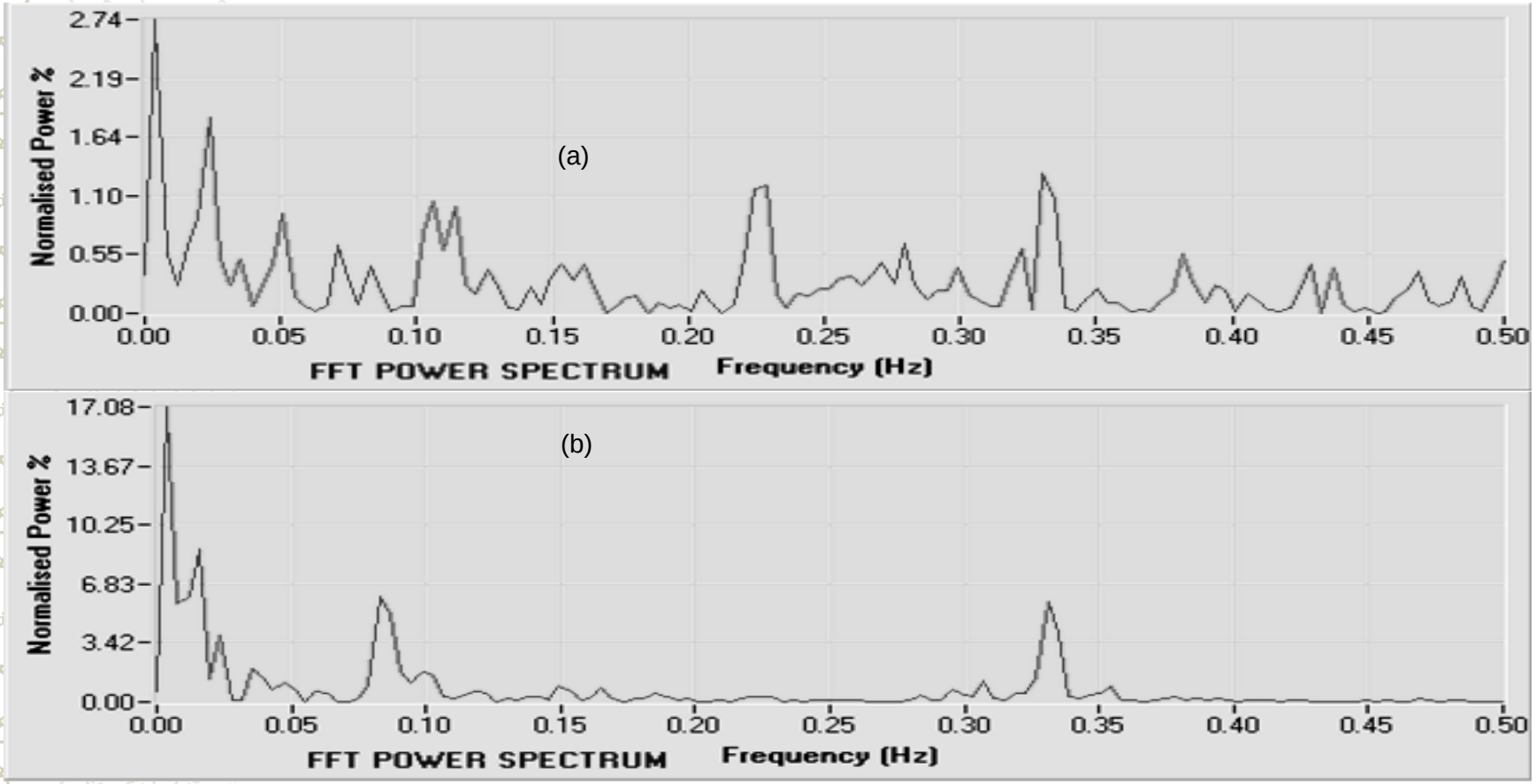
$$X_7=x_0W^0+x_1W^7+x_2W^6+-------+x_7W^1$$

There by reducing the number of computations. In a sample size of N, the computations needed for DFT are N^2 whereas that for FFT is $N*\log_2 N$.

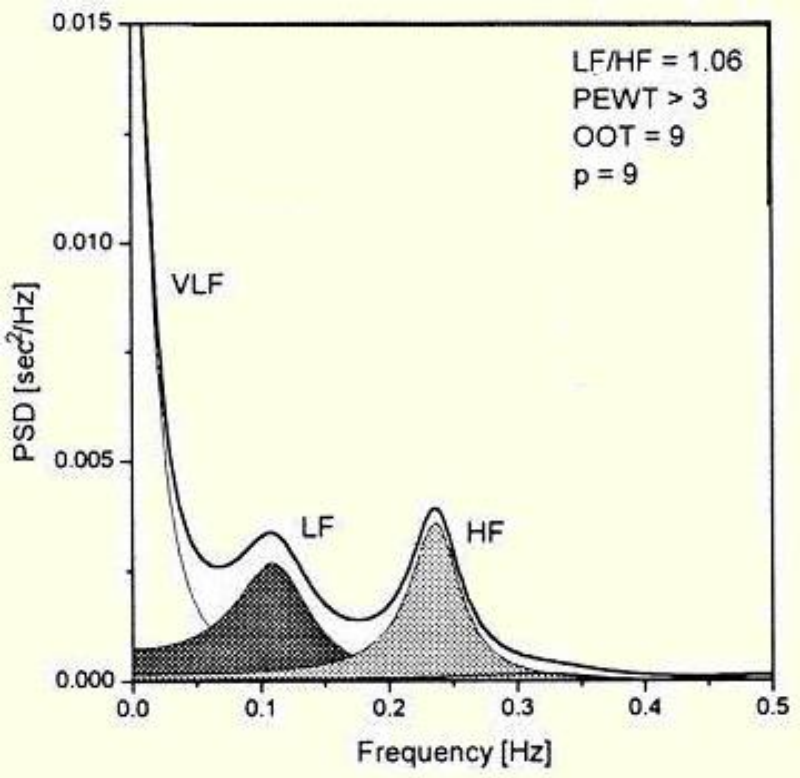
Spectral Leakage

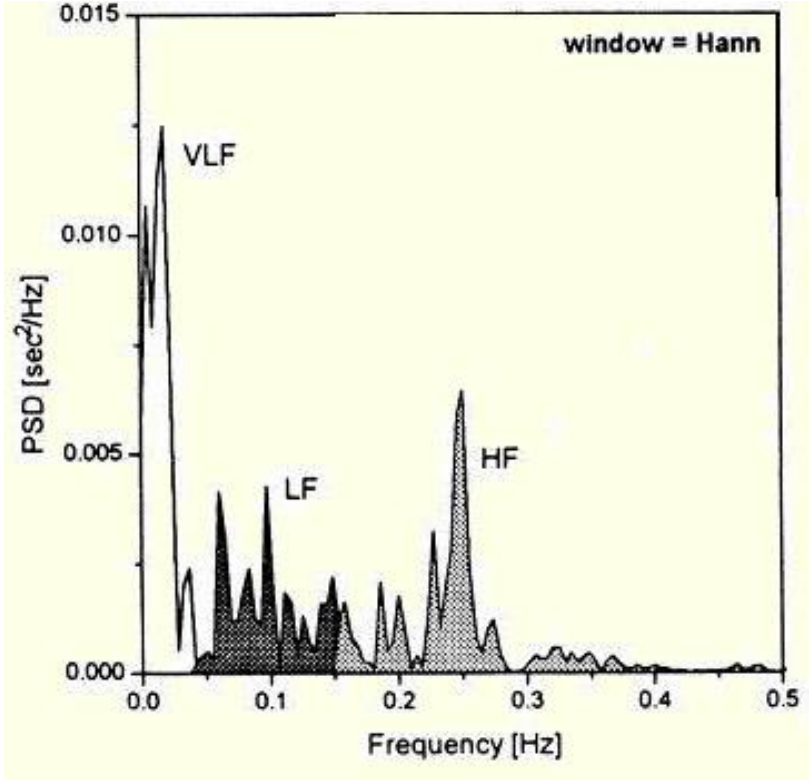


Interpolation



Power Spectral Density



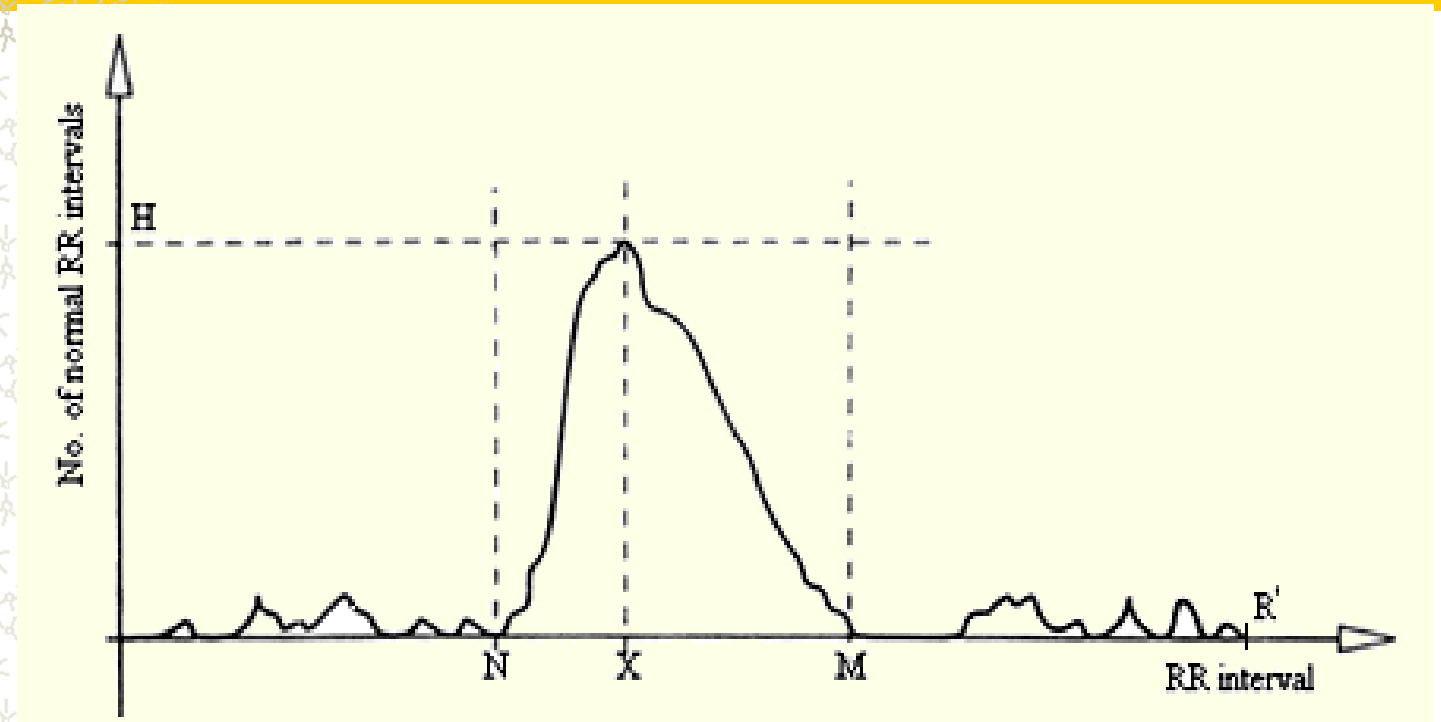


Power Spectral Density

Variable	*Unit*	*Frequency Range*	*Description*
Total Power	ms^2	< 0.4 Hz	The variance of RR intervals over the selected time interval
VLF Power	ms^2	≤ 0.04 Hz	Power of very low frequency component
LF Power	ms^2	0.04–0.15 Hz	Power of low frequency component
HF Power	ms^2	0.15 – 0.4 Hz	Power of high frequency component

Method ➔ Region ➓	**AR Modeling**			**FFT**	
	Frequency (Hz)	***Power ($msec^2$)***	***Power (n.u.)***	***Frequency (Hz)***	***Power ($msec^2$)***
VLF	0.00	786	-	0.00	266
LF	0.11	479	47.95	0.10	164
HF	0.24	450	45.05	0.25	214

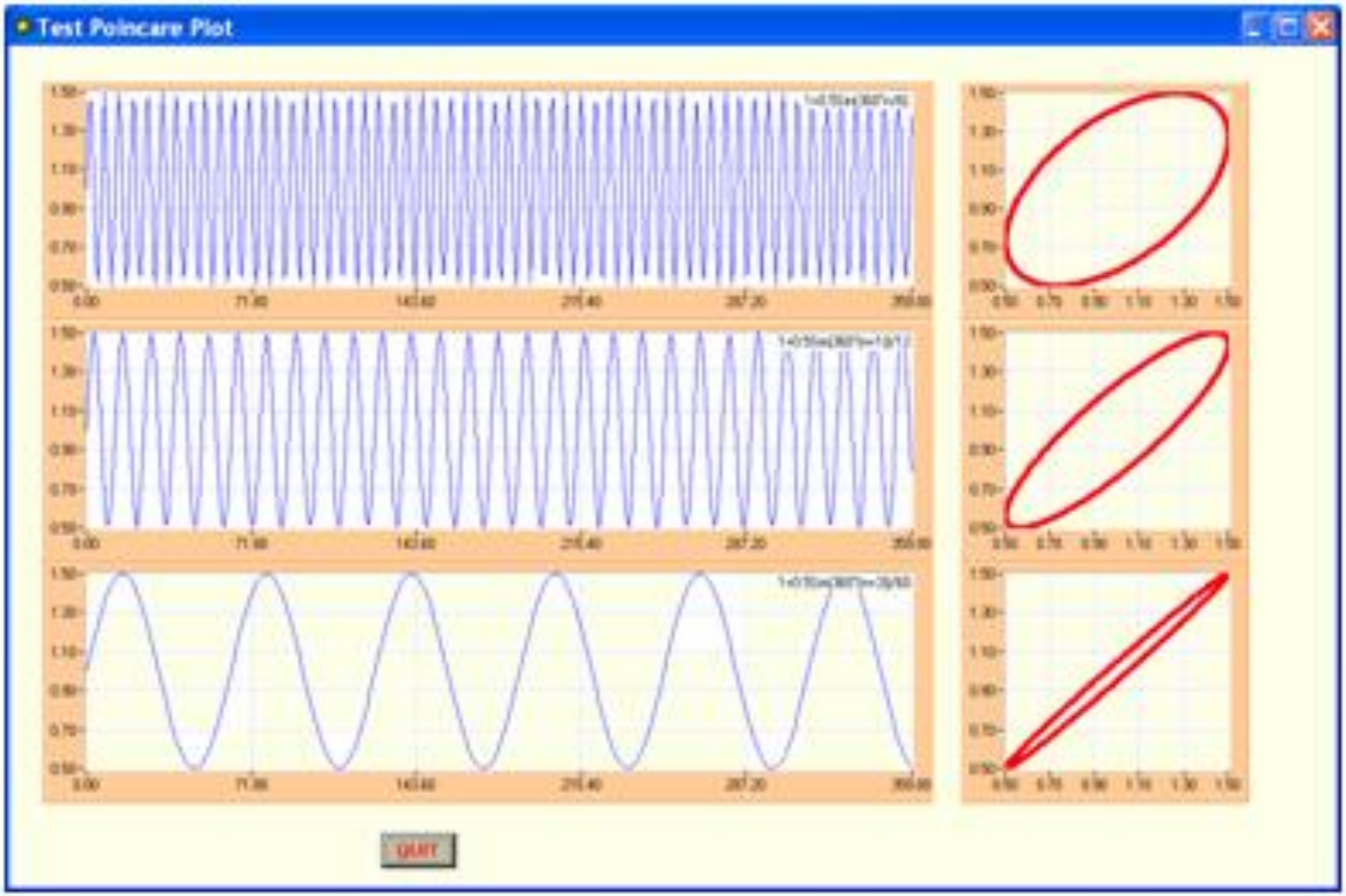
Geometric Method



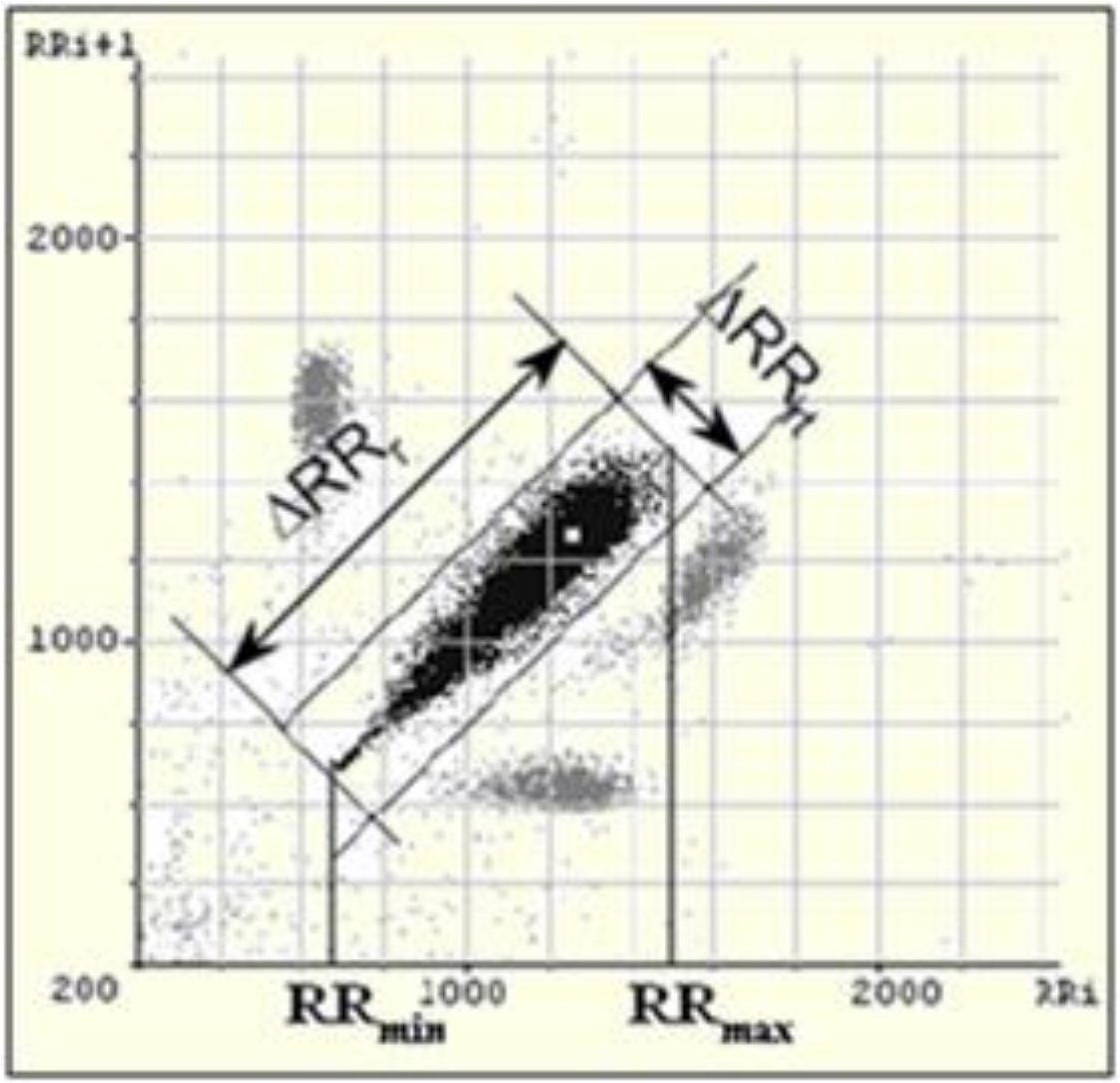
TINN = M – N

$$HTI = \frac{\text{No. of RR Intervals}}{H}$$

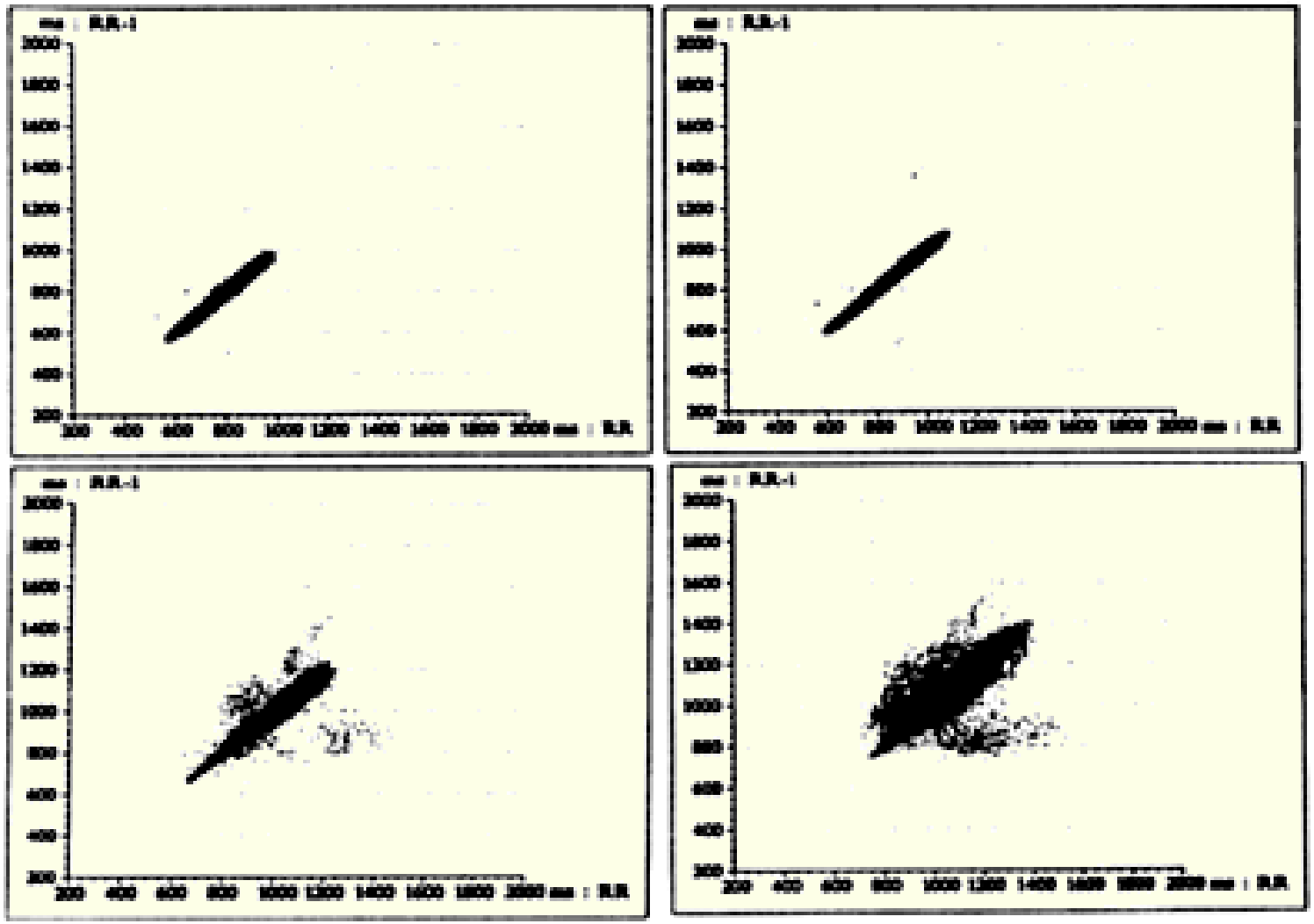
Poincare Plot



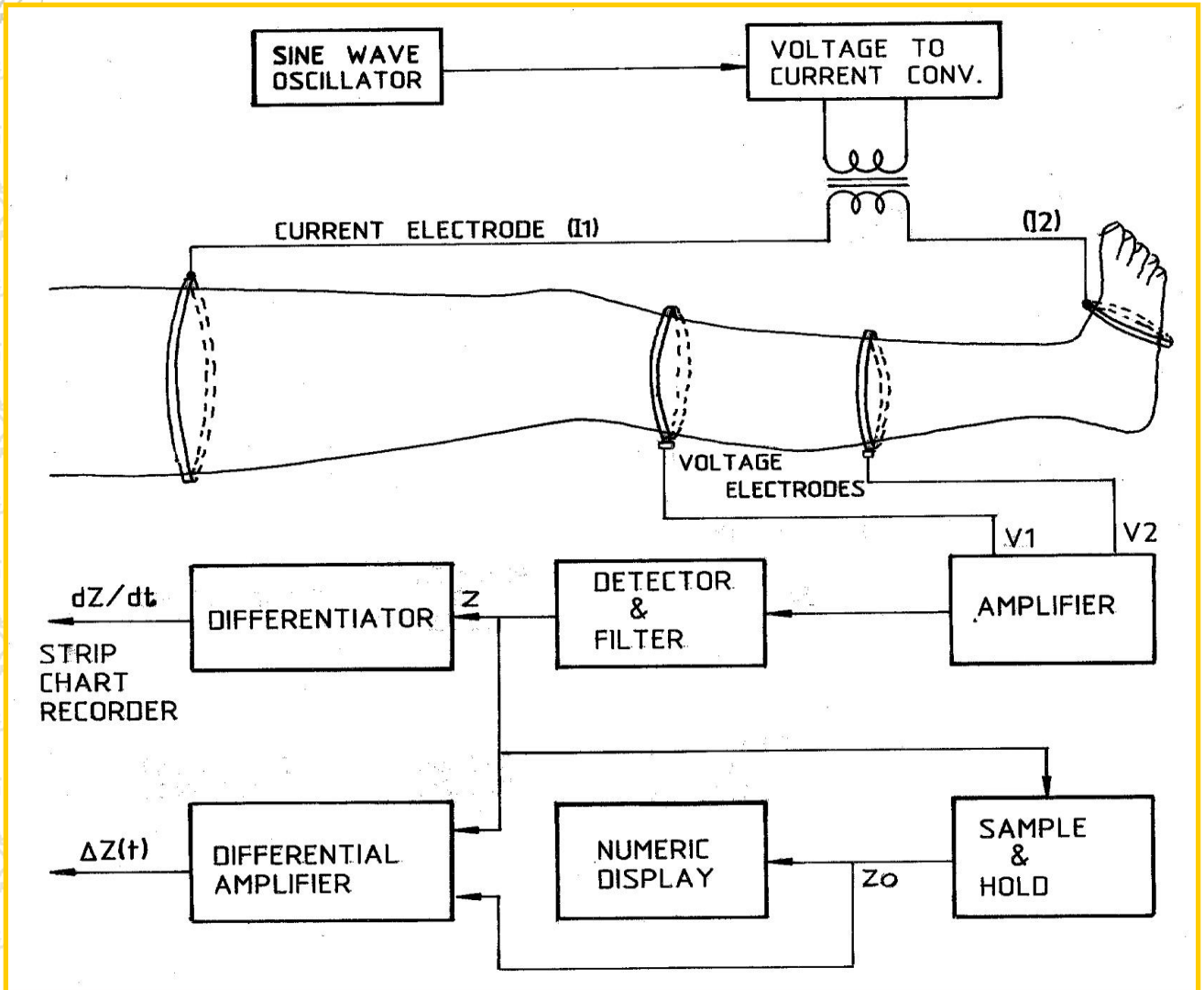
Poincare Plot



Poincare Plot : *Effect of placebo & bisoprolol*



Typical IPG


SINE WAVE OSCILLATOR
VOLTAGE TO CURRENT CONV.
CURRENT ELECTRODE (I1)
(I2)
VOLTAGE ELECTRODES
V1
V2
dZ/dt
DIFFERENTIATOR
Z
DETECTOR & FILTER
AMPLIFIER
STRIP CHART RECORDER
ΔZ(t)
DIFFERENTIAL AMPLIFIER
NUMERIC DISPLAY
Zo
SAMPLE & HOLD

Diseases Affecting the Variabilty

TABLE 1.
Outline classification and examples of disorders that cause cardiac autonomic dysfunction

PRIMARY
- ACUTE/SUBACUTE DYSAUTONOMIAS
  - Pure cholinergic dysautonomia
  - Pure pandysautonomia
  - Pandysautonomia with neurological features
- CHRONIC AUTONOMIC FAILURE SYNDROMES
  - Pure autonomic failure
  - Multiple system atrophy (Shy-Drager syndrome)
  - Autonomic failure with Parkinson's disease

SECONDARY
- CONGENITAL
  - Nerve growth factor deficiency
- HEREDITARY
  - *Autosomal dominant trait*
    - Familial amyloid neuropathy
    - Porphyria
  - *Autosomal recessive trait*
    - Familial dysautonomia – Riley-Day syndrome
    - Dopamine beta-hydroxylase deficiency
    - Friedrich's ataxia
- METABOLIC DISEASES
  - Diabetes mellitus
  - Chronic renal failure
  - Chronic liver disease
  - Thyroid disease (thyrotoxicosis & myxoedema)
  - Vitamin B_{12} deficiency
  - Alcohol-induced
- INFLAMMATORY
  - Guillain-Barre syndrome
  - Transverse myelitis
- INFECTIONS
  - Bacterial – tetanus
  - Viral– human immunodeficiency virus infection
  - Parasitic – Trypanosomiasis Cruzi; Chagas' disease
  - Prion – fatal familial insomnia

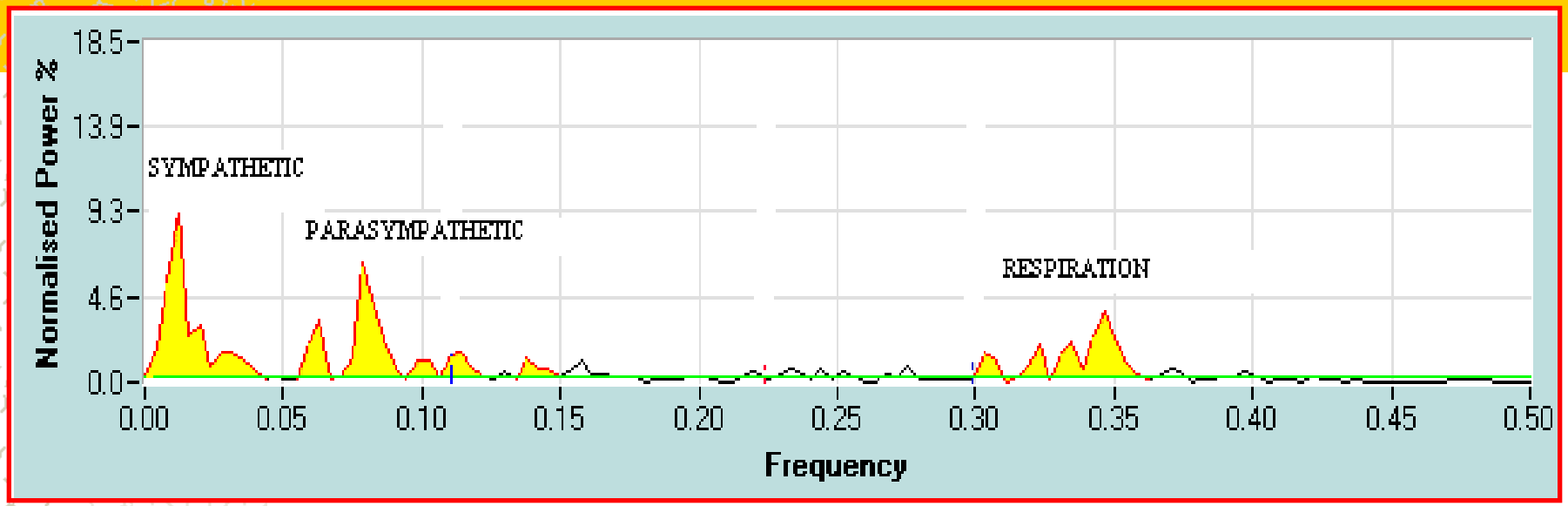
TABLE 1.
Continued

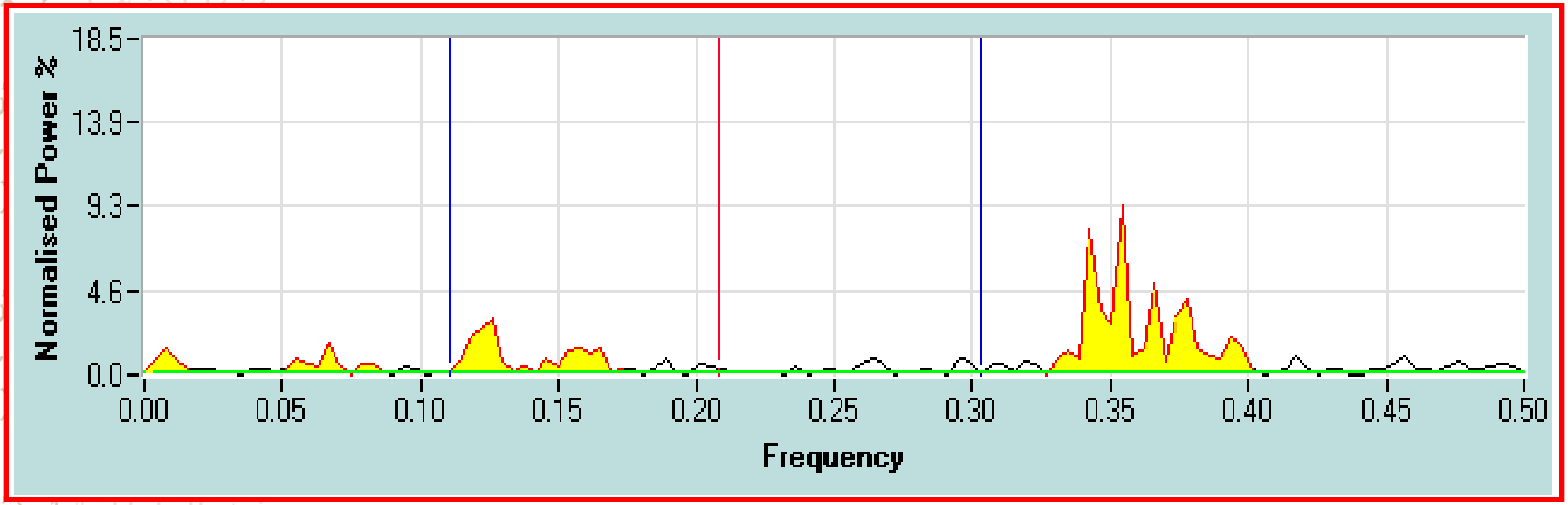
SECONDARY
- NEOPLASIA
  - Brain tumours – esp of third ventricle or posterior fossa
  - Paraneoplastic – adenocarcinomas:
    - lung, pancreas, and Lambert-Eaton syndrome
- SURGERY
  - Organ transplantation – heart, kidney
  - Vagotomy and drainage procedures – 'dumping syndrome'
  - Regional sympathectomy – splanchnic
- TRAUMA
  - Spinal cord transection
- MISCELLANEOUS NEUROLOGICAL DISORDERS
  - Subarachnoid haemorrhage
  - Epilepsy
  - Narcolepsy

POSTURAL TACHYCARDIA SYNDROME

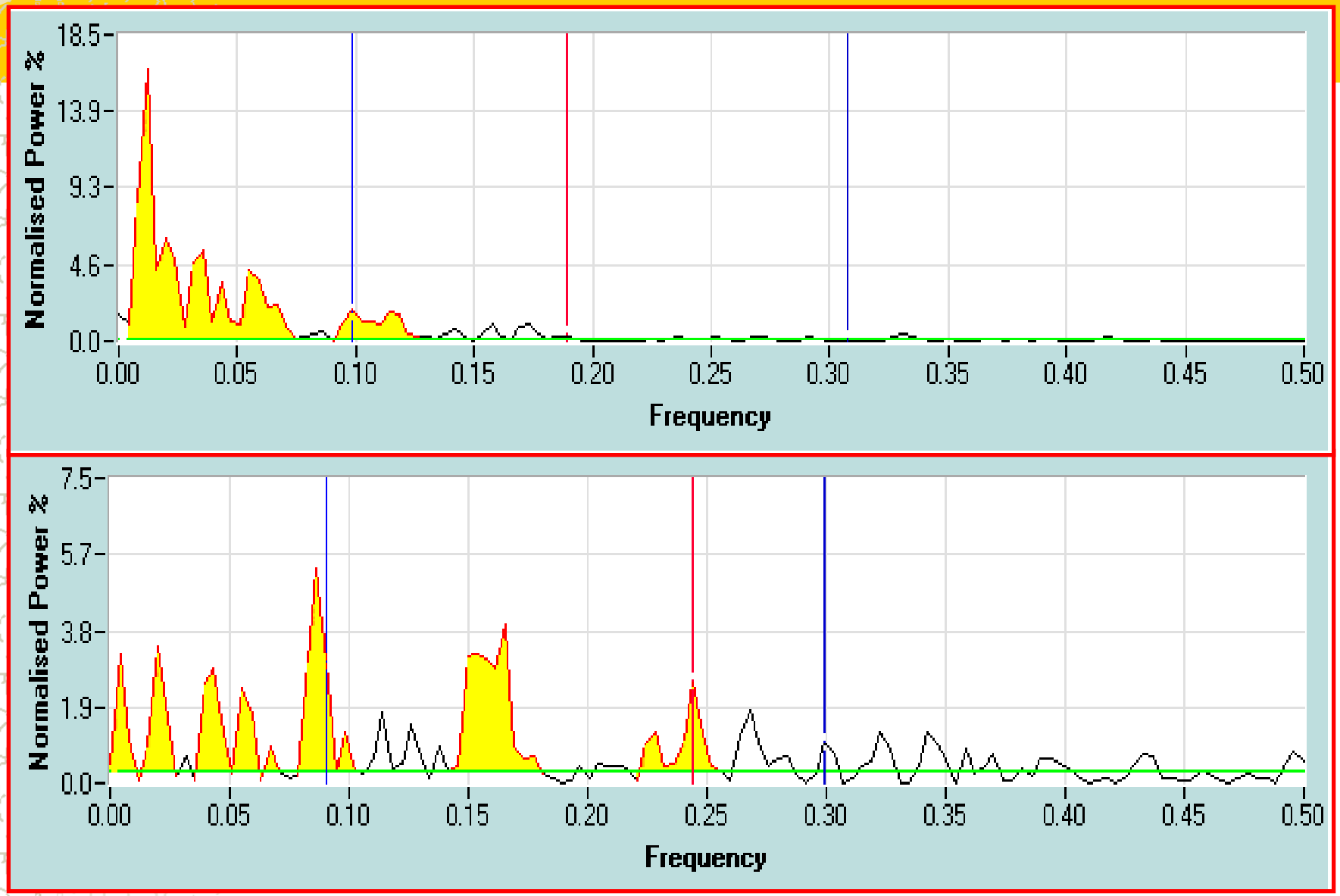
NEURALLY MEDIATED SYNCOPE
- Vasovagal syncope
- Carotid sinus hypersensitivity
- Micturition syncope
- Cough syncope
- Swallow syncope
- Associated with glossopharyngeal neuralgia

HRV in Disease Characterization

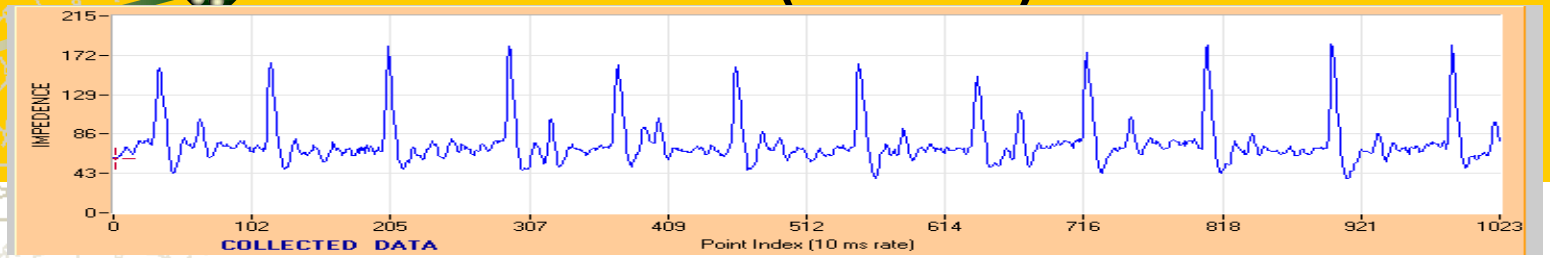




Blood Flow Variability in AIDs



Data (MAN)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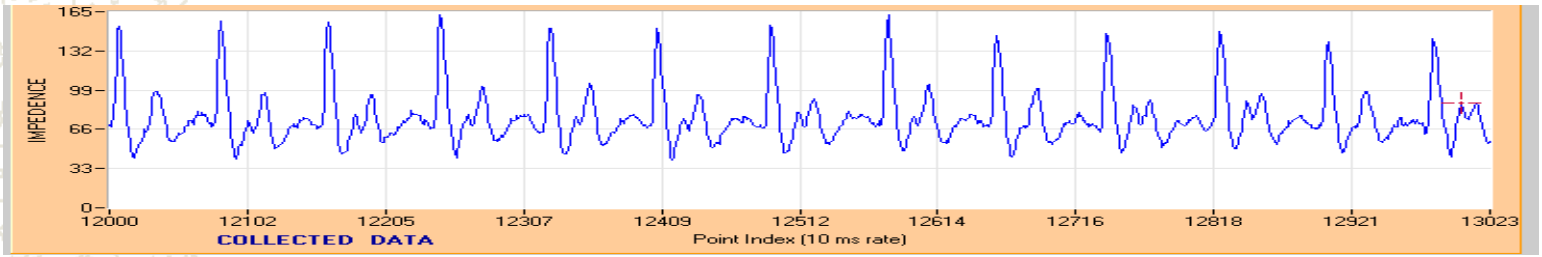
COLLECTED DATA
Point Index (10 ms rate)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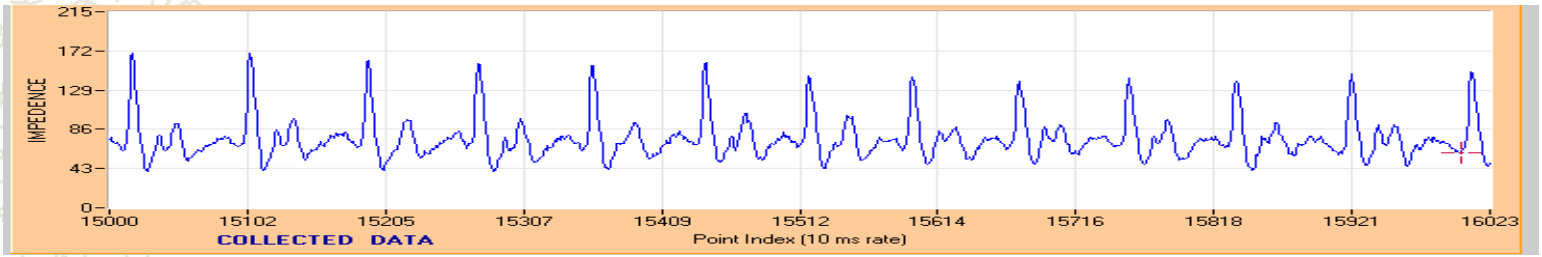
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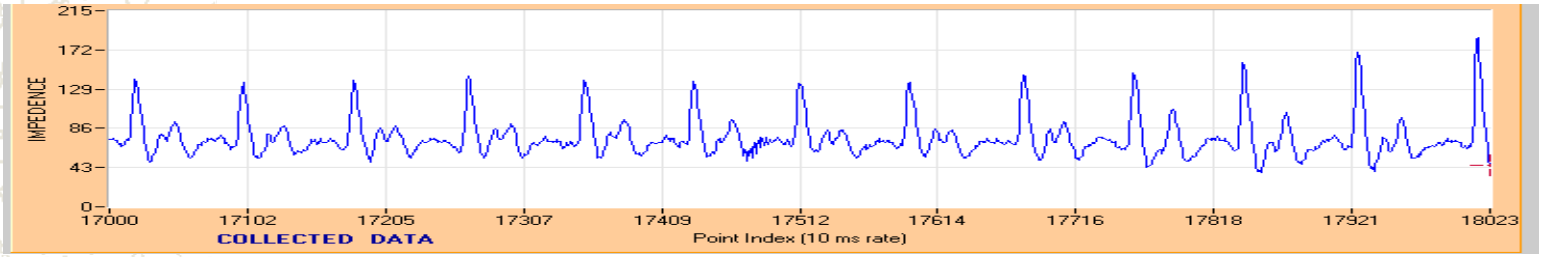
Point Index (10 ms rate)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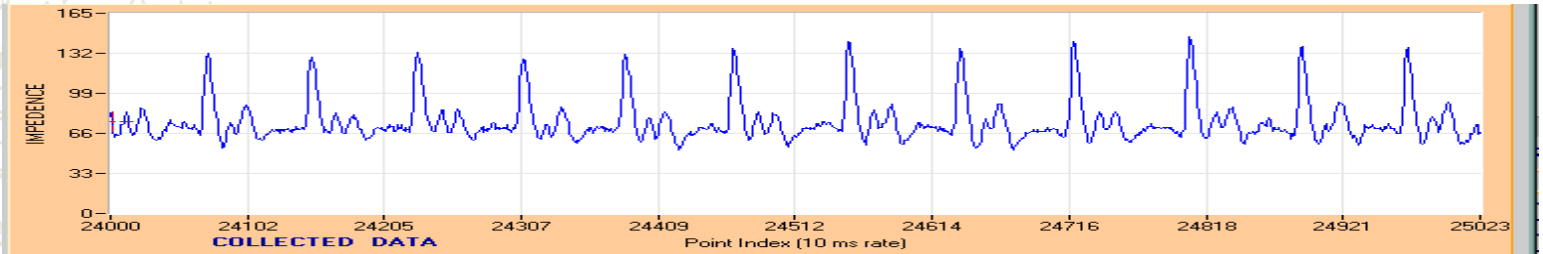
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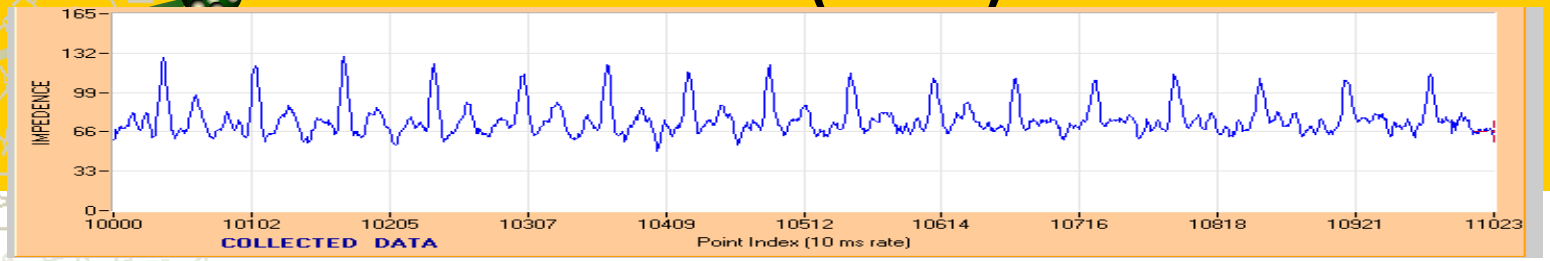
Point Index (10 ms rate)

Data (VM)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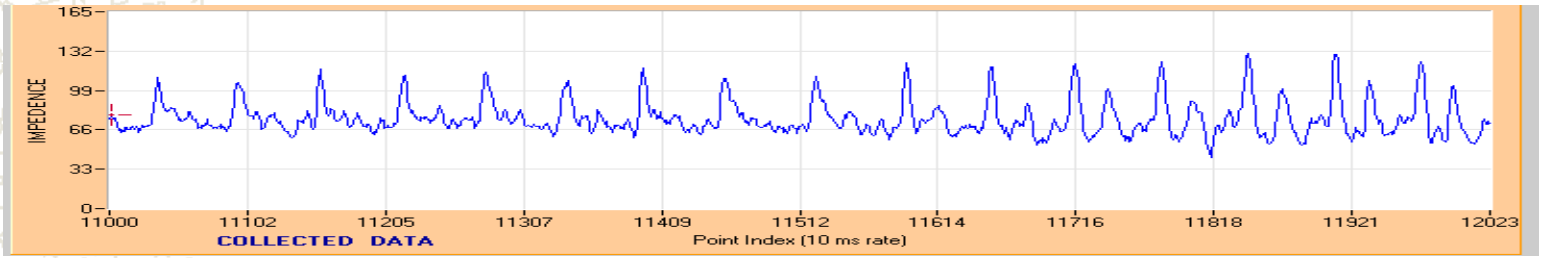
Point Index (10 ms rate)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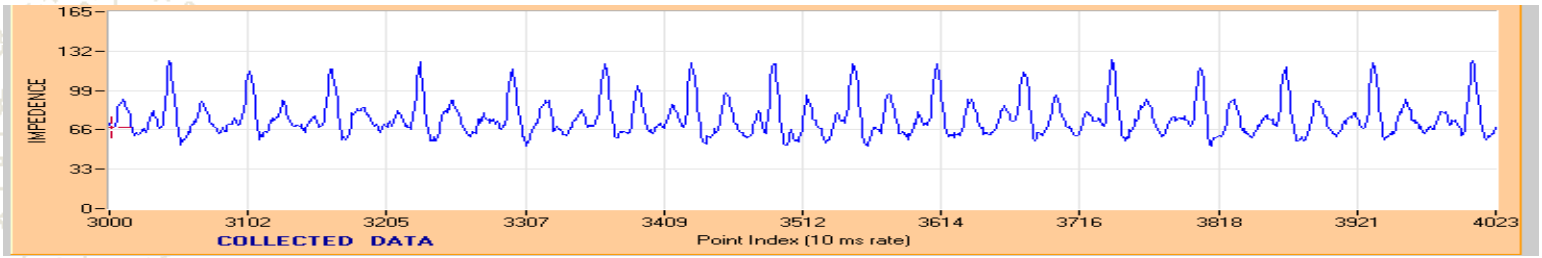
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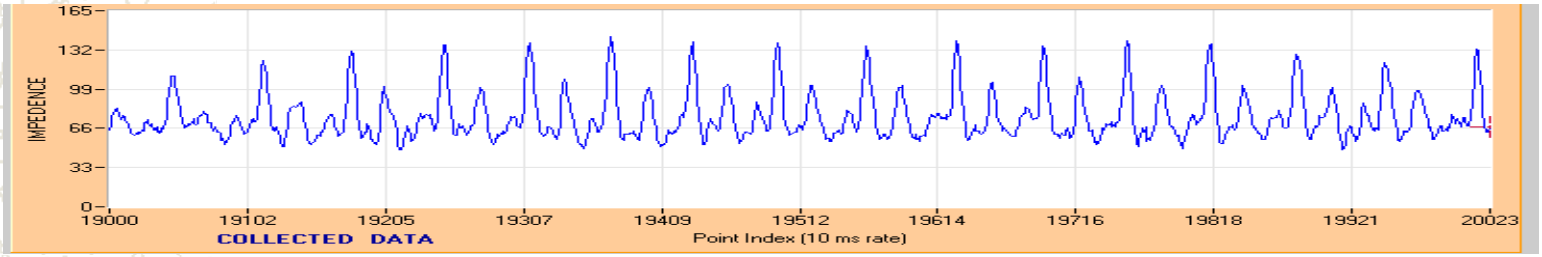
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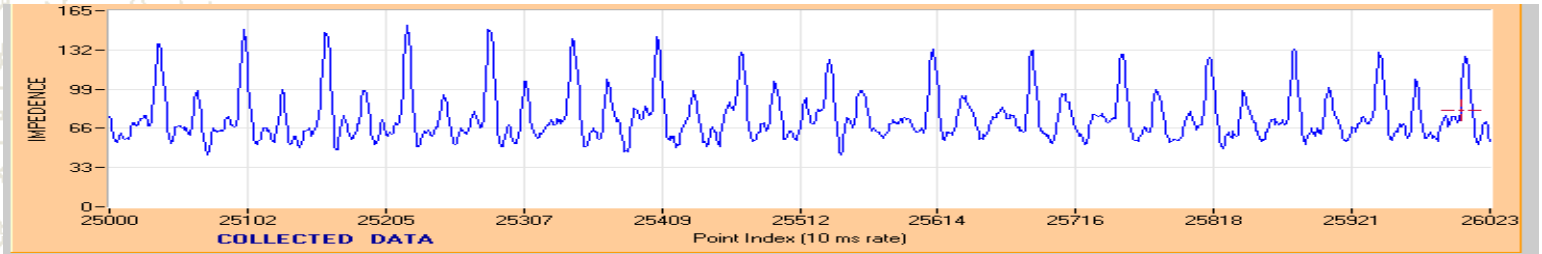
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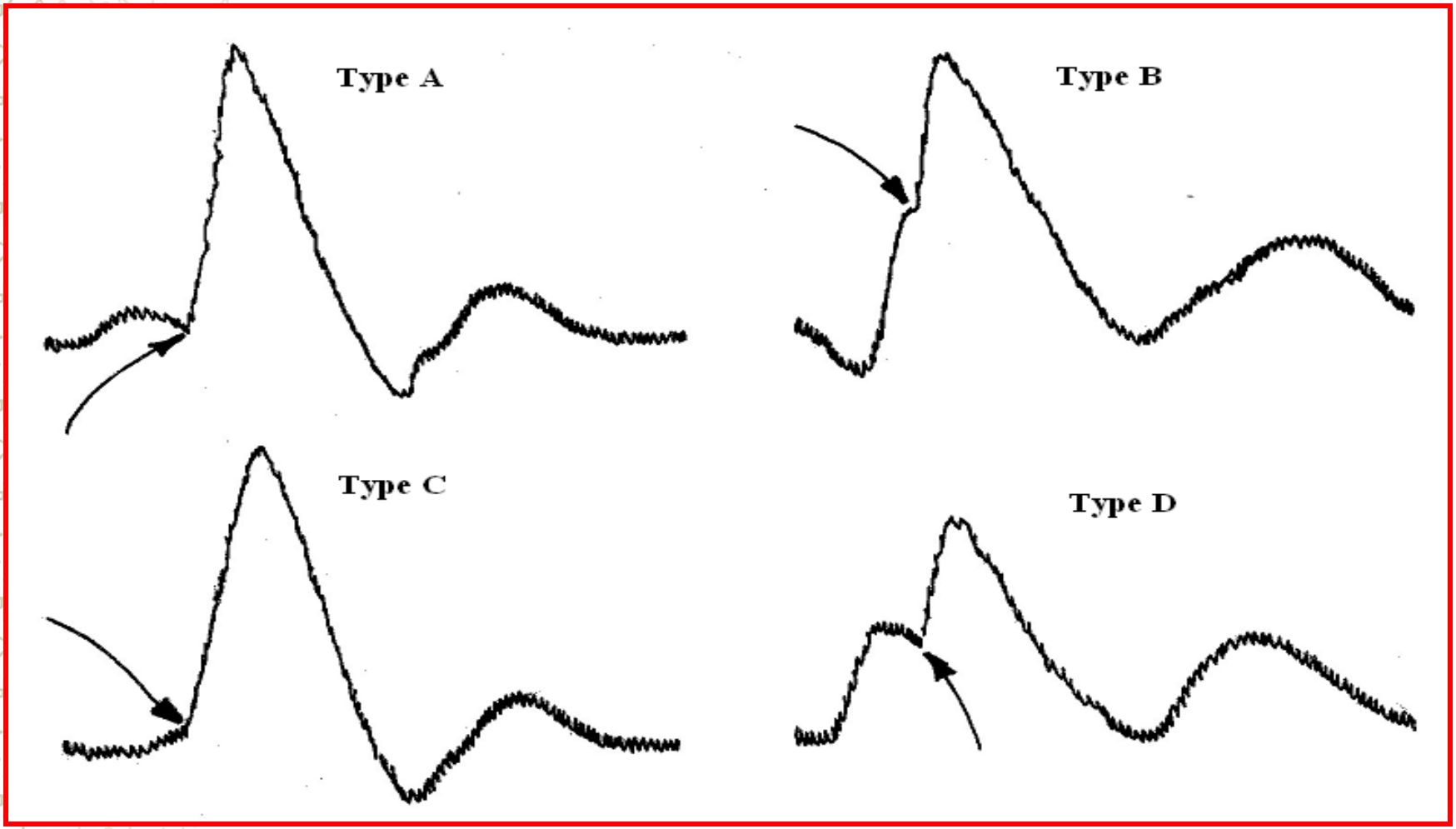
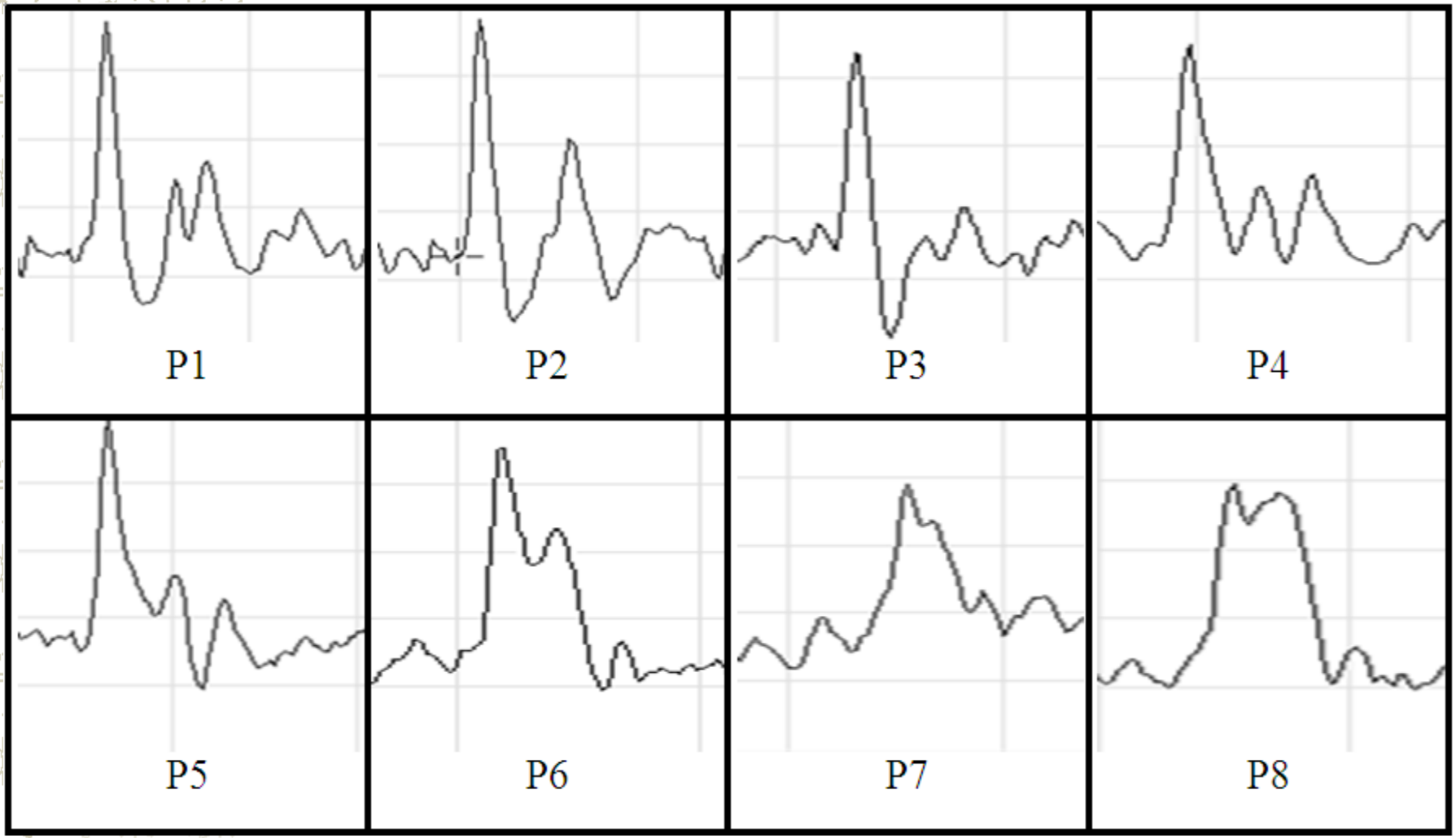
Point Index (10 ms rate)

Pulse Morphology and Variability

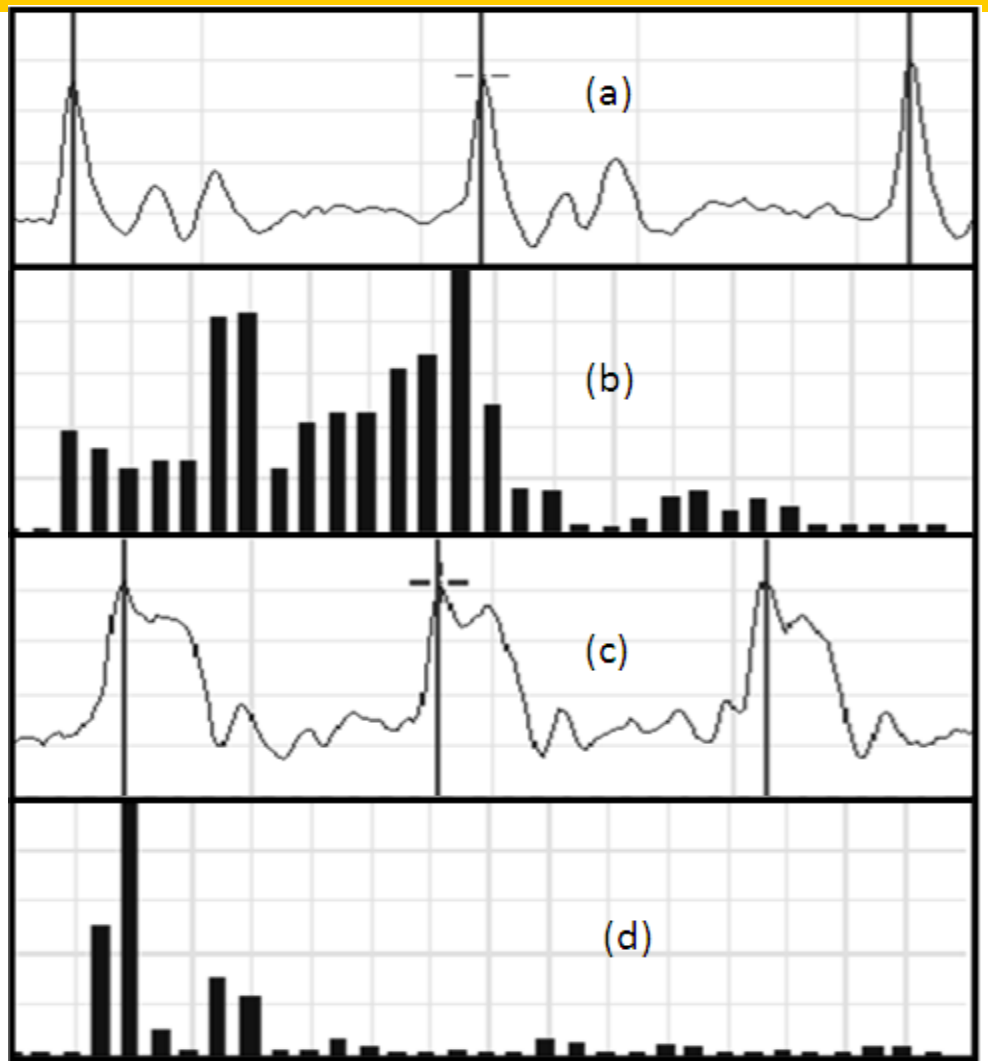


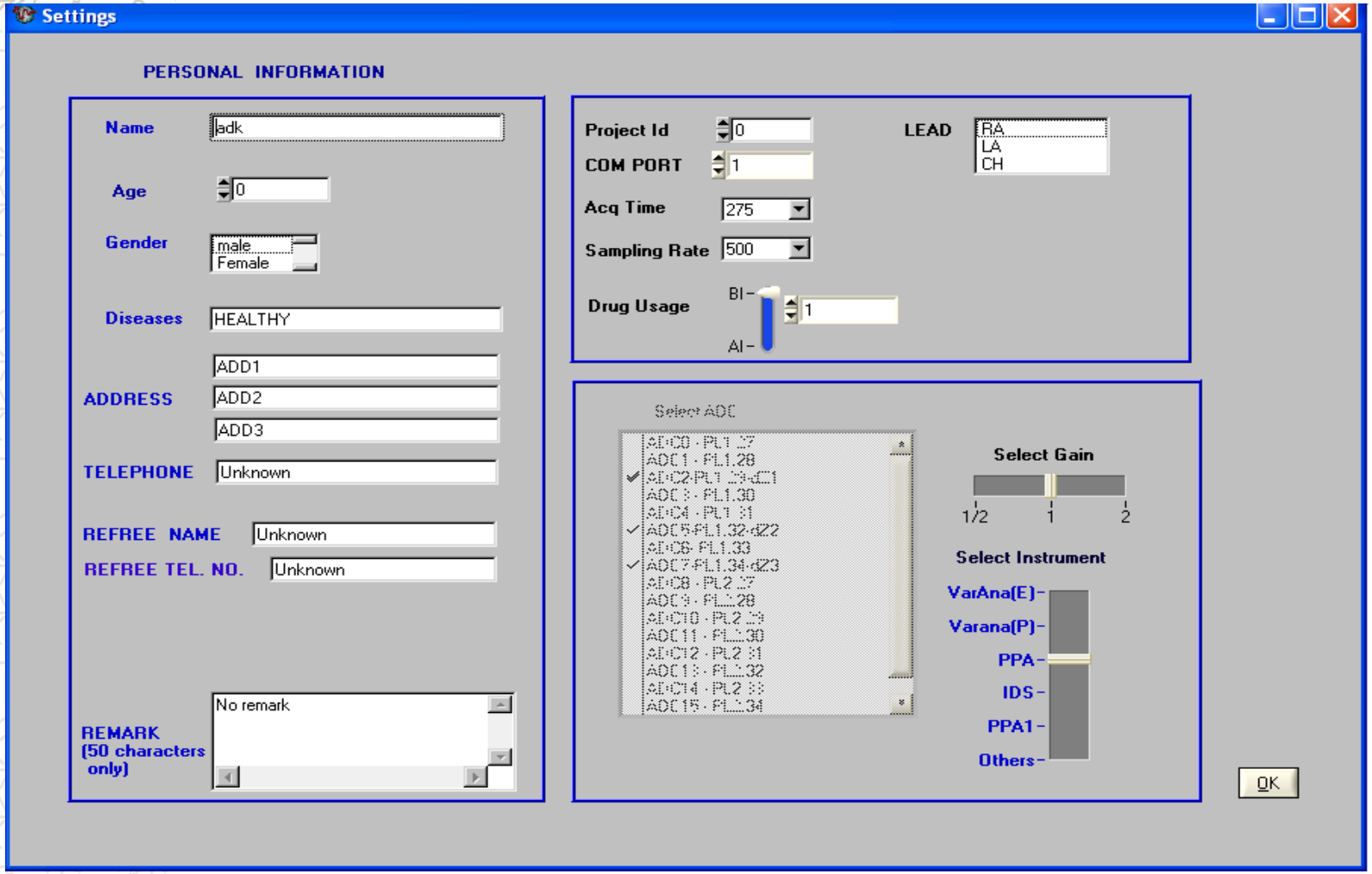
Peripheral Pulse Morphology



Morphology Index

$$MIx = \frac{\sum_{i=6}^{i=127} PSD(i)}{\sum_{i=2}^{i=127} PSD(i)}$$

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HEALTHY
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ADD2
ADD3
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REFREE NAME
Unknown
REFREE TEL. NO.
Unknown
REMARK
(50 characters only)
No remark
Project Id
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COM PORT
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Acq Time
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Sampling Rate
500
Drug Usage
BI
AI
1
LEAD
RA
LA
CH
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Select Gain
1/2
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2
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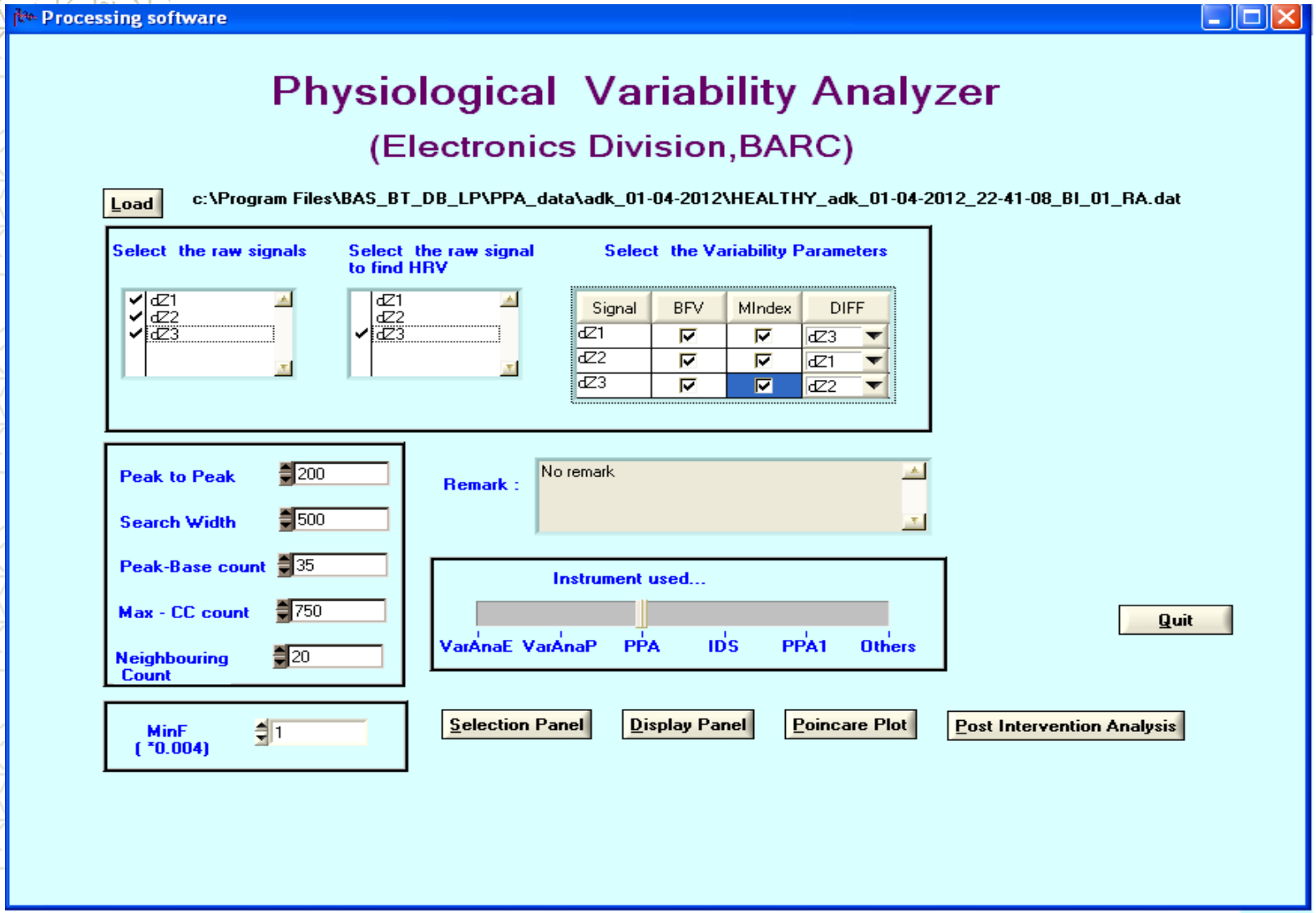
VarAna(E)
Varana(P)
PPA
IDS
PPA1
Others
OK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Physiological Variability Analyzer
(Electronics Division,BARC)
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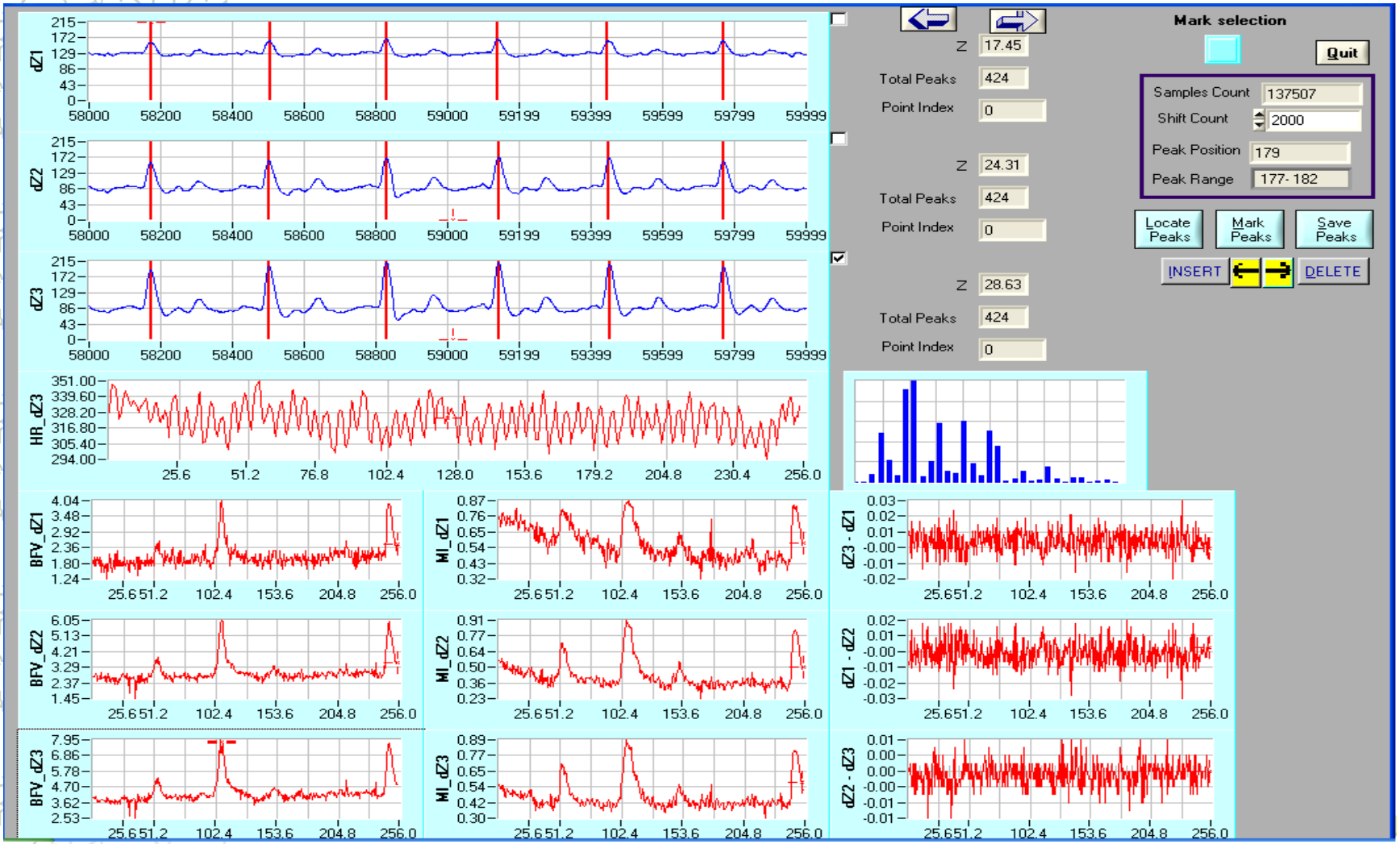
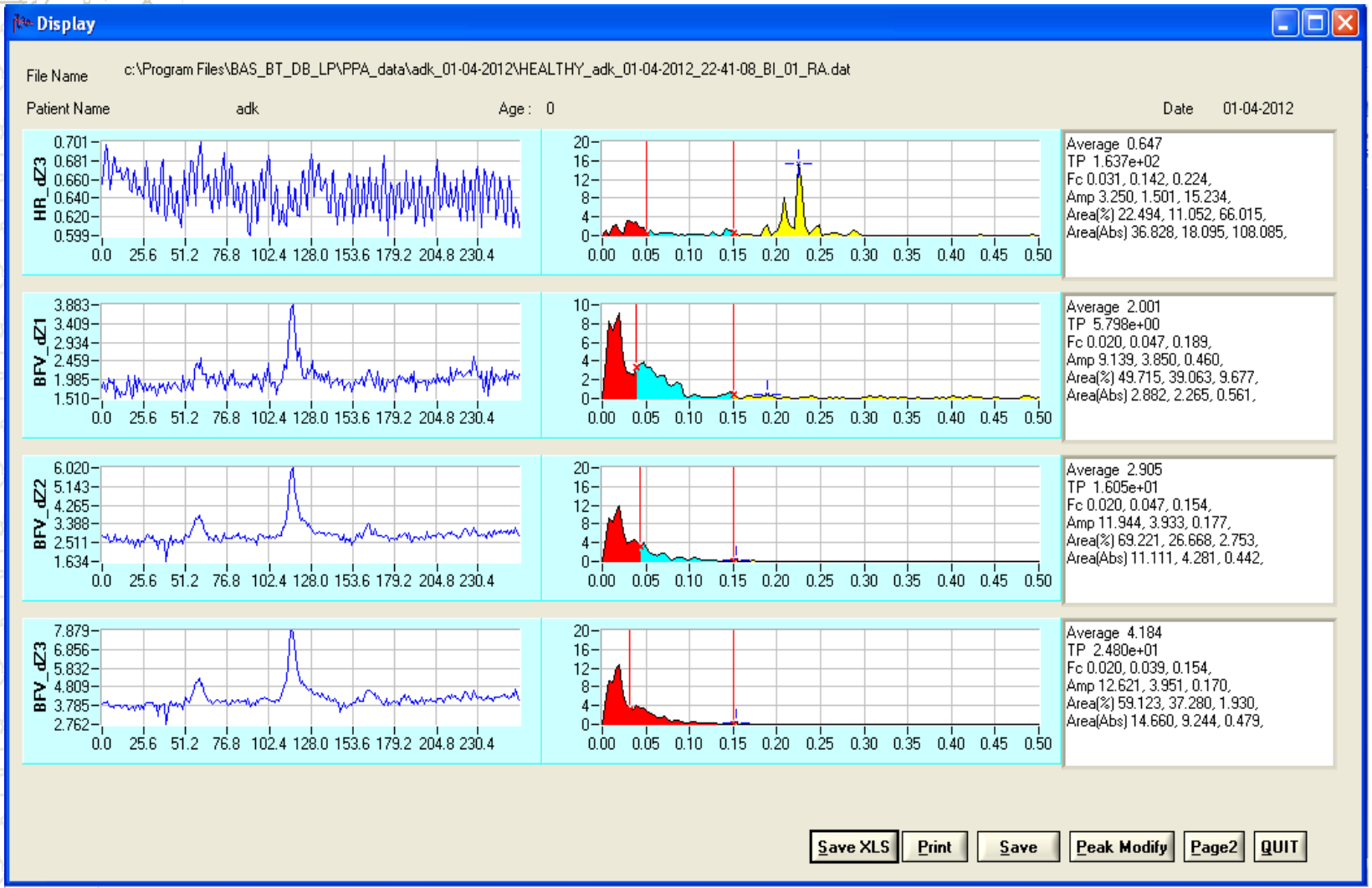
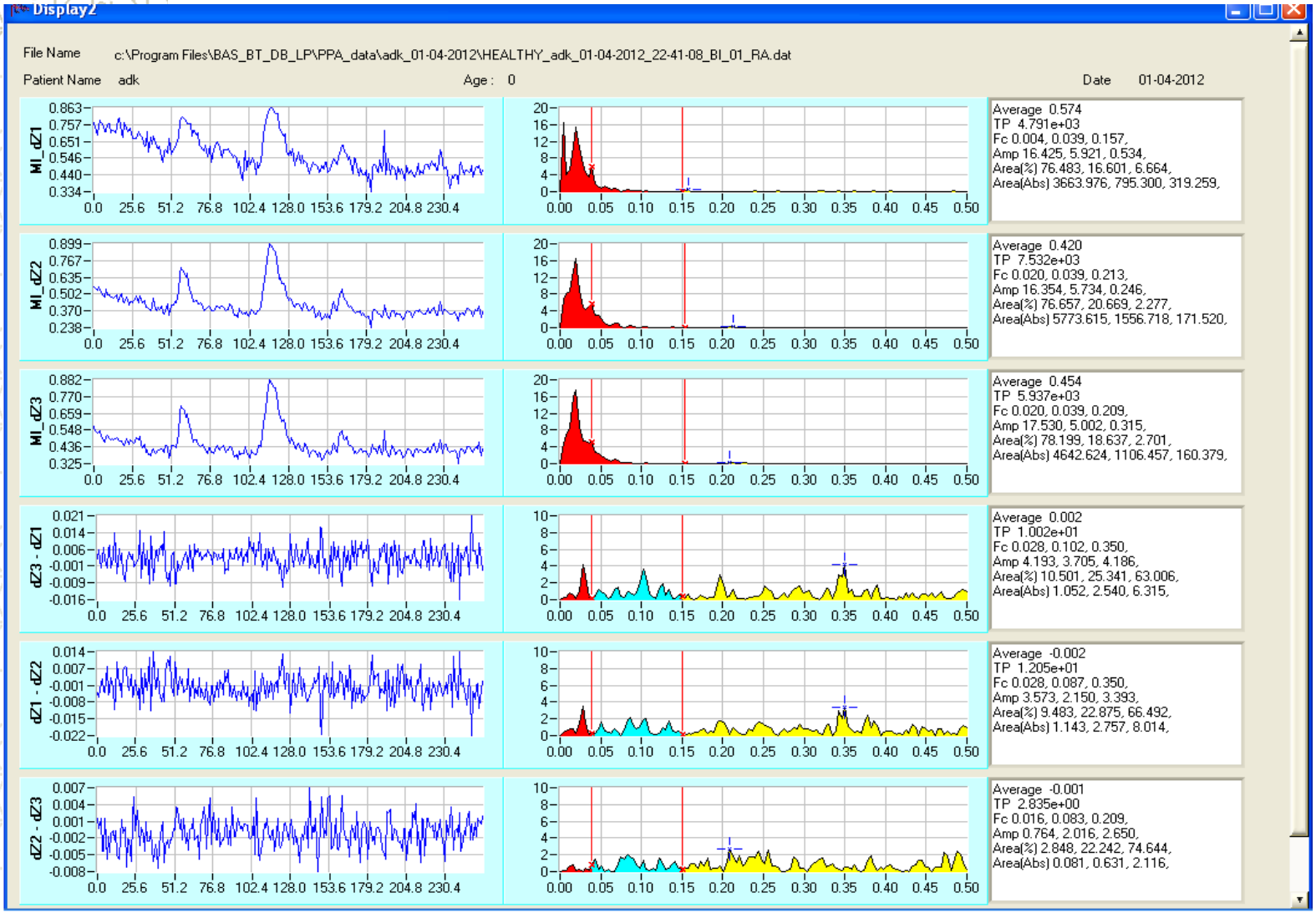
dZ2
dZ3
Select the raw signal to find HRV
dZ1
dZ2
dZ3
Select the Variability Parameters
Signal
BFV
MIndex
DIFF
dZ1
dZ3
dZ2
dZ1
dZ3
dZ2
Peak to Peak
200
Search Width
500
Peak-Base count
35
Max - CC count
750
Neighbouring Count
20
Remark :
No remark
Instrument used...
VarAnaE
VarAnaP
PPA
IDS
PPA1
Others
Quit
MinF (*0.004)
1
Selection Panel
Display Panel
Poincare Plot
Post Intervention Analysis


dZ1
dZ2
dZ3
HR_dZ3
BFV_dZ1
BFV_dZ2
BFV_dZ3
MI_dZ1
MI_dZ2
MI_dZ3
dZ3 - dZ1
dZ1 - dZ2
dZ2 - dZ3
Z 17.45
Total Peaks 424
Point Index 0
Z 24.31
Total Peaks 424
Point Index 0
Z 28.63
Total Peaks 424
Point Index 0
Mark selection
Quit
Samples Count 137507
Shift Count 2000
Peak Position 179
Peak Range 177- 182
Locate Peaks
Mark Peaks
Save Peaks
INSERT
DELETE


Display
File Name
c:\Program Files\BAS_BT_DB_LP\PPA_data\adk_01-04-2012\HEALTHY_adk_01-04-2012_22-41-08_BI_01_RA.dat
Patient Name
adk
Age : 0
Date 01-04-2012
HR_dZ3
BFV_dZ1
BFV_dZ2
BFV_dZ3
Average 0.647
TP 1.637e+02
Fc 0.031, 0.142, 0.224,
Amp 3.250, 1.501, 15.234,
Area(%) 22.494, 11.052, 66.015,
Area(Abs) 36.828, 18.095, 108.085,
Average 2.001
TP 5.798e+00
Fc 0.020, 0.047, 0.189,
Amp 9.139, 3.850, 0.460,
Area(%) 49.715, 39.063, 9.677,
Area(Abs) 2.882, 2.265, 0.561,
Average 2.905
TP 1.605e+01
Fc 0.020, 0.047, 0.154,
Amp 11.944, 3.933, 0.177,
Area(%) 69.221, 26.668, 2.753,
Area(Abs) 11.111, 4.281, 0.442,
Average 4.184
TP 2.480e+01
Fc 0.020, 0.039, 0.154,
Amp 12.621, 3.951, 0.170,
Area(%) 59.123, 37.280, 1.930,
Area(Abs) 14.660, 9.244, 0.479,
Save XLS
Print
Save
Peak Modify
Page2
QUIT


Display2
File Name c:\Program Files\BAS_BT_DB_LP\PPA_data\adk_01-04-2012\HEALTHY_adk_01-04-2012_22-41-08_BI_01_RA.dat
Patient Name adk
Age : 0
Date 01-04-2012
MI_dZ1
Average 0.574
TP 4.791e+03
Fc 0.004, 0.039, 0.157,
Amp 16.425, 5.921, 0.534,
Area(%) 76.483, 16.601, 6.664,
Area(Abs) 3663.976, 795.300, 319.259,
MI_dZ2
Average 0.420
TP 7.532e+03
Fc 0.020, 0.039, 0.213,
Amp 16.354, 5.734, 0.246,
Area(%) 76.657, 20.669, 2.277,
Area(Abs) 5773.615, 1556.718, 171.520,
MI_dZ3
Average 0.454
TP 5.937e+03
Fc 0.020, 0.039, 0.209,
Amp 17.530, 5.002, 0.315,
Area(%) 78.199, 18.637, 2.701,
Area(Abs) 4642.624, 1106.457, 160.379,
dZ3 - dZ1
Average 0.002
TP 1.002e+01
Fc 0.028, 0.102, 0.350,
Amp 4.193, 3.705, 4.186,
Area(%) 10.501, 25.341, 63.006,
Area(Abs) 1.052, 2.540, 6.315,
dZ1 - dZ2
Average -0.002
TP 1.205e+01
Fc 0.028, 0.087, 0.350,
Amp 3.573, 2.150, 3.393,
Area(%) 9.483, 22.875, 66.492,
Area(Abs) 1.143, 2.757, 8.014,
dZ2 - dZ3
Average -0.001
TP 2.835e+00
Fc 0.016, 0.083, 0.209,
Amp 0.764, 2.016, 2.650,
Area(%) 2.848, 22.242, 74.644,
Area(Abs) 0.081, 0.631, 2.116,

Thank You…