# Modeling of Phase, Amplitude and Transfer Function of Carotid Arterial Pulse Pressure and Intracranial Pulse Pressure in Dogs


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# Thanks!

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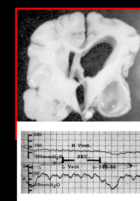
We thank Siv, Jim, Pino and the Fields Institute for organizing this meeting and for their hospitality and for this opportunity to collaborate

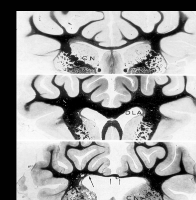
# There is evidence that abnormalities of pulsatility are important in hydrocephalus

- **Bering (1964)**

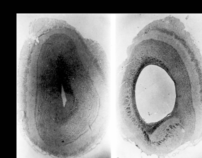


- **Wilson and Bertan (1966)**

- **DiRocco (1978)**



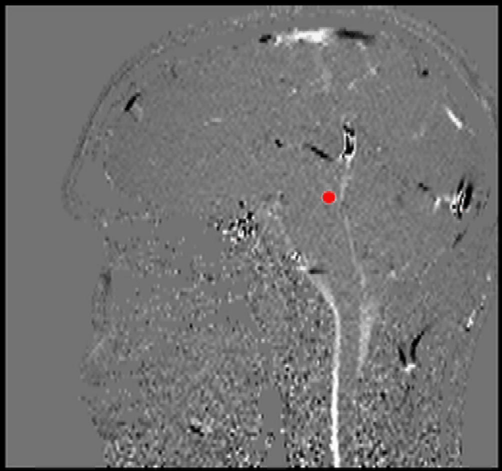
- **Guinane (1977)**



- **Greitz, Alperin, Bateman (1993-2006)**

# How can we understand intracranial pulsatility?

- Monroe-Kellie model is essentially a model of mass conservation
- Monroe-Kellie model is best suited to describe smooth convective *gradual* dynamics
- Virtually all of the motion of CSF is pulsatile!
- Pulsations (oscillations) involve phenomena that are best described with terms that are different from those that describe convective dynamics

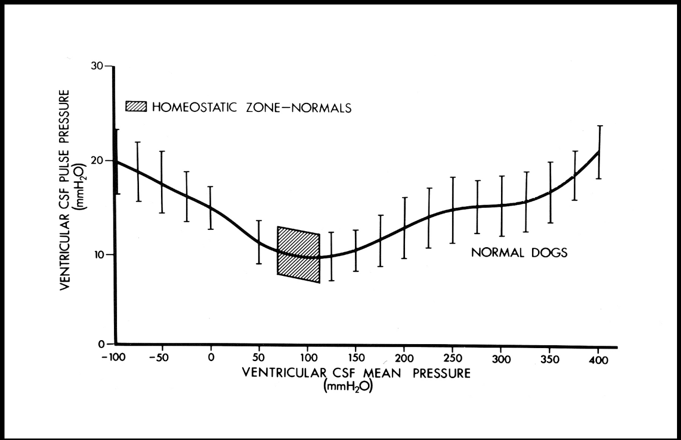


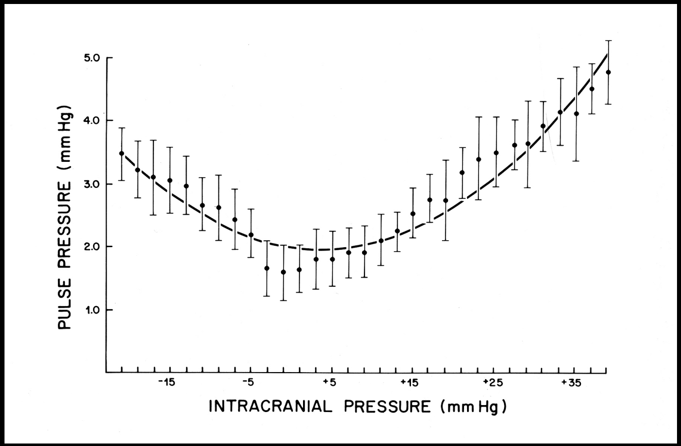
# Intracranial pulsatility

There are several aspects of intracranial pulsatility that cannot be readily explained by the Monroe-Kellie Model

# ICP pulse pressure amplitude: the low ICP anomaly

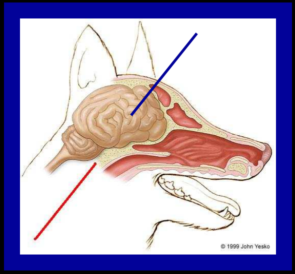
- Foltz (1984)
- Sklar (1985)
- Amplitude of ICP pulse pressure increases with increasing ICP
- Amplitude of ICP pulse pressure also *increases with decreasing ICP*
- **The U-shaped curve becomes linear in hydrocephalus!**

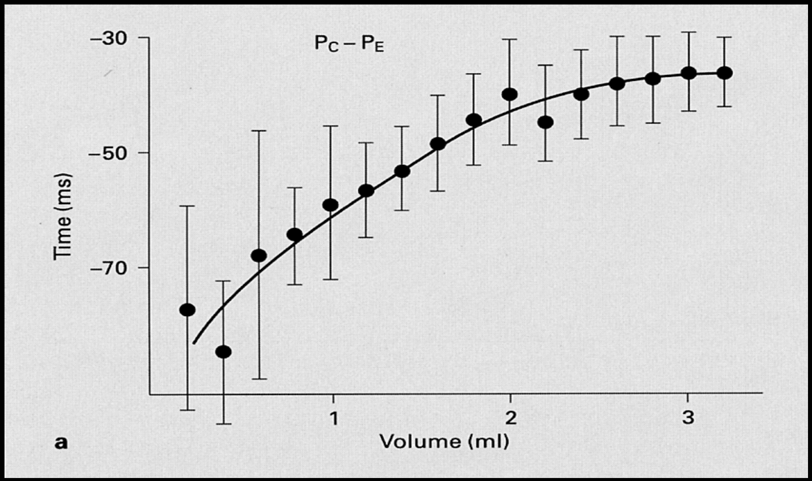


# Nitta

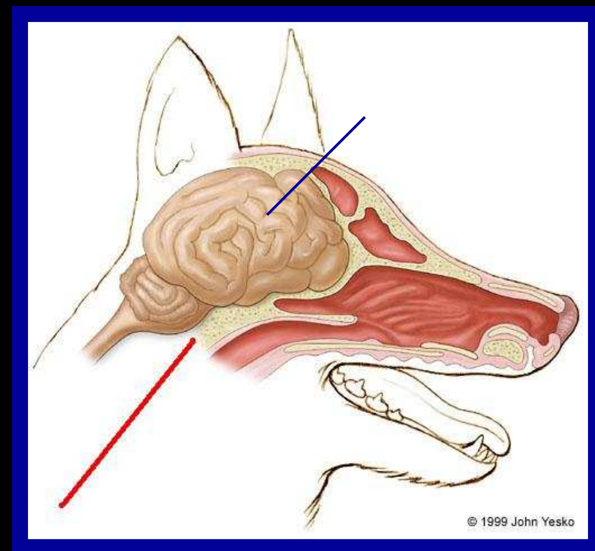
- Nitta (1985) measured "transmission delay" between carotid arterial pressure pulse and ICP pulse
- Transmission delay was *lengthened* by increasing ICP (and decreasing compliance), o*pposite* what would be expected of wave propagation
- Normal dynamics were characterized by an ICP pulse that led the carotid arterial pulse
- The normal ICP pulse *precedes* the carotid arterial pulse!

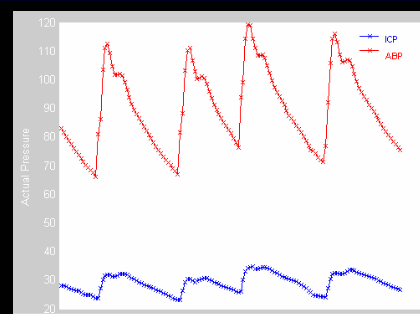




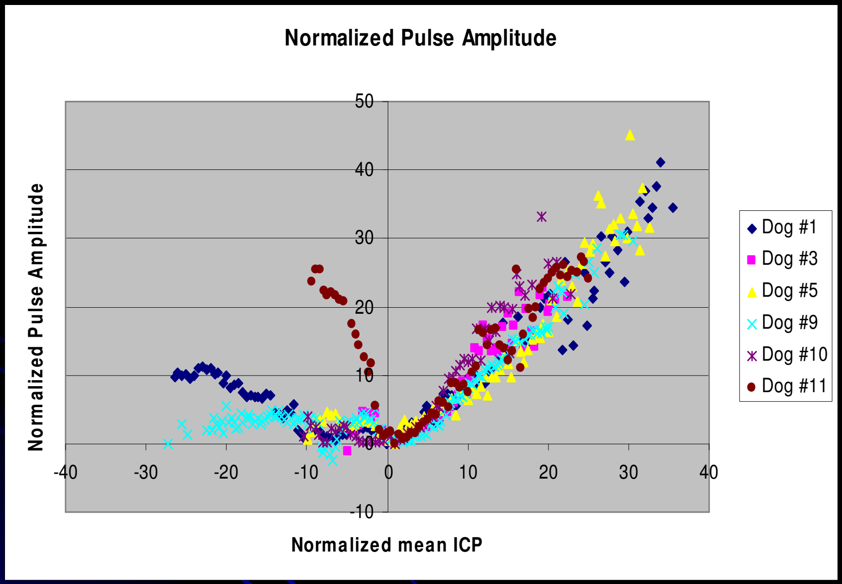
# Methods:
# Dog model of intracranial amplitude and phase

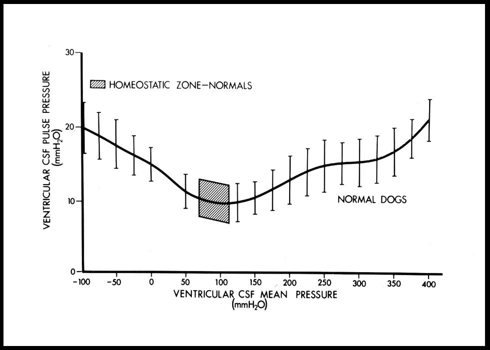
- **12 dogs**
- **Carotid arterial pressure**
- **Parenchymal brain pressure**
- **Venous pressure**
- **Vary ICP by lumbar/cisternal injection and withdrawal of CSF**
- **Analyze amplitude and phase of vascular and ICP pulses**

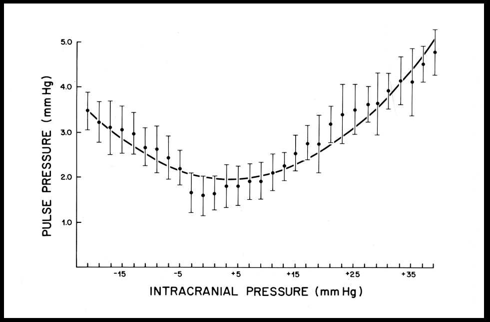


# Results: Amplitude



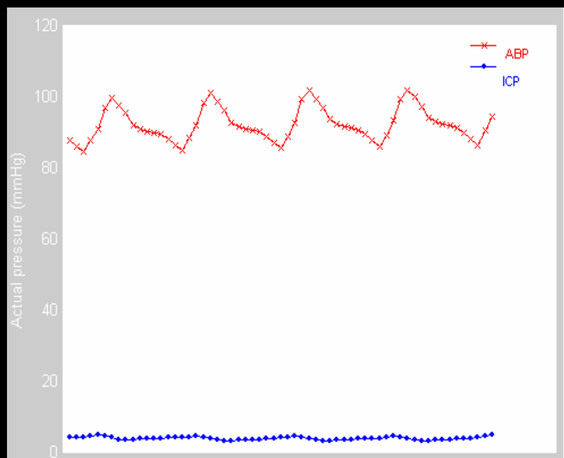



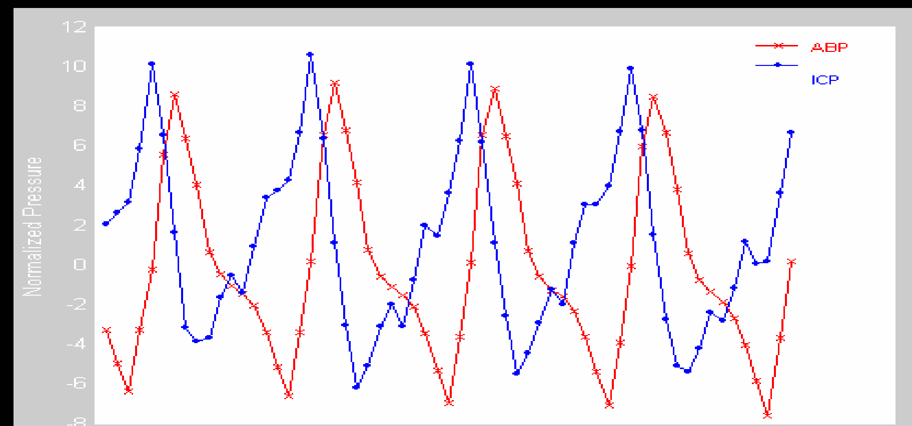
# Results: qualitative phase

Actual Pressures

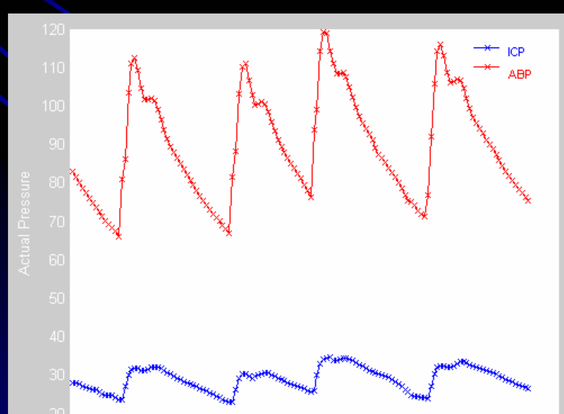
Normalized Pressures

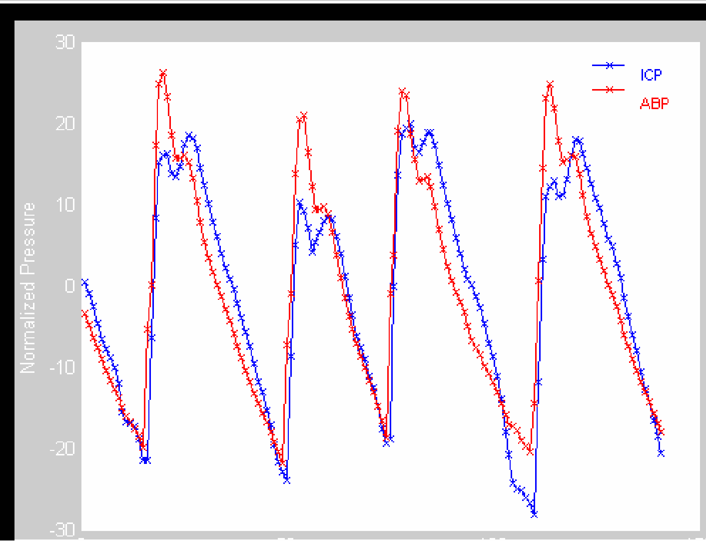
Low ICP (5mmHg)



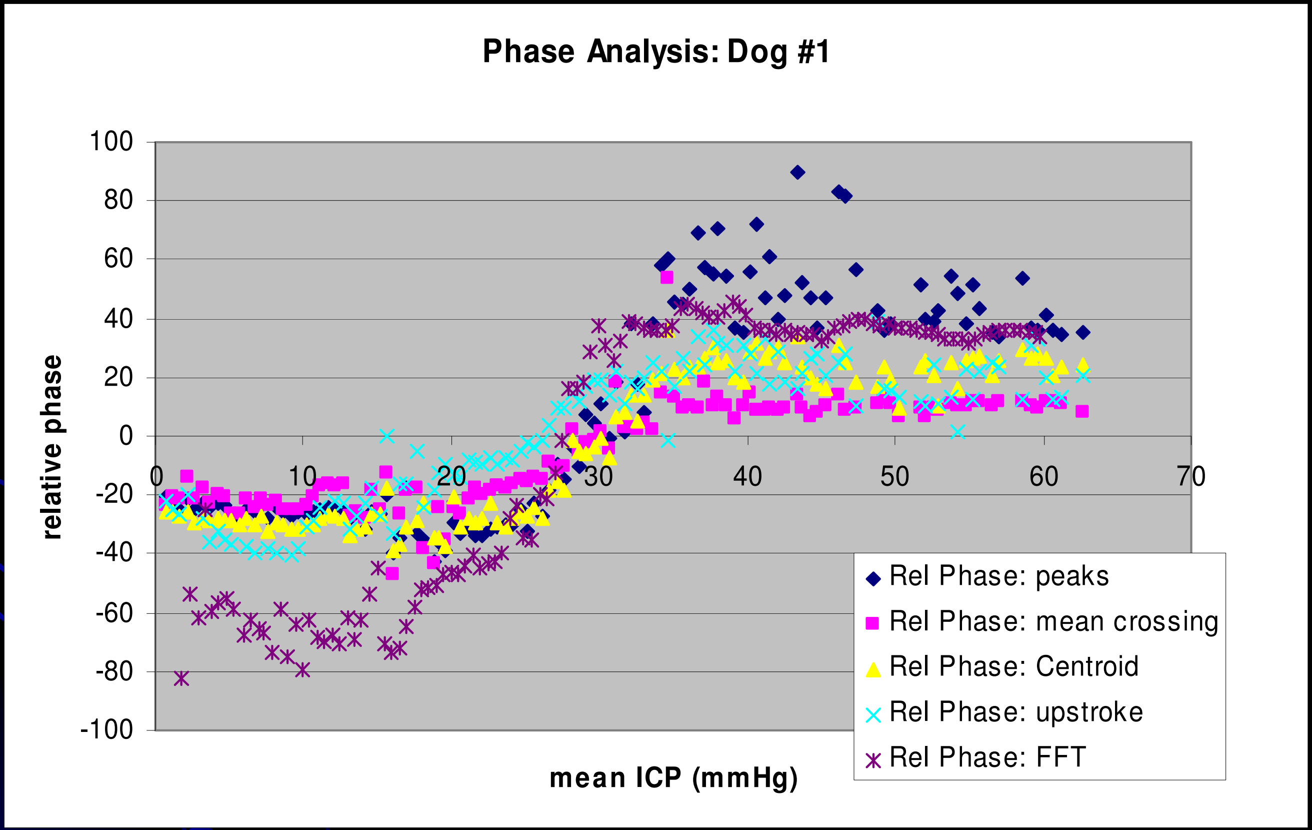




Elevated ICP (30mmHg)



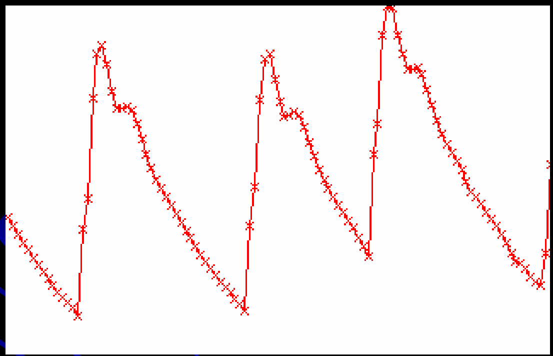
# ICP Phase

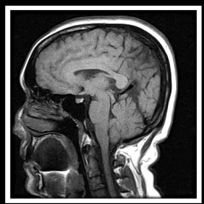


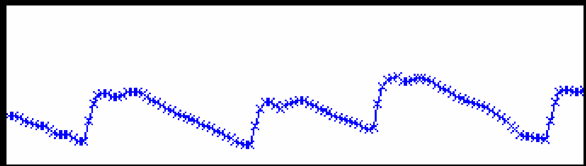
Phase Analysis: Dog #1
relative phase
mean ICP (mmHg)
100
80
60
40
20
0
-20
-40
-60
-80
-100
0
10
20
30
40
50
60
70
Rel Phase: peaks
Rel Phase: mean crossing
Rel Phase: Centroid
Rel Phase: upstroke
Rel Phase: FFT

# Transfer function

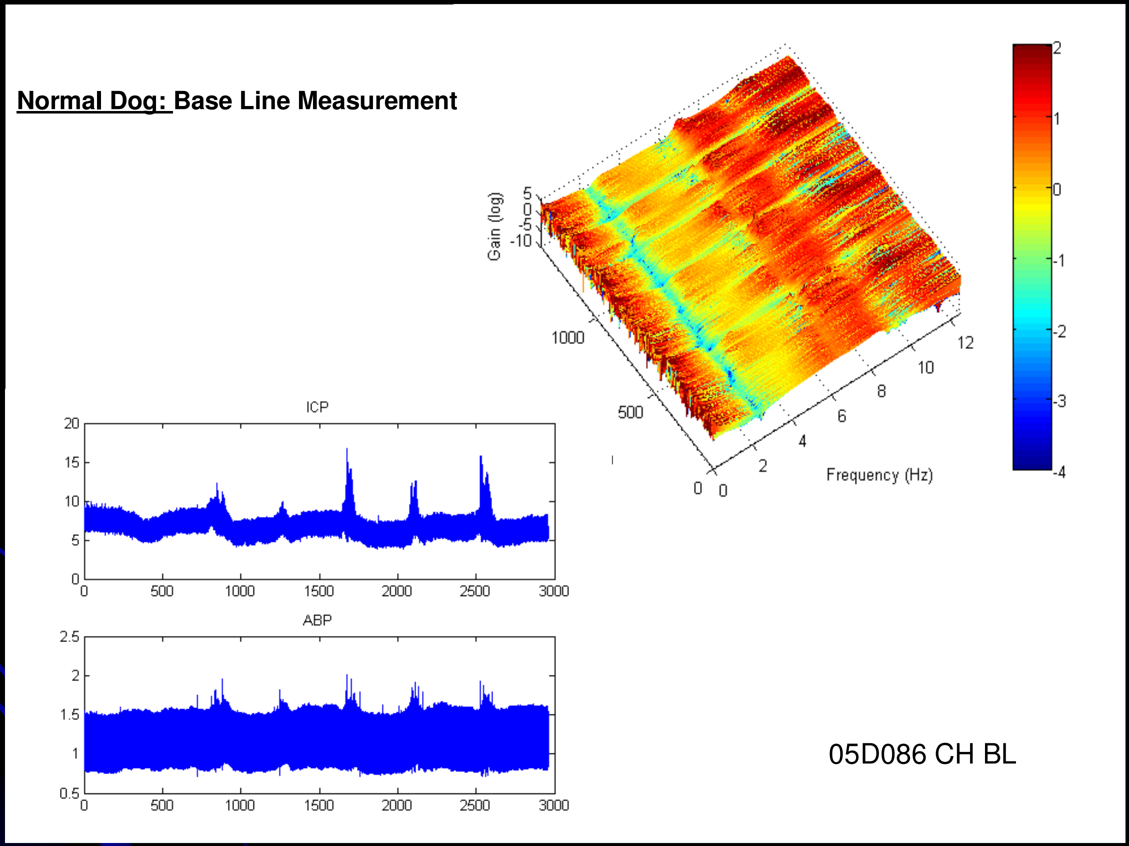
How does the cranium *process* the arterial pulse?



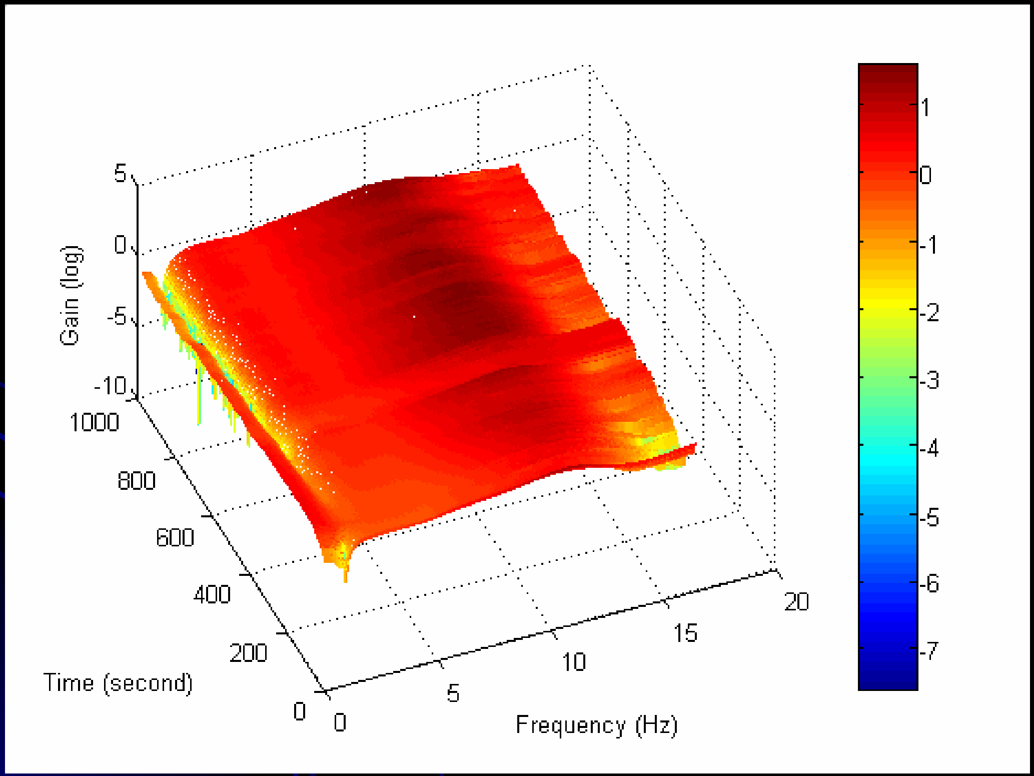


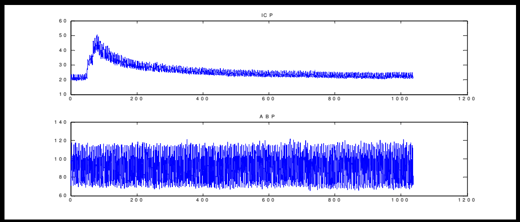


# Phase, amplitude and the 'notch' of the ABP-ICP transfer function (ARMA analysis: Joe Madsen, Rai Zou)



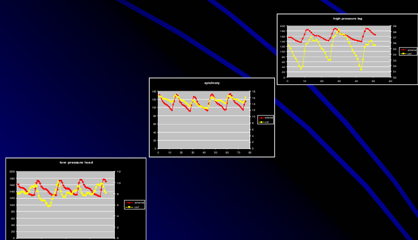
# Disappearance and reappearance of the notch

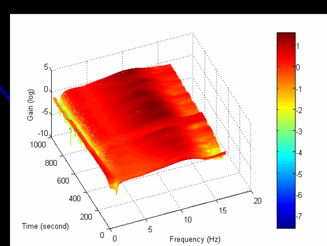


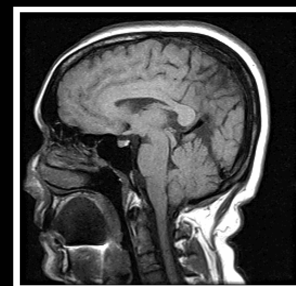



# The violin analogy

- The ICP pulse is a **standing wave**, *not* a transmitted wave
- The cranium is a resonating chamber
- An external source excites standing waves in a chamber, but the standing waves may lead or lag the source, depending on the elastance (and other properties) of the chamber
- Analogous to sound waves in a violin

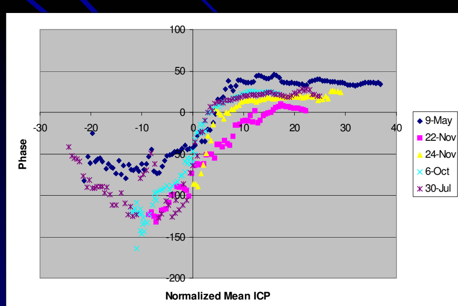




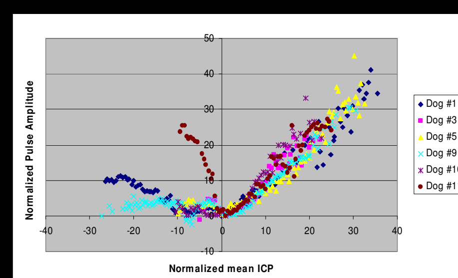



# Understanding phase and amplitude

- **Phase of ICP**
- **Phase is impedance phase of effort/flow**
- **Reference phasor is waveform of CBF in systole/diastole**
- High Elastance ICP lags flow
- Low Elastance ICP leads flow
- (Analogous to phase of voltage in a.c. RLC electrical circuit)

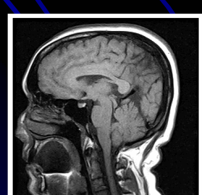


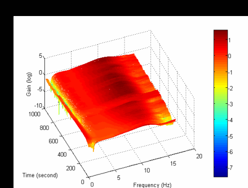
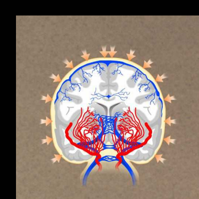
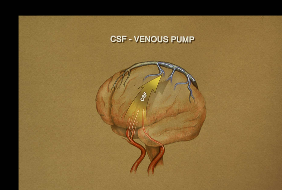

- **Amplitude of ICP**
- Normal physiology is at high impedance resonance (anti-resonance)
- 'Tuned notch': normal ICP amplitude: cranial cavity suppresses fundamental of arterial pulse
- 'Detuned notch': low and high ICP



# The physiological importance of the notch filter: the windkessel mechanism

- A resonating chamber such as the cranium will suppress certain frequencies of input
- There is evidence that the cranium normally suppresses the fundamental frequency of the arterial pulse, which may protect the microvasculature
- ‘Phase’ determines the frequency of the notch, which will represent anti-resonance for the fundamental of the arterial pulse
- The high impedance windkessel reflects cardiac pulse to veins (‘CSF-venous pump’)
- Maximizes CBF by transforming pulsatile arterial flow to smooth capillary flow
- The windkessel is ***tuned***, and can be altered by heart rate, inertia, compliance, and damping



# Communicating hydrocephalus is an *asymmetrically* broken notch filter

- CSF *links* different parts of the cranial cavity, and solves the mechanical problems associated with complex geometry in a tuned notch filter
- CBF, ICP, and capillary integrity depend on integrity of the notch filter
- Hydrocephalus disturbs the dynamics of the intracranial notch filter by changing CSF pathway impedance

•In hydrocephalus, CSF pulsations are unevenly distributed

•Asymmetrical breakdown of the notch filter dilates ventricles, and increases capillary and venous pulse pressure, which may contribute to malabsorption of CSF

•Slit ventricle can be modeled as a ‘narrow’ notch with an excessively high Q factor

•The notch filter model suggests that therapeutic alterations of intracranial compliance and heart rate may be of value in improving intracranial dynamics in hydrocephalus

# Current research

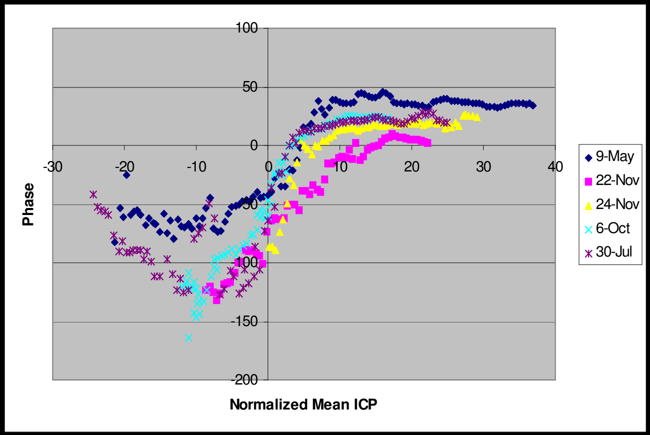
- Anatomically-selective kaolin induced hydrocephalus in a rat model (Pat, Gia)
- 9.4 T MRI vascular and CSF flow studies (Mark)
- Lymphatic absorption of CSF (Miles Johnston)
- Histopathological studies (Pat)
- Carotid pressure and ICP analysis of notch filter in rat model of hydrocephalus
- Two-photon confocal microscopy of capillary flow and pulsatility in Pat's hydrocephalus model (Mark, Mike and Bryan Bertoglio)
- ICP waveform analysis in clinical hydrocephalus (Per)

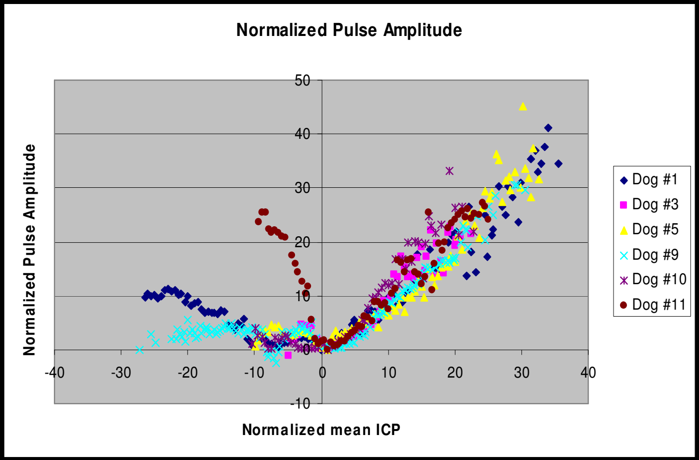
- Feyerabend wikipedia anarchy in science

John von Neumann fathered mathematical game theory and had a big hand in launching theoretical computer science-surely two major recent examples of science fertilizing mathematics. So his thoughts on our question carry great weight. In an essay called "The Mathematician," von Neumann sermonized memorably in terms that the advocate could approve of: As a mathematical discipline travels far from its empirical source, or still more, if it is a second and third generation only indirectly inspired by ideas coming from "reality," it is beset with very grave dangers. It becomes more and more purely aestheticizing, more and more purely l'art pour l'art. This need not be bad, if the field is surrounded by correlated subjects, which still have closer empirical connections, or if the discipline is under the influence of men with an exceptionally well-developed taste. But there is a grave danger that the subject will develop along the line of least resistance, that the stream, so far from its source, will separate into a multitude of insignificant branches, and that the discipline will become a disorganized mass of details and complexities. In other words, at a great distance from its empirical source, or after much "abstract" inbreeding, a mathematical subject is in danger of degeneration. At the inception the style is usually classical; when it shows signs of becoming baroque, then the danger signal is up.2

# Normalized phase and amplitude

- Graph of ICP normalized to each dog's baseline pressure shows that normal phase in at the mid-point (inflection point) of the curve
- Normal pulse amplitude is at a minimum



# The intracranial windkessel is a *tuned* notch filter, a rectifier, and a venous pump

- Maximizes protection of brain capillaries from cardiac pulsatility
- Maximizes CBF by transforming pulsatile arterial flow to smooth capillary flow
- Reflects cardiac pulse to veins ('CSF-venous pump')
- The windkessel is ***tuned***, and can be altered by heart rate, inertia, compliance, and damping