# QUELS

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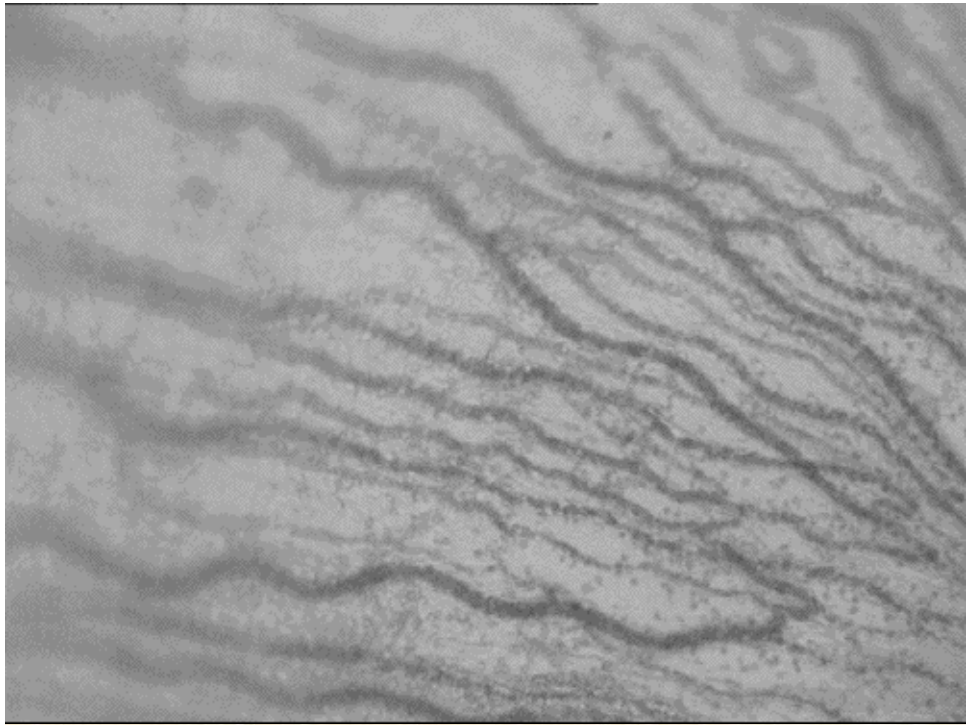
# Evolution

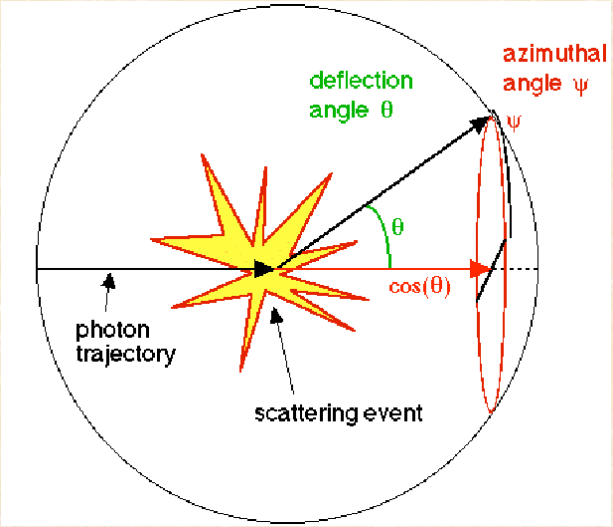
- The first measurements of micro-vascular blood flow employing the Doppler shift of monochromatic light
  - Rabbit eye: Riva et al. 1972
    - *Velocimetry and doppler principle*
  - Skin microcirculation: Stern 1975
    - *Diffuse backscattered with speckle analysis*



# Theory principle

- **Coherent** light directed toward a tissue will be scattered by moving objects and by static tissue structures
- Changes in the frequency of the light will occur according to the **Doppler principle**,
- If the remitted light is detected by a photodetector, **optical mixing** of light shifted and unshifted in frequency will result in a stochastic photocurrent
- The power spectral density of which depends on the *number* of RBCs and their *shape* and *velocity distribution* within the *scattering volume*.

# Anisotropy g




# Anisotropy definition

$$g = \int_0^{\pi} p(\theta)\cos\theta 2\pi \sin\theta d\theta = <\cos\theta>, \text{ where } \int_0^{\pi} p(\theta) 2\pi \sin\theta d\theta = 1$$

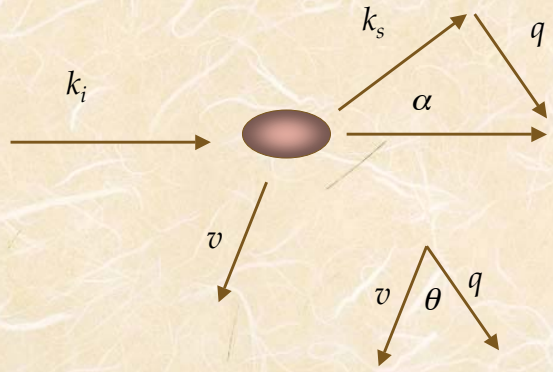
$$g = \int_{-1}^{1} p(\cos\theta)\cos\theta d(\cos\theta), \text{ where } \int_{-1}^{1} p(\cos\theta) d(\cos\theta) = 1$$

# Scattering function

- The angular dependence of scattering is called the scattering function, p(θ) which has units of [$sr^{-1}$] and describes the probability of a photon scattering into a unit solid angle oriented at an angle relative to the photons original trajectory.

# *Single scattering event*

$$\mathbf{E_i} = E_{io} e^{i(\omega t + \mathbf{k}_i \mathbf{r})}$$



## The scattered wave

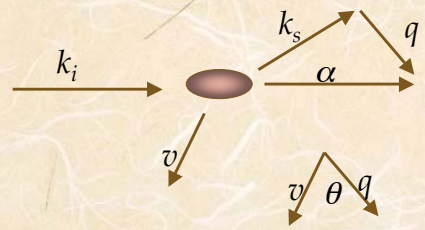
$$\mathbf{E}_s = E_{so} e^{i((\omega - \mathbf{k_i v})t - \mathbf{k_i r_o} - \mathbf{k_s}(\mathbf{r_1} - \mathbf{v}t))} \Rightarrow$$

$$\mathbf{E}_s = E_{so} e^{i\omega t} e^{-i(\mathbf{k_i} - \mathbf{k}_s)\mathbf{v}t} \underbrace{e^{-i(\mathbf{k_i r_0} + \mathbf{k_s r_1})}}_{\text{Time-invariant phase factor}} \Rightarrow$$

## The scattered wave

If $\mathbf{q} = \mathbf{k_i} - \mathbf{k}_s$

$$\mathbf{E}_s = E_{so} e^{i\omega t} e^{-i(\mathbf{q})\mathbf{v}t}$$

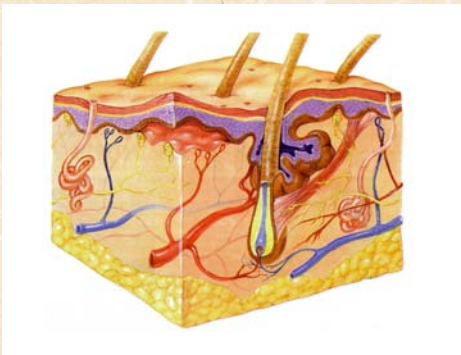



## Scattering and doppler

$$\text{Scattering vector} = q = 2k\sin(\frac{\alpha}{2}) = \frac{4\pi}{\lambda_t}\sin(\frac{\alpha}{2})$$

$$\text{Angular doppler freq.} = \omega_D = \frac{4\pi}{\lambda_t}\sin(\frac{\alpha}{2})v\cos(\theta)$$

## Detection model

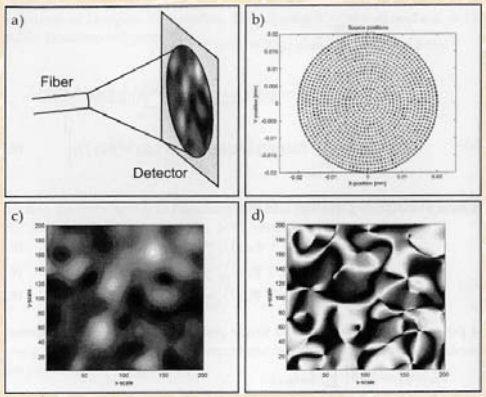


# Coherence area

- When the backscattered light impinges on the surface of a photo detector, a fluctuating speckle pattern is formed
- The frequency and magnitude of intensity fluctuations in the individual coherence areas of this speckle pattern are related to the average speed and number of moving objects within the scattering volume

# Coherence area

- Pertaining to an electro-magnetic wave, the area of a surface perpendicular to the direction of propagation, over which the electromagnetic wave maintains a specified degree of coherence. *Note:* The specified degree of coherence is usually taken to be 0.88 or greater.




# Coherence area

- The area of a single speckle (A) is determined by the
  - distance (D) between source and detector,
  - size of the source ($r_0$) and
  - laser wavelength λ

$$A_c = \frac{\lambda^2}{\Omega} = \frac{\lambda^2 D^2}{2\pi r_0}$$

# Coherence area

- The total number of coherence areas (N) are:

$$N = \frac{A_{\text{det}}}{A_c} = \frac{2\pi r_0 A_{\text{det}}}{\lambda^2 D^2}$$

# Coherence area

- Each speckle area independent and therefore the stationary current and the time-varying current scale differently against the number of coherence areas:

$$i_{dc} \propto N$$

$$i_{ac} \propto \sqrt{N}$$

# Photocurrent

Total photocurrent $i(t) = \sum_{j=1}^{N} (< i_c > + \Delta i_{cj}(t))$

$< i_c >$ = average photocurrent for area j

$\Delta i_{cj}(t)$ = fluctuating photocurrent for area j

N = number of coherence areas

Note:
Noise factors neglected

# A stochastic process is best described with the autocorrelation function

$$< i(0) i^*(\tau) > = \sum_{j=1}^{N} (< i_c > + \Delta i_{cj}(0)) \sum_{l=1}^{N} (< i^*_c > + \Delta i^*_{cl}(\tau)) =$$

$$\sum_{j=1}^{K} \sum_{l=1}^{N} < i_c > < i^*_c > + \sum_{j=1}^{N} \sum_{l=1}^{N} \Delta i_{cj}(0) \Delta i^*_{cl}(\tau) =$$

$$N^2 < i_c >^2 + N < \Delta i_c(0) \Delta i_c^*(\tau) >$$

# Photocurrent acf

Since the photo detector is a square-law detector

$$\left\langle \boldsymbol{i_c}(0) \boldsymbol{i}^*_{\boldsymbol{c}}(\tau) \right\rangle \propto \left\langle \mathbf{E}(0) \mathbf{E}^*(0) \mathbf{E}(\tau) \mathbf{E}^*(\tau) \right\rangle$$

Where the E vector represents the sum of the electromagnetic field vectors impinging on the actual coherence area

# Photocurrent acf

This can also be described by the second order correlation function

$$g^{(2)}(\tau) = 1 + \left|g^{(1)}(\tau)\right|^2 = \left\langle I(t)I(t+\tau)\right\rangle$$

and

$$g^{(1)}(\tau) = \left\langle E(t)E(t+\tau)\right\rangle$$

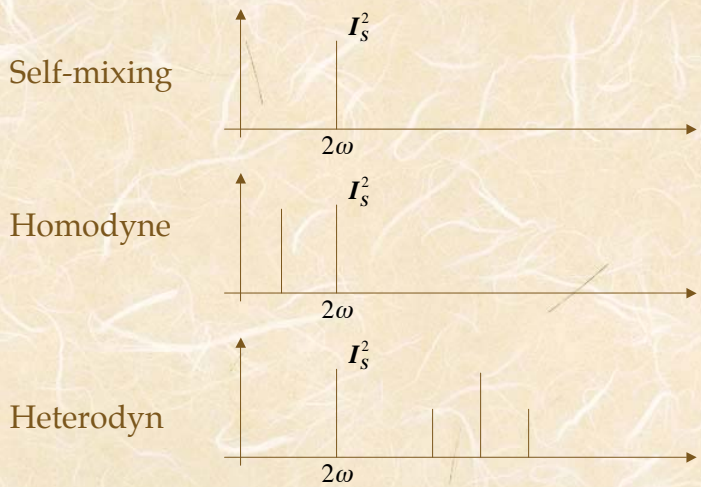
# Sixteen terms of E-fields

| | |
|---|---|
| $\left\langle E_S(0)E_S^*(0)E_S(\tau)E_S^*(\tau)\right\rangle$ | $Homodyn$ |
| $\left\langle E_S(0)E_S^*(0)E_R(\tau)E_R^*(\tau)\right\rangle$ | $\langle i_S\rangle\langle i_R\rangle = DC$ |
| $\left\langle E_S(0)E_S^*(0)E_S^*(\tau)E_R(\tau)\right\rangle$ | 0 |
| $\left\langle E_S(0)E_S^*(0)E_S(\tau)E_R^*(\tau)\right\rangle$ | 0 |
| $\left\langle E_R(0)E_R^*(0)E_S(\tau)E_S^*(\tau)\right\rangle$ | $\langle i_R\rangle\langle i_S\rangle = DC$ |
| $\left\langle E_R(0)E_R^*(0)E_R(\tau)E_R^*(\tau)\right\rangle$ | $\langle i_R\rangle^2 = DC$ |
| $\left\langle E_R(0)E_R^*(0)E_S^*(\tau)E_R(\tau)\right\rangle$ | 0 |
| $\left\langle E_R(0)E_R^*(0)E_S(\tau)E_R^*(\tau)\right\rangle$ | 0 |

# Sixteen terms of E-fields

| | |
|---|---|
| $\left\langle E_S^*(0)E_R(0)E_S(\tau)E_S^*(\tau)\right\rangle$ | 0 |
| $\left\langle E_S^*(0)E_R(0)E_R(\tau)E_R^*(\tau)\right\rangle$ | 0 |
| $\left\langle E_S^*(0)E_R(0)E_S^*(\tau)E_R(\tau)\right\rangle$ | $Heterodyn, HP$ |
| $\left\langle E_S^*(0)E_R(0)E_S(\tau)E_R^*(\tau)\right\rangle$ | $Heterodyn, LP$ |
| $\left\langle E_S(0)E_R^*(0)E_S(\tau)E_S^*(\tau)\right\rangle$ | 0 |
| $\left\langle E_S(0)E_R^*(0)E_R(\tau)E_R^*(\tau)\right\rangle$ | 0 |
| $\left\langle E_S(0)E_R^*(0)E_S^*(\tau)E_R(\tau)\right\rangle$ | $Heterodyn, LP$ |
| $\left\langle E_S(0)E_R^*(0)E_S(\tau)E_R^*(\tau)\right\rangle$ | $Heterodyn, HP$ |

# Light beat detection



# The overall acf of the photocurrent

$$\left\langle i_c(0) i^*_c(\tau) \right\rangle = \underbrace{2 i_{Re} i_{Sc} + i_{Re}^2 + i_{Sc}^2}_{\text{Stationary}} +$$

$$\underbrace{i_{Re} i_{Sc} \left( \left\langle e^{i\mathbf{q}\mathbf{v}\tau} \right\rangle + \left\langle e^{-i\mathbf{q}\mathbf{v}\tau} \right\rangle \right)}_{\text{heterodyne - mixing}} +$$

$$\underbrace{i_{Sc}^2 \left\langle \frac{1}{S^2} \sum_{k=1, k \neq l}^{S} \sum_{l=1}^{S} e^{i(\mathbf{q}_k \mathbf{v}_k - \mathbf{q}_l \mathbf{v}_l)\tau} \right\rangle}_{\text{homodyne - mixing}}$$

# The overall acf of the photocurrent

For a low and moderate RBC concentration ($C_{RBC}$), $i_{Sc}$ is proportional to the total photocurrent produced by a single coherence area and $i_{Sc} \approx C_{RBC} i_{Re}$ for $i_{Re} >> i_{Sc}$.

# The Doppler component

$$\left\langle e^{i\mathbf{q}\mathbf{v}\tau} \right\rangle = \left\langle \frac{1}{S} \sum_{k=1}^{S} e^{i(\mathbf{q}_k \mathbf{v}_k \tau)} \right\rangle$$

# Derivation of $\left\langle e^{i\mathbf{q}\mathbf{v}\tau} \right\rangle_{\mathbf{v}}$

$$\left\langle e^{i\mathbf{q}\mathbf{v}\tau} \right\rangle_{\mathbf{v}} = \int_{\mathbf{v}} N_0(\mathbf{v}) e^{i\mathbf{q}\mathbf{v}\tau} d\mathbf{v}$$

Assuming that the RBCs move randomly without any preferential direction, and making the transformation to spherical coordinates,

$$\left\langle e^{i\mathbf{q}\mathbf{v}\tau} \right\rangle_{\mathbf{v}} = \int_{\mathrm{v}=0}^{\infty} N(\mathrm{v}) \frac{\sin(\mathrm{q}\mathrm{v}\tau)}{\mathrm{q}\mathrm{v}\tau} \mathrm{dv}$$

One-dimensional distribution $N(v) = 4\pi \mathrm{v}^2 N_0(\mathbf{v})$

# Derivation of $\left\langle\left\langle e^{i\mathbf{q}\mathbf{v}\tau}\right\rangle_{\mathbf{v}}\right\rangle_{\mathbf{q}}$

$$\left\langle\left\langle e^{i\mathbf{q}\mathbf{v}\tau}\right\rangle_{\mathbf{v}}\right\rangle_{\mathbf{q}} = \int_{\alpha=0}^{\pi}\left\langle e^{i\mathbf{q}\mathbf{v}\tau}\right\rangle_{\mathbf{v}} S_o(\mathbf{q}(\alpha))d\alpha$$

Where $S_o$ is the scattering vector distribution

Assuming circular symmetry with respect to $\mathbf{k}_i$ then

$$S(q(\alpha)) = \frac{2S_0(\mathbf{q}(\alpha))}{\sin(\alpha)}$$

# continue

$$\left\langle\left\langle e^{i\mathbf{q}\mathbf{v}\tau}\right\rangle_{\mathbf{v}}\right\rangle_{\mathbf{q}} = \int_{\alpha=0}^{\pi}\int_{\mathrm{v}=0}^{\infty} N(\mathrm{v})\frac{\sin(\mathrm{q}\mathrm{v}\tau)}{2\mathrm{q}\mathrm{v}\tau} S(\mathrm{q}(\alpha))\sin(\alpha)d\mathrm{v}d\alpha$$

This is the relation for a one-dimensional RBC velocity N(v) and a scattering vector $S_o(q)$ distribution to the measured photocurrent acf produced by the heterodyn mixing

# Wiener-Khintchine Theorem

Let x(n) be a WSS random process with autocorrelation sequence

$$r_{xx}(m) = E\left[x(n+m)x^*(n)\right]$$

The power spectral density is defined as the Discrete Time Fourier Transform of the autocorrelation sequence

$$P_{xx}(f) = T\sum_{n=-\infty}^{\infty} r_{xx}(m)e^{-i2\pi fmT}$$

where T is the sampling interval.

The signal is assumed to be bandlimited in frequency to ± 1/2T
And periodic in frequency with period 1/T

# Wiener-Khintchine Theorem

The inverse DTFT is

$$r_{xx}(m) = \int_{-1/2T}^{1/2T} P_{xx}(f)e^{i2\pi fmT}df$$

And, $r_{xx}(0)$ is the average power

$$r_{xx}(0) = \int_{-1/2T}^{1/2T} P_{xx}(f)df$$

Due to the property $r_{xx}(-m)= r^*_{xx}(m)$, the PSD must be a strictly real, nonnegative function.

# Power Spectral Density

Using the Wiener-Khintchine theorem, the power spectral density $P_c(\omega)$ of the heterodyne mixing term can be calulated

$$P_c(\omega) \propto C_{RBC} i_{Re}^{\ 2} \int_{v=0}^{\infty} N(v) \int_{\alpha=0}^{\pi} \sin(\alpha) S(q(\alpha)) \int_{\tau=-\infty}^{\infty} \frac{\sin(qv\tau)}{qv\tau} e^{i\omega\tau} d\tau d\alpha dv$$

If we assume $q = \frac{4\pi}{\lambda_t} \sin(\frac{\alpha}{2})$ then

$$P_c(\omega) \propto C_{RBC} i_{Re}^{\ 2} \int_{v=\frac{\lambda_t \omega}{4\pi}}^{v_{max}} \frac{N(v)}{v} \int_{q=\frac{\omega}{v}}^{\frac{4\pi}{\lambda_t}} S(q) dq dv$$

# continue

Since $i_{re}$ scales with $N^2$ and $i_{sc}$ scales with N normalisation with the total light intensity gives:

$$\boldsymbol{P}(\omega) \propto \frac{C_{RBC}}{N} \int_{v=\frac{\lambda_t \omega}{4\pi}}^{v_{max}} \frac{\boldsymbol{N}(v)}{v} \int_{q=\frac{\omega}{v}}^{\frac{4\pi}{\lambda_t}} \boldsymbol{S}(\boldsymbol{q}) \boldsymbol{dq} dv$$

# Perfusion value

To calculate $\int \omega^n P(\omega) d\omega$ we assume an arbitrary velocity distribution:

$$N(v) = \sum N_{v_o} \delta(v - v_0)$$

The contribution to $\int \omega^n \boldsymbol{P}(\omega) \boldsymbol{d}\omega$ from $N_0(v)$ is:

$$\int \omega^n \boldsymbol{P}(\omega) \boldsymbol{d}\omega \propto \frac{C_{RBC}}{\boldsymbol{K}} \int_{\omega=0}^{\infty} \omega^n \int_{v=\frac{\lambda_t \boldsymbol{w}}{4\pi}}^{v_{max}} \frac{\boldsymbol{N}(v)}{v} \int_{q=\frac{\omega}{v}}^{\frac{4\pi}{\lambda_t}} \boldsymbol{S}(\boldsymbol{q}) \boldsymbol{dq} dv \boldsymbol{d}\omega$$

$$= \frac{C_{RBC} \boldsymbol{N}_{v_0}}{\boldsymbol{K}} \int_{\omega=0}^{\infty} \omega^n \int_{v=\frac{\lambda_t \boldsymbol{w}}{4\pi}}^{\infty} \frac{\delta(v - v_0)}{v} \int_{q=\frac{\omega}{v}}^{\frac{4\pi}{\lambda_t}} \boldsymbol{S}(\boldsymbol{q}) \boldsymbol{dq} dv d\omega$$

$$= \frac{C_{RBC} N_{v_0}}{K} \int_{x=0}^{\infty} (x v_0)^n \int_{v=\frac{\lambda_t x v_0}{4\pi}}^{\infty} \frac{\delta(v - v_0) v_0}{v} \int_{q=\frac{x v_0}{v}}^{\frac{4\pi}{\lambda_t}} S(q) dq dv dx$$

$$= \frac{C_{RBC} N_{v_0} v_0^n}{K} \underbrace{\int_{x=0}^{\infty} x^n \int_{q=x}^{\frac{4\pi}{\lambda_t}} S(q) dq dx}_{constant}$$

# Contribution from the complete velocity spectrum

$$\int \omega^n P(\omega) d\omega \propto \frac{C_{RBC}}{K} \underbrace{\int_{v=0}^{\infty} v^n N(v)\, dv}_{\langle v^n \rangle} \propto C_{RBC} \langle v^n \rangle$$

# Sampling volume

If the spatial distribution of those photons within the sampling volume that are available for detection is described by a weighing function H(**r**) that is dependent on the tissue optical properties at location **r**, the output signal from the laser Doppler flowmeter is proposed to be

$$\int_{\mathbf{r}^3} H(\mathbf{r}) v(\mathbf{r}) C_{RBC}(\mathbf{r}) d\mathbf{r}^3$$

# Advantages

- LDF makes possible noninvasive recording and imaging of tissue perfusion with minimal impact on microcirculation.
- LDF devices are easy to use.
- Continuous recordings over unlimited periods of time can be made with LDPM.
- Two-dimensional perfusion maps can be visualized by LDPI.
- The theoretical basis of LDF is well established.

# Disadvantages

- No absolute calibration is possible, and results obtained from different organs cannot be directly
- compared because of variations in photon path lengths due to the different optical properties of the tissue.
- Results obtained by recording at a single site using LDPM may not be representative for the entire tissue.
- LDF does not distinguish between nutritive (capillary) perfusion and global tissue perfusion.
- LDPI assumes steady-state conditions in perfusion during the image-capturing period, which may amount to 4 min or longer.