Russian Federal Nuclear Center –
Zababakhin Institute of Applied Physics

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“ROSATOM” STATE CORPORATION

Early photon fluorescence molecular tomography with Lyubimov reconstruction model: sensitivity functions and resolution estimates

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SFM 2017, Saratov,
September 25-30 2017

Contents

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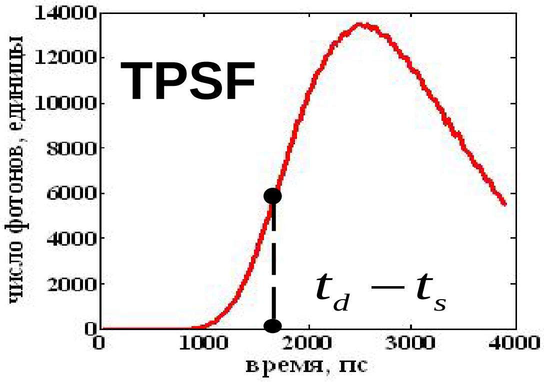
Measurement data: comparison with DOT

❑ Time-resolved optical projections (DOT)

$$g(\mathbf{r}_s,t_s,\mathbf{r}_d,t_d)=\frac{\Gamma_0(\mathbf{r}_s,t_s,\mathbf{r}_d,t)\big|_{t=t_d}-\Gamma(\mathbf{r}_s,t_s,\mathbf{r}_d,t)\big|_{t=t_d}}{\Gamma_0(\mathbf{r}_s,t_s,\mathbf{r}_d,t)\big|_{t=t_d}}$$

$\Gamma(\mathbf{r}_s,t_s,\mathbf{r}_d,t)$ **is the temporal point spread function (TPSF)**



❑ Ratio of fluorescence flux to exciting radiation flux (FMT)

$$g_f(\mathbf{r}_s,t_s,\mathbf{r}_d,t_d)=\frac{\Gamma_f(\mathbf{r}_s,t_s,\mathbf{r}_d,t)\big|_{t=t_d}}{\Gamma_e(\mathbf{r}_s,t_s,\mathbf{r}_d,t)\big|_{t=t_d}}$$

Here $e,\ f$ **are indices with respect to exciting radiation and fluorescence, respectively**

Basic equations

System of diffusion equations

$$\frac{1}{c}\frac{\partial}{\partial t}\varphi_e(\mathbf{r},t) - D_e\Delta\varphi_e(\mathbf{r},t) + \mu_{ae}(\mathbf{r})\varphi_e(\mathbf{r},t) = S(\mathbf{r},t)$$

$$\frac{1}{c}\frac{\partial}{\partial t}\varphi_f(\mathbf{r},t) - D_f\Delta\varphi_f(\mathbf{r},t) + \mu_{af}(\mathbf{r})\varphi_f(\mathbf{r},t) = S_f(\mathbf{r},t)$$

$$S_f(\mathbf{r},t) = \gamma\int_{t_s}^{t}\frac{\delta\mu_{af}(\mathbf{r})}{\tau_n}\varphi_e(\mathbf{r},t')\exp\left(-\frac{t-t'}{t_n}\right)dt'$$

Asymptotic estimate for the source function

$$S_f(\mathbf{r},t) = \frac{\gamma\delta\mu_{af}(\mathbf{r})\cdot 4D_e ct^2}{\tau_n\,|\mathbf{r}|^2 + 4D_e ct^2}\varphi_e(\mathbf{r},t)$$

V.V. Lyubimov, Opt. Spectrosc. 88: 282 (2000)

Solutions for the photon densities

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$$\varphi_f(\mathbf{r},t) = \int_{t_s}^{t} c\,dt' \int_V \frac{\gamma\delta\mu_{af}(\mathbf{r}') \cdot 4D_e c t'^2}{\tau_n |\mathbf{r}'|^2 + 4D_e c t'^2} \varphi_e(\mathbf{r}',t') G_f(\mathbf{r}-\mathbf{r}',t-t') d^3r'$$

$$\varphi(\mathbf{r},t) = \int_V G(\mathbf{r}-\mathbf{r}',t-t')\varphi(\mathbf{r}',t) d^3r'$$

$$\frac{\varphi_f(\mathbf{r},t)}{\varphi_e(\mathbf{r},t)} = \int_{t_s}^{t} c\,dt' \int_V \frac{\gamma\delta\mu_{af}(\mathbf{r}') \cdot 4D_e c t'^2}{\tau_n |\mathbf{r}'|^2 + 4D_e c t'^2} \frac{C_f(\mathbf{r}-\mathbf{r}',t-t')}{G_e(\mathbf{r}-\mathbf{r}',t-t')} \times \frac{\varphi_e(\mathbf{r}',t') G_e(\mathbf{r}-\mathbf{r}',t-t')}{\int_V \varphi_e(\mathbf{r}',t') G_e(\mathbf{r}-\mathbf{r}',t-t') d^3r'} d^3r'$$

Equation for the flux ratio

$$\frac{\Gamma_f(\mathbf{r}_s,t_s,\mathbf{r}_d,t)\,|_{t=t_d}}{\Gamma_e(\mathbf{r}_s,t_s,\mathbf{r}_d,t)\,|_{t=t_d}} = \gamma \int_{t_s}^{t_d} c\,dt \int_V \frac{\delta\mu_{af}(\mathbf{r})\cdot 4D_e c t^2}{\tau_n\,|\,\mathbf{r}\,|^2 + 4D_e c t^2}$$

$$\times \frac{\frac{\partial}{\partial\eta}G_f(\mathbf{r}_d-\mathbf{r},t_d-t)}{\frac{\partial}{\partial\eta}G_e(\mathbf{r}_d-\mathbf{r},t_d-t)} \times \frac{\varphi_e(\mathbf{r},t)\frac{\partial}{\partial\eta}G_e(\mathbf{r}_d-\mathbf{r},t_d-t)}{\int_V \varphi_e(\mathbf{r},t)\frac{\partial}{\partial\eta}G_e(\mathbf{r}_d-\mathbf{r},t_d-t)\,d^3r}\,d^3r$$

$\partial/\partial\eta$ **is the derivative in direction of the outer normal to the boundary at the point** $\mathbf{r}_d$

Our simplifying assumptions

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- The scattering medium and the fluorescence inhomogeneity have identical optical parameters $\mu_{ae} \cong \mu_{af}$ and $D_e \cong D_f$.
- The Green function derivatives of exciting radiation and fluorescence are equal each other.
- The velocity of the center of instantaneous photon distributions is constant in the most part of the volume.

Resulting equation that describes the model

$$\frac{\Gamma_f(\mathbf{r}_s,t_s,\mathbf{r}_d,t)\big|_{t=t_d}}{\Gamma_e(\mathbf{r}_s,t_s,\mathbf{r}_d,t)\big|_{t=t_d}} \cong \int_V W_{\delta\mu_{af}}(\mathbf{r}_s,t_s,\mathbf{r}_d,t_d,\mathbf{r})\,\delta\mu_{af}(\mathbf{r})\,d^3r,$$

where

$$W_{\delta\mu_{af}}(\mathbf{r}_s,t_s,\mathbf{r}_d,t_d) = \int_{t_s}^{t_d} \frac{4\gamma D_e c^2 t^2}{\tau_n|\mathbf{r}|^2+4D_e c t^2} \times \frac{G_e(\mathbf{r}-\mathbf{r}_s,t-t_s)\dfrac{\partial}{\partial\eta}G_e(\mathbf{r}_d-\mathbf{r},t_d-t)}{\dfrac{\partial}{\partial\eta}G_e(\mathbf{r}_d-\mathbf{r}_s,t_d-t_s)}\,dt$$

is the sensitivity function that is responsible for reconstruction of the fluorophore absorption coefficient

Comparison of FMT with DOT

❑ Diffuse optical tomography of absorbing inhomogeneities

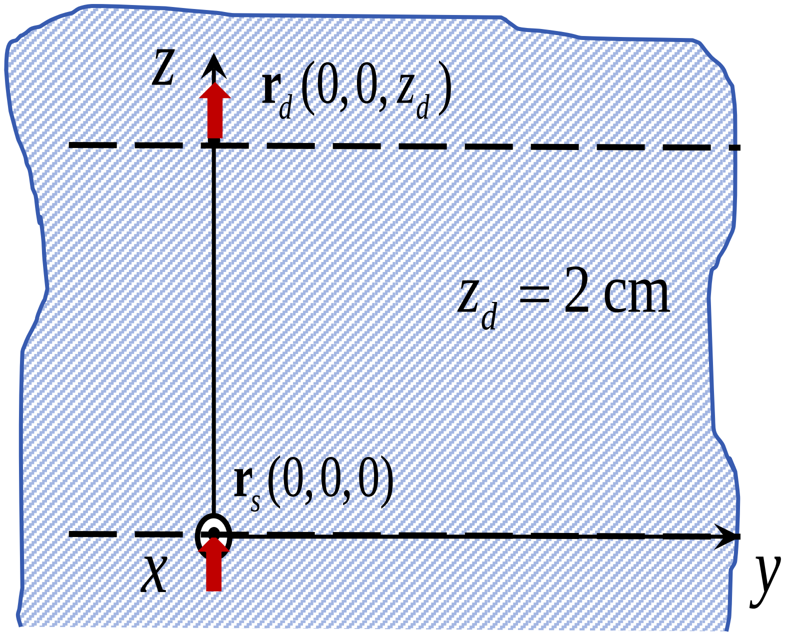
$$W_{\mu_a}(\mathbf{r}_s,\mathbf{r}_d,\mathbf{r},t_d) = c\int_0^{t_d} \frac{G(\mathbf{r}-\mathbf{r}_s,t)\,\partial G(\mathbf{r}_d-\mathbf{r},t_d-t)/\partial\eta}{\partial G(\mathbf{r}_d-\mathbf{r}_s,t_d)/\partial\eta}\,dt$$

A.B. Konovalov, V.V. Vlasov, Quantum Electron. 44: 719 (2014)

❑ Fluorescence molecular tomography

$$W_{\delta\mu_{af}}(\mathbf{r}_s,\mathbf{r}_d,\mathbf{r},t_d) = c\gamma\int_0^{t_d} \frac{4Dct^2}{\tau_n\,|\mathbf{r}|^2 + 4Dct^2}\,\frac{G(\mathbf{r}-\mathbf{r}_s,t)\,\partial G(\mathbf{r}_d-\mathbf{r},t_d-t)/\partial\eta}{\partial G(\mathbf{r}_d-\mathbf{r}_s,t_d)/\partial\eta}\,dt$$

Transmission geometry as a simplest example



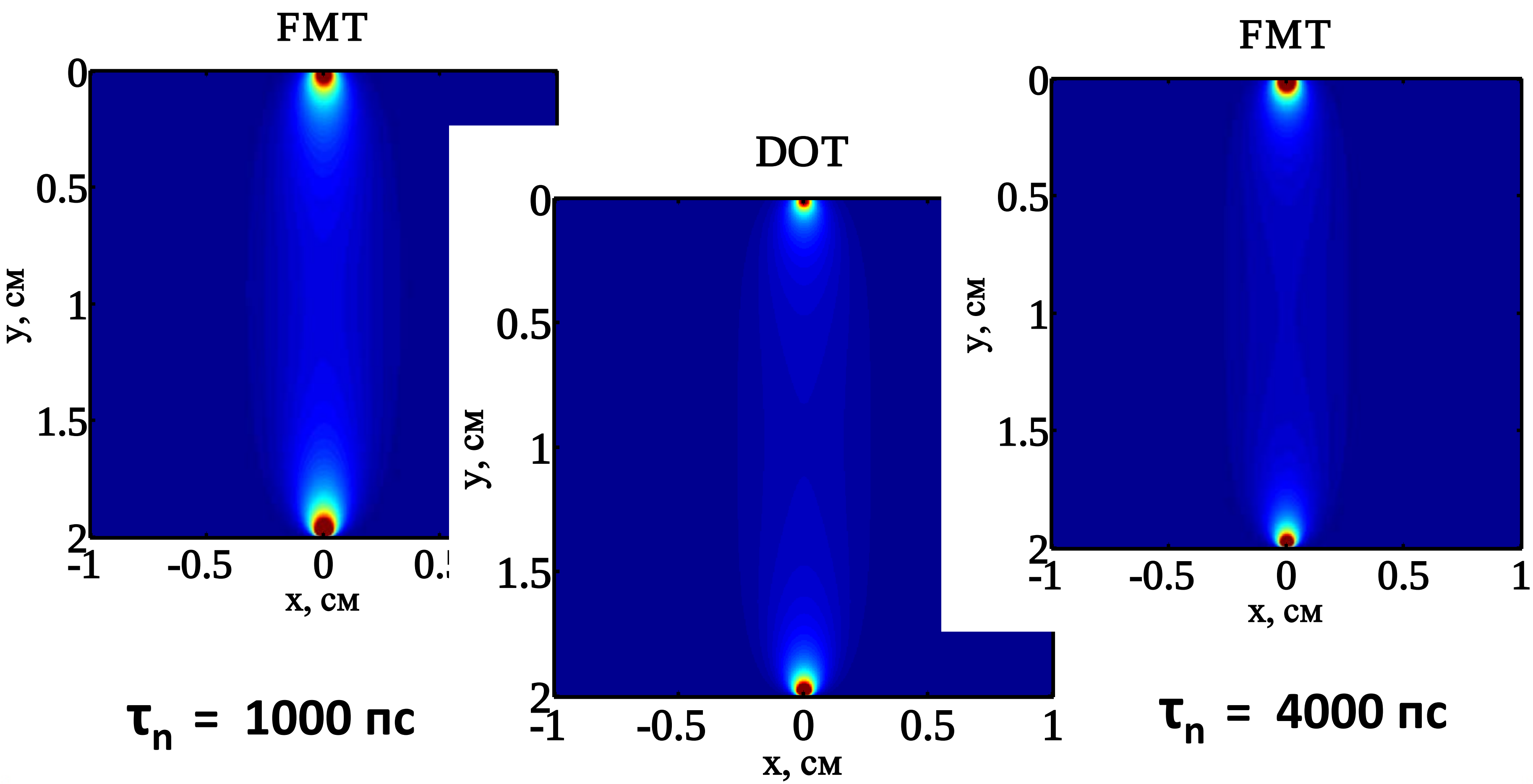
$$G_e(\mathbf{r}',\mathbf{r},t',t) = \left[4\pi Dc(t-t')\right]^{-3/2} \exp\left[-\mu_a c(t-t') - \frac{(x-x')^2+(y-y')^2+(z-z')^2}{4Dc(t-t')}\right]$$

$$\frac{G(\ldots)\partial G(\ldots)/\partial\eta}{\partial G(\ldots)/\partial\eta} = \frac{z_d - z}{z_d}(4\pi Dct)^{-3/2}\left(\frac{t_d}{t_d - t}\right)^{5/2} \exp\left[-\frac{x^2t_d^2 + y^2t_d^2 + (zt_d - z_d t)^2}{4Dc(t_d - t)tt_d}\right]$$

The banana-shaped distributions

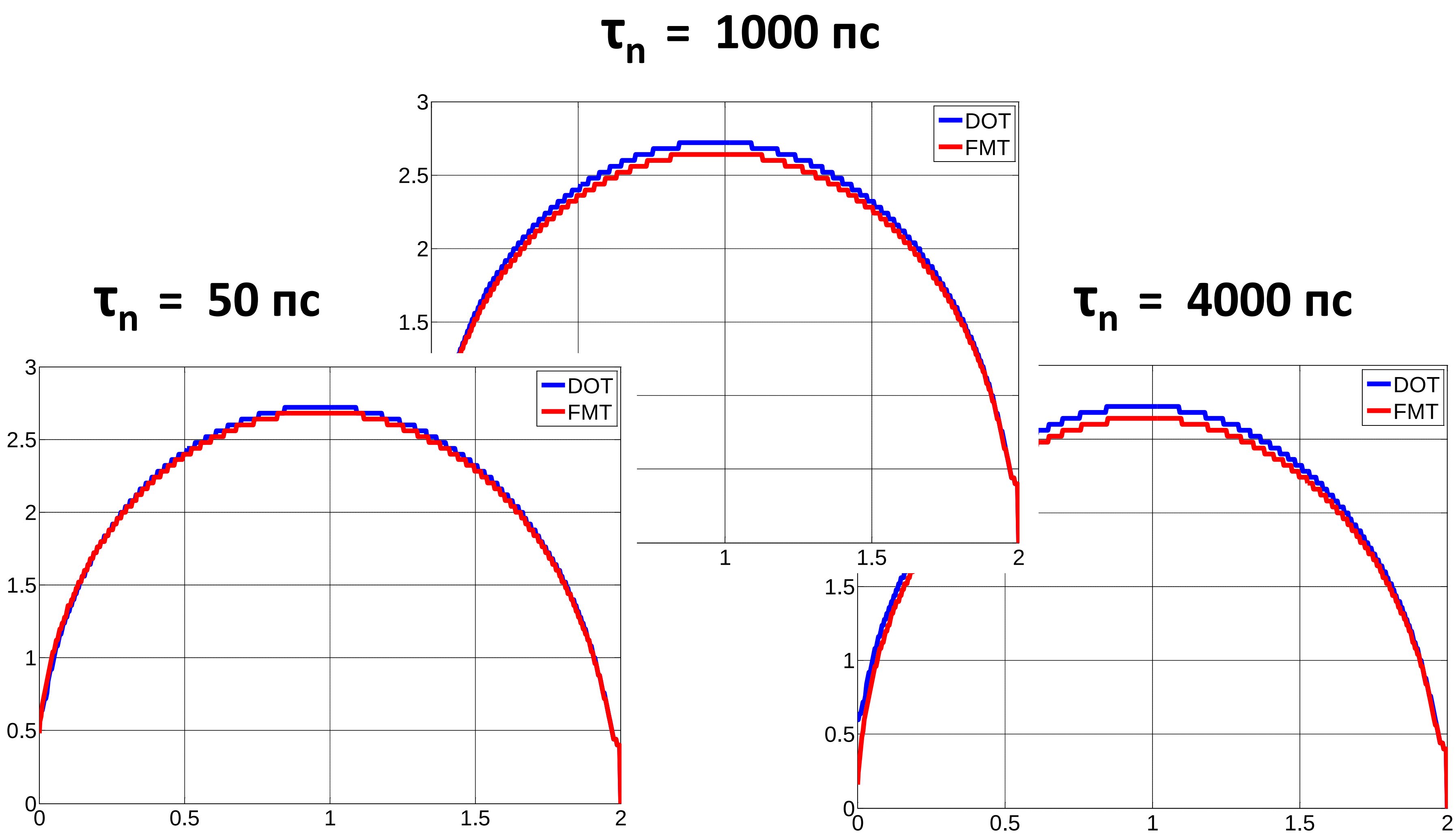
$\mu_a = 0.05 \;\; мм^{-1}$ $\mu_s' = 1.6 \;\; мм^{-1}$ $t_d = 200 \;\; пс$

$c = 0.214 \;\; мм/пс$ $D = 0.19 \;\; мм$



τ_n = 1000 пс **τ_n = 4000 пс**

Standard deviation plots



Characteristics for photon distributions

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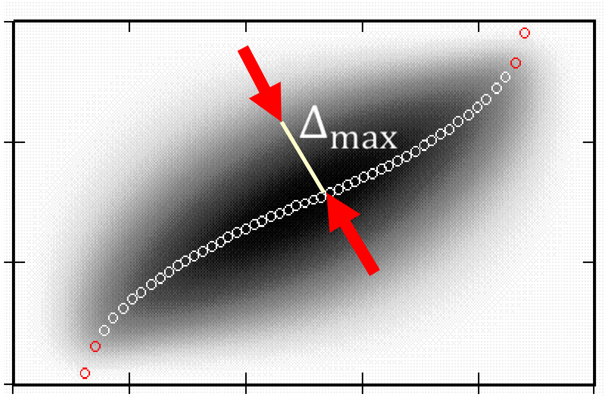


B

- The photon average trajectory (PAT)

$$\mathbf{R}(\mathbf{r}_s,t_s,\mathbf{r}_d,t) = \int_V \mathbf{r} \frac{G(\mathbf{r}-\mathbf{r}_s,t-t_s)\dfrac{\partial}{\partial\eta}G(\mathbf{r}_d-\mathbf{r},t_d-t)}{\dfrac{\partial}{\partial\eta}G(\mathbf{r}_d-\mathbf{r}_s,t_d-t_s)} d^3r$$

- The root-mean-square deviation of photons from the PAT

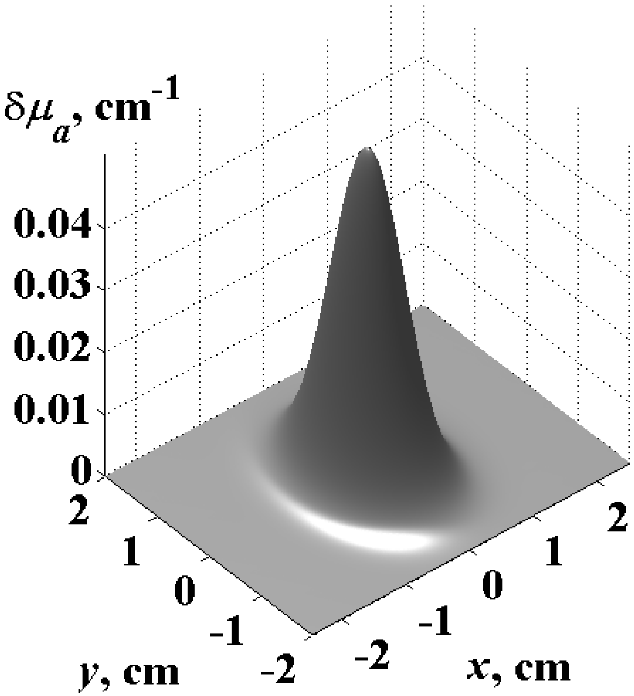
$$\Delta(\mathbf{r}_s,t_s,\mathbf{r}_d,t) = \left[\int_V \left|\mathbf{r}-\mathbf{R}(\mathbf{r}_s,t_s,\mathbf{r}_d,t)\right|^2 \frac{G(\mathbf{r}-\mathbf{r}_s,t-t_s)\dfrac{\partial}{\partial\eta}G(\mathbf{r}_d-\mathbf{r},t_d-t)}{\dfrac{\partial}{\partial\eta}G(\mathbf{r}_d-\mathbf{r}_s,t_d-t_s)} d^3r\right]^{1/2}$$

V.V. Lyubimov, Opt. Spectrosc. 86: 251 (1999)

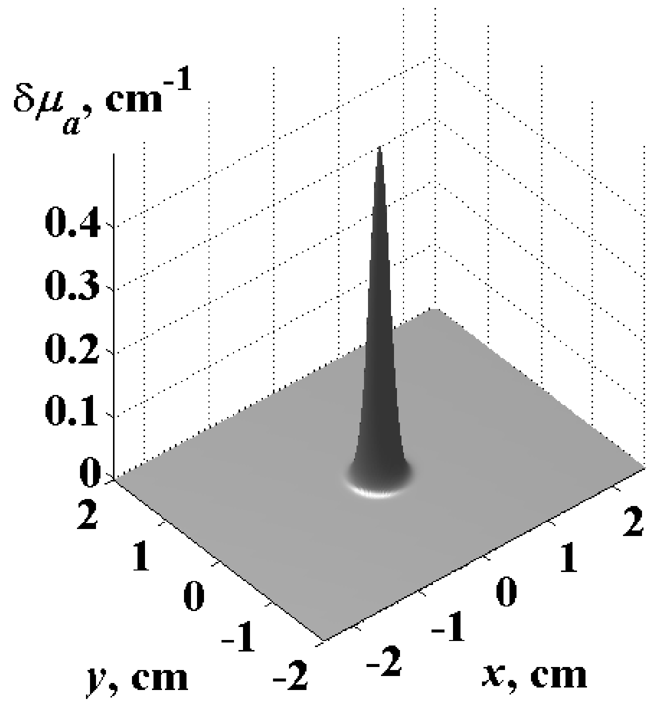
V.V. Lyubimov et al., Phys. Med. Biol. 47: 2109 (2002)

PSFs for transmission geometry

Average trajectories



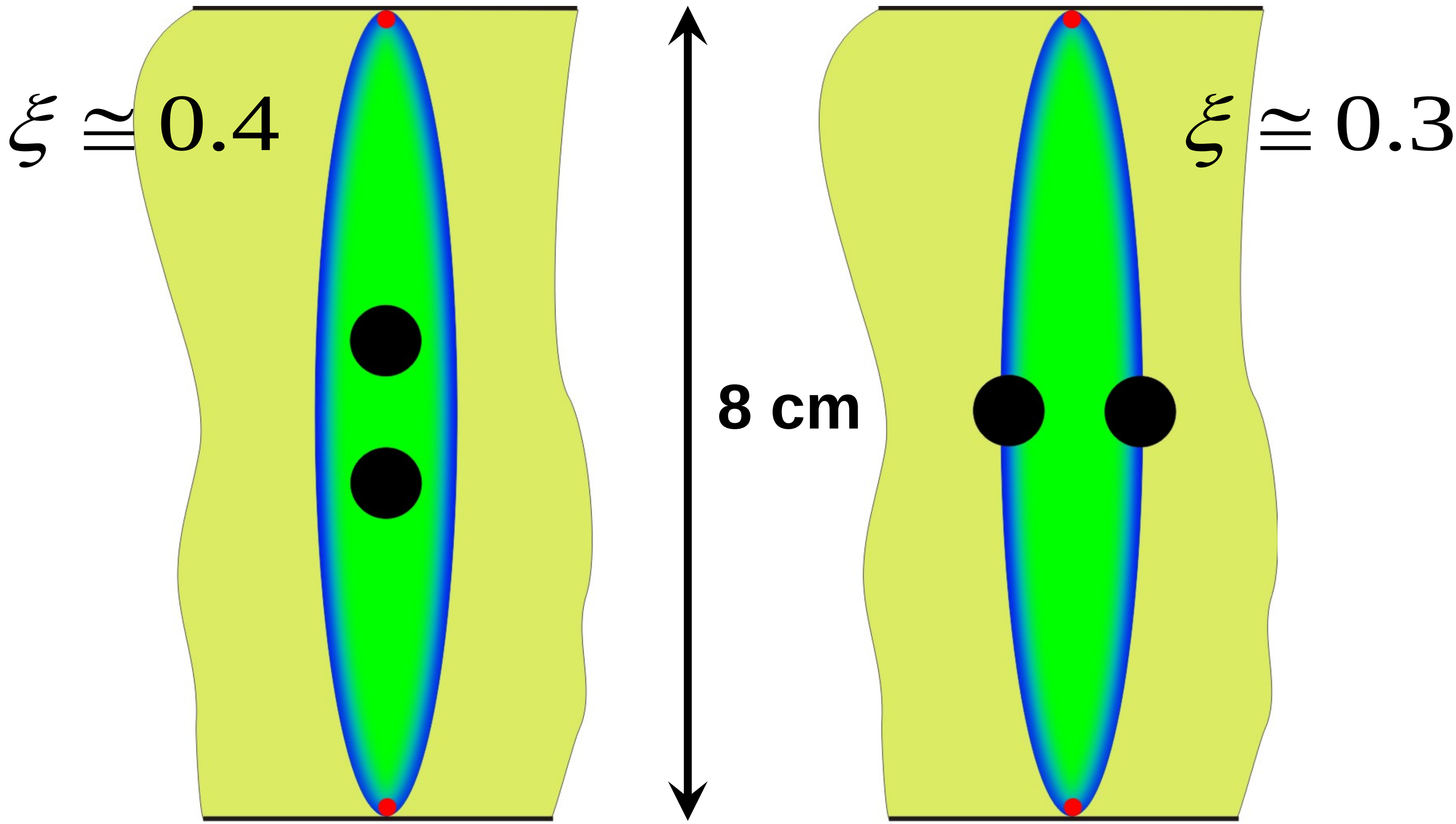
Banana-shaped distributions



$\delta_{\lim} \cong \xi \cdot \Delta_{\max}$, where ξ is a coefficient that depends on the geometry and the reconstruction technique

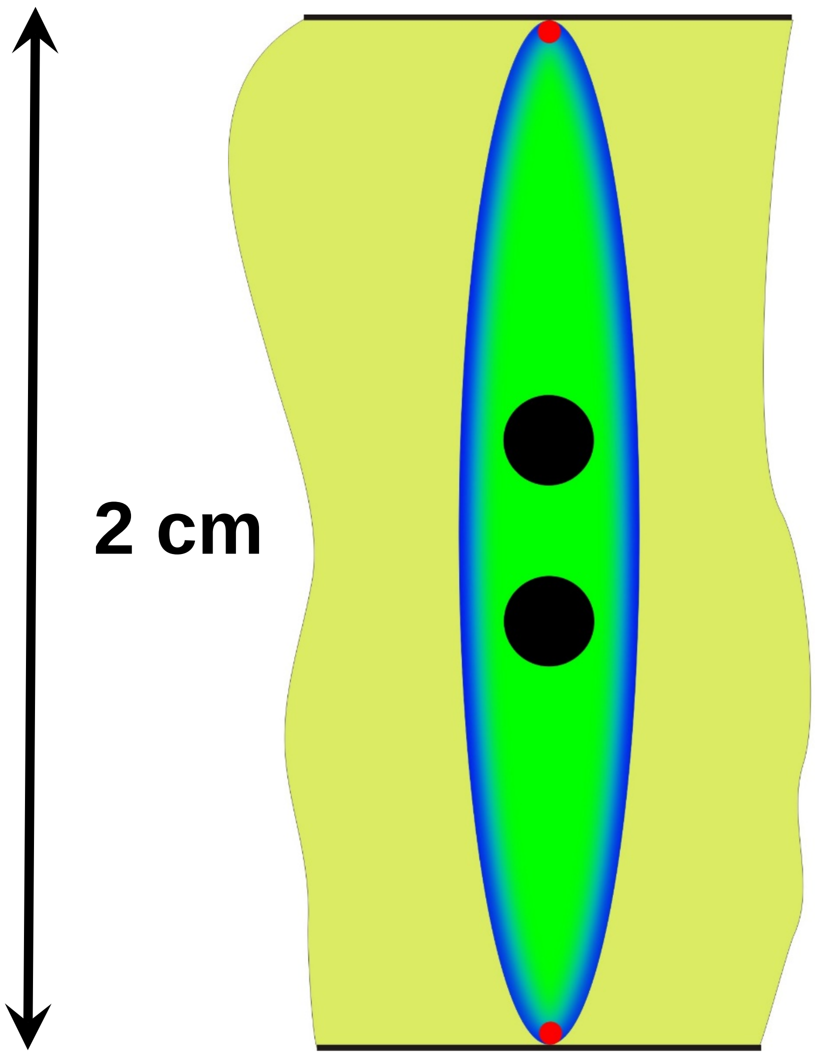
A.B. Konovalov, V.V. Vlasov, Quantum Electron. 44: 239 (2014)

Some estimates for coefficient ξ

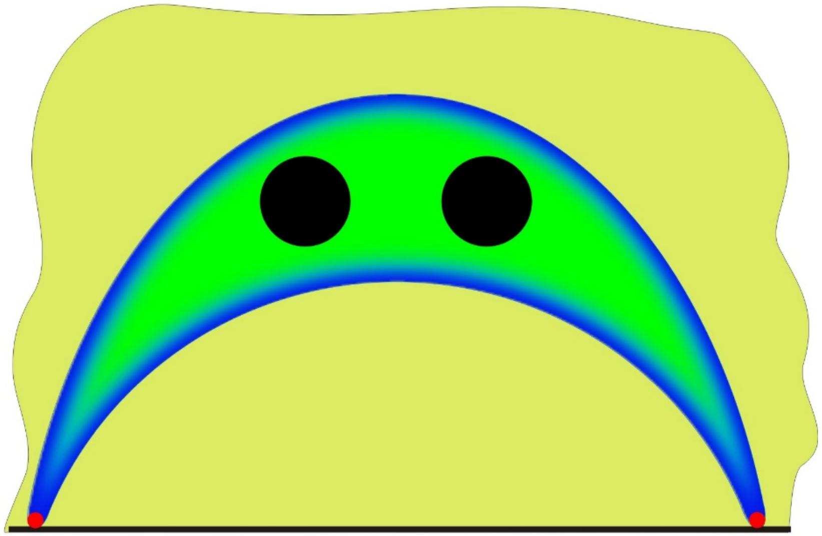


A.B. Konovalov, V.V. Vlasov, Quantum Electron. 44: 719 (2014)

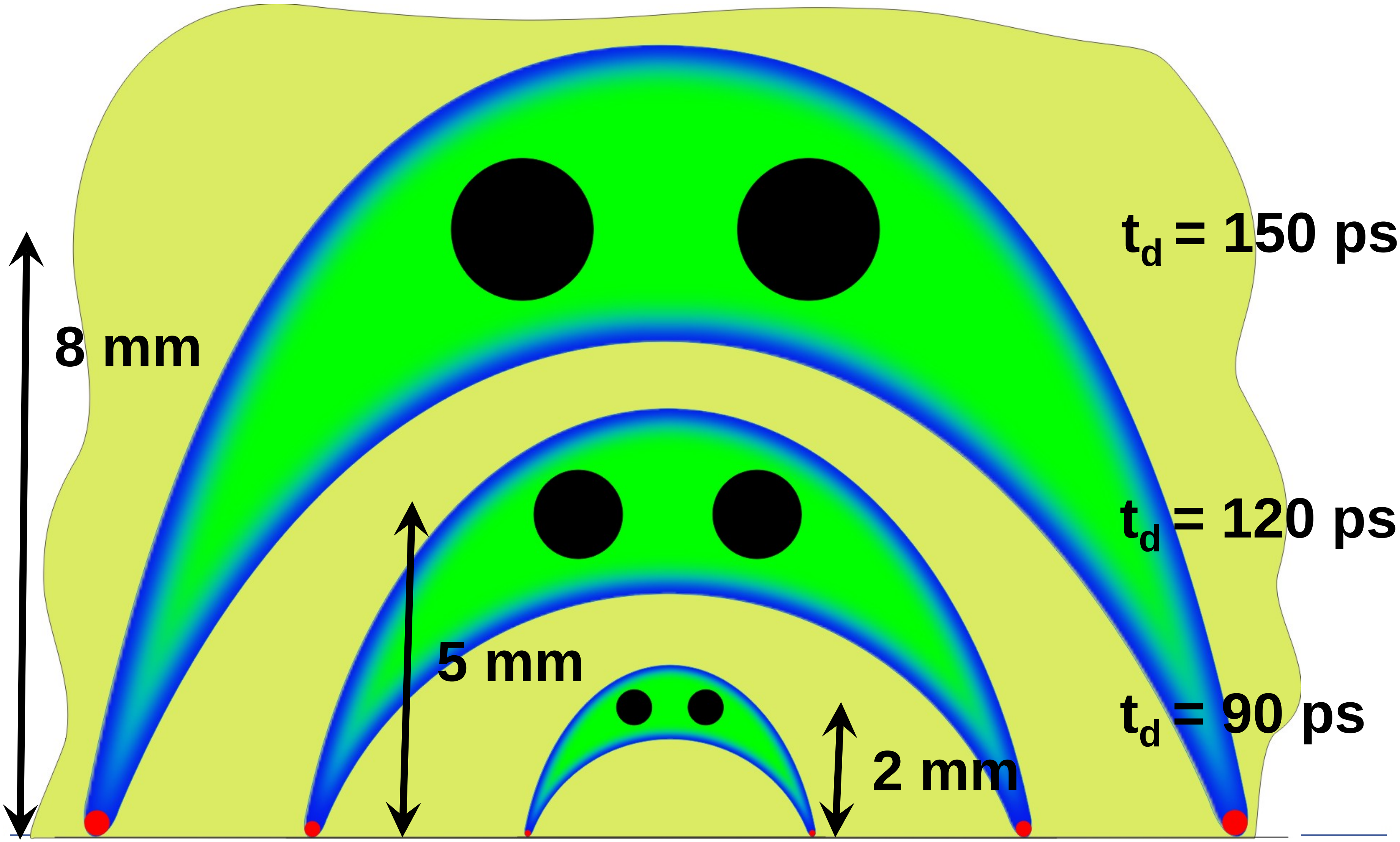
Comparison of two geometries



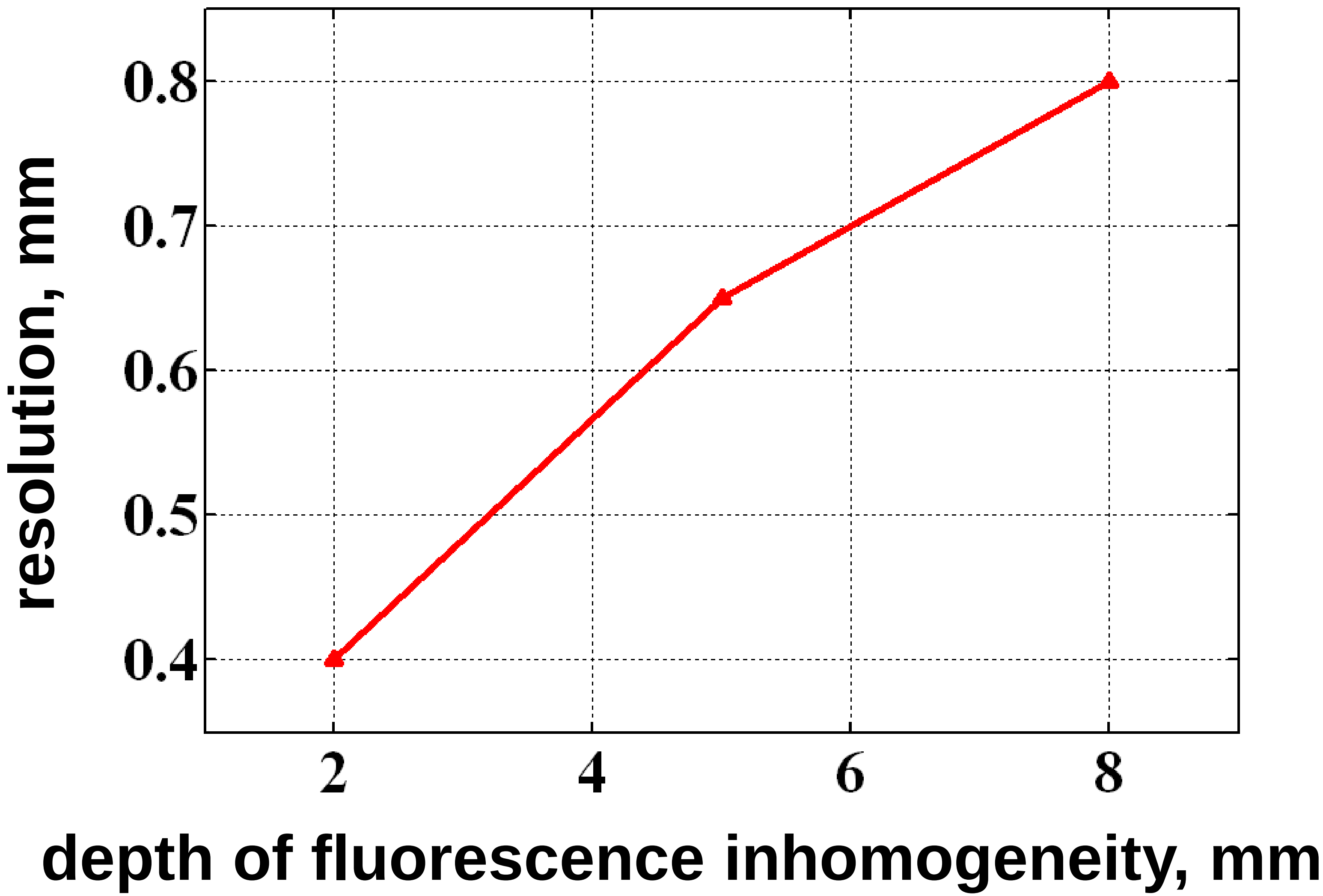
$$\xi \simeq 0.4$$



Banana-shaped zones for different depths



Resolution for reflectance FMT



Conclusion and further research

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- According to our theoretical estimates Lyubimov model can reconstruct fluorescence tomograms with high – submillimeter – resolution .
- Our further research is aimed at developing a numerical experiment to verify the theoretical results .

Publications we refer to

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The authors thank you for your time!

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