Combined studies of cell response to electric pulses
A simple approach

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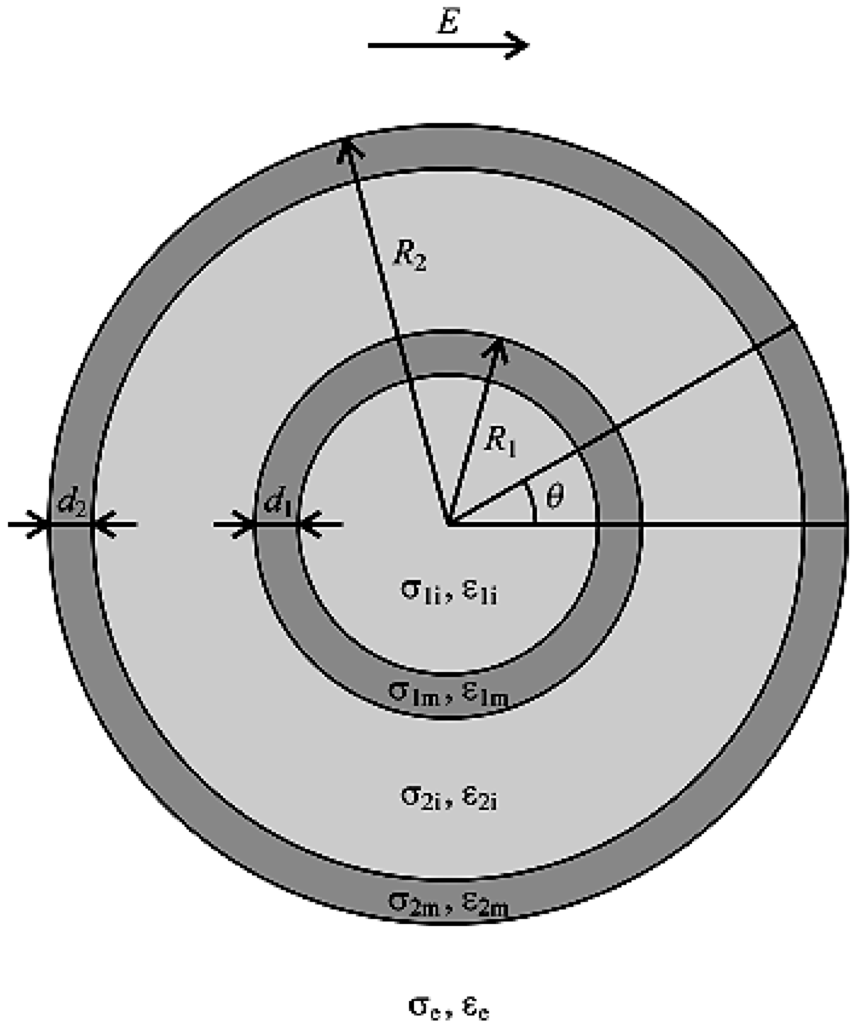
OUTLINE

1. Kotnik’s approach
2. Joshi’s approach
3. The approximated model
4. The combined method
5. Result & Conclusion

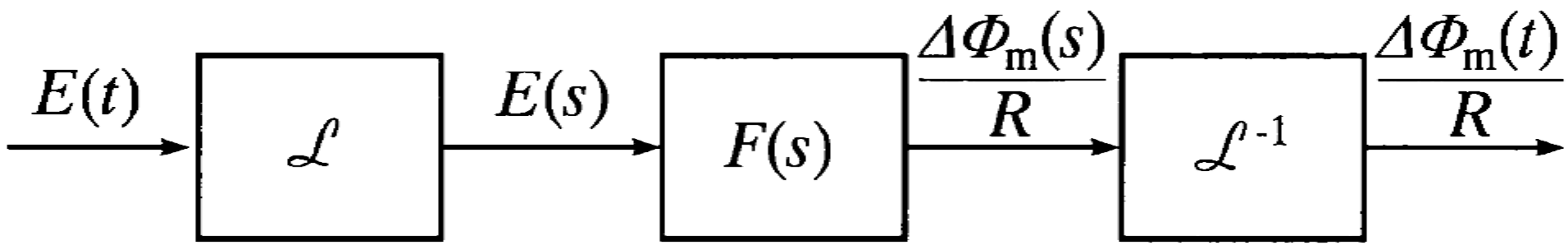
- the effects of electric pulses on the cell responses, including the electroporation phenomenon .

- investigated the dependance of membrane potentials of outer (plasma) and inner (organelle) membranes, the membrane currents and pore densities on the electric pulses

MODEL: ***a spherical cell with a concentric spherical organelle, both covered by bimembranes, interacting with a trapezoidal electric pulse***



1. Kotnik’s approach



$$\Delta\Phi_m = fER\cos\theta$$

$$\Delta\Psi_{cell}(t) = L^{-1}\left[\Delta\Psi_{cell}(s)\right]$$

$$\Delta\Psi_{org}(t) = L^{-1}\left[\Delta\Psi_{org}(s)\right]$$

f is a function reflecting the electrical and geometrical properties of the cell

- Kotnik’s approach: [1] Tadej Kotnik and Damijan Miklavcic, *Biophys J.* 2006, **90**(2), 480491

2. Joshi's Approach

- The pores are controlled by the Smoluchowski equation:

$$n_r' - \frac{D}{k_B T}(nE_r')_r' - Dn_r'' = S(r)$$

r is the pore radius

- The effective conductivity:

$$\sigma_{eff-mem} = \frac{A_p}{A_0}\sigma_{out} + \left(1 - \frac{A_p}{A_0}\right)\sigma_{mem}$$

- The dynamic pore area $$A_p = A_0\left(\int_0^r 2\pi r^* n(r^*,t)dr^*\right)$$

- Joshi, R.P., Qin Hu, Schoenbach, K.H., *Plasma Science, IEEE Transactions*,**32**, 4, 2004, 1677 – 1686

3. Approximate Mehod

- The approximated model of pore creation and pore current

$$\frac{dN}{dt} = \alpha e^{(Vm/V_{ep})^2}\left(1 - \frac{N}{N_0} e^{-q(Vm/V_{ep})^2}\right)$$

$$i_{ep} = \frac{\pi r_m^2 \sigma v_m RT e^{v_m - 1} / Fh}{\frac{w_0 \exp(w_0 - nv_m) - nv_m}{w_0 - nv_m} e^{v_m} - \frac{w_0 \exp(w_0 + nv_m) + nv_m}{w_0 + nv_m}}$$

John C. Neu and Wanda Krassowska, *Phys. Rev. E*, **59**, 3471 - 3482 (1999).

4.the combined method

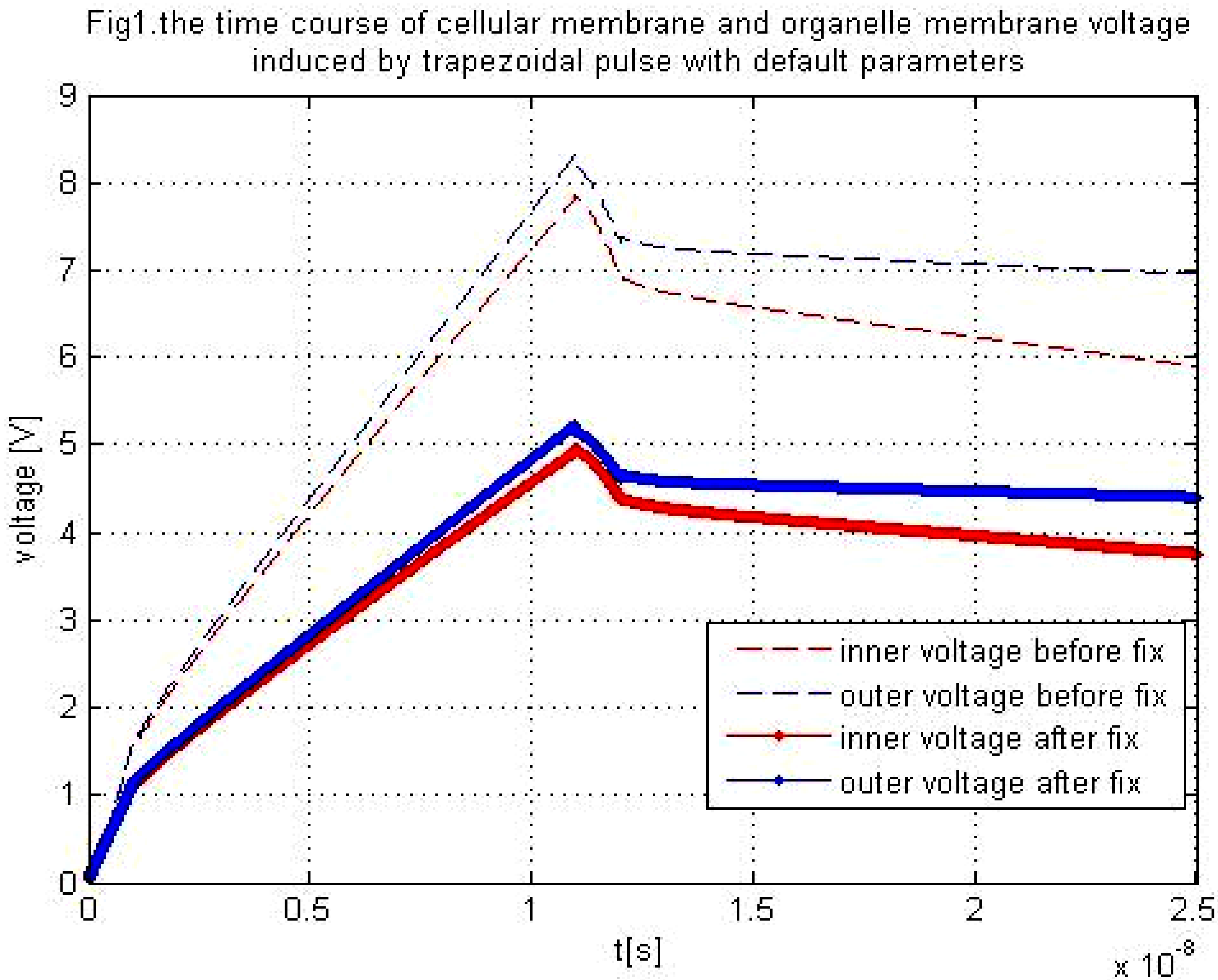
- Use the analytical equations of voltage from Kotnik
- Include the dynamic conductivity properties by the approximated model of Wanda.
- The updated potentials can be calculated

$$\Delta\Psi_{comb} = \Delta\Psi_{kotnik} - i_{ep} R_{pore}$$

$$i_{ep} = \frac{\pi r_m^2 \sigma v_m R T e^{v_m - 1} / Fh}{\dfrac{w_0 \exp(w_0 - n v_m) - n v_m}{w_0 - n v_m} e^{v_m} - \dfrac{w_0 \exp(w_0 + n v_m) + n v_m}{w_0 + n v_m}} \quad \& \quad R_{pore} = R_p + R_i$$

- Our results are not only good agreement with Joshi's results but also applied to many models of cell membrane such as the tri-layer membrane...

the differences between the effect of default and adjusted parameters of cell on the membranes potentials



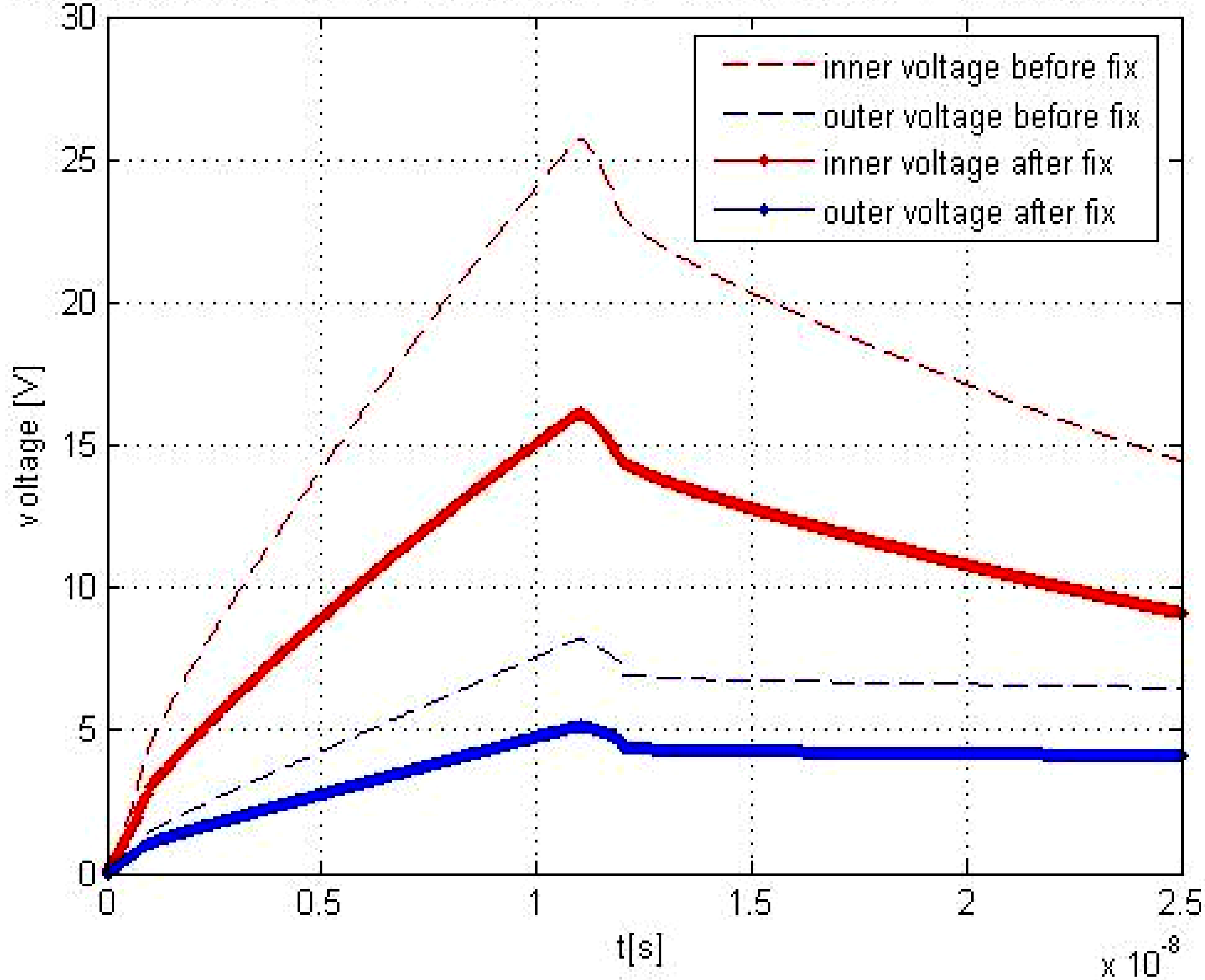
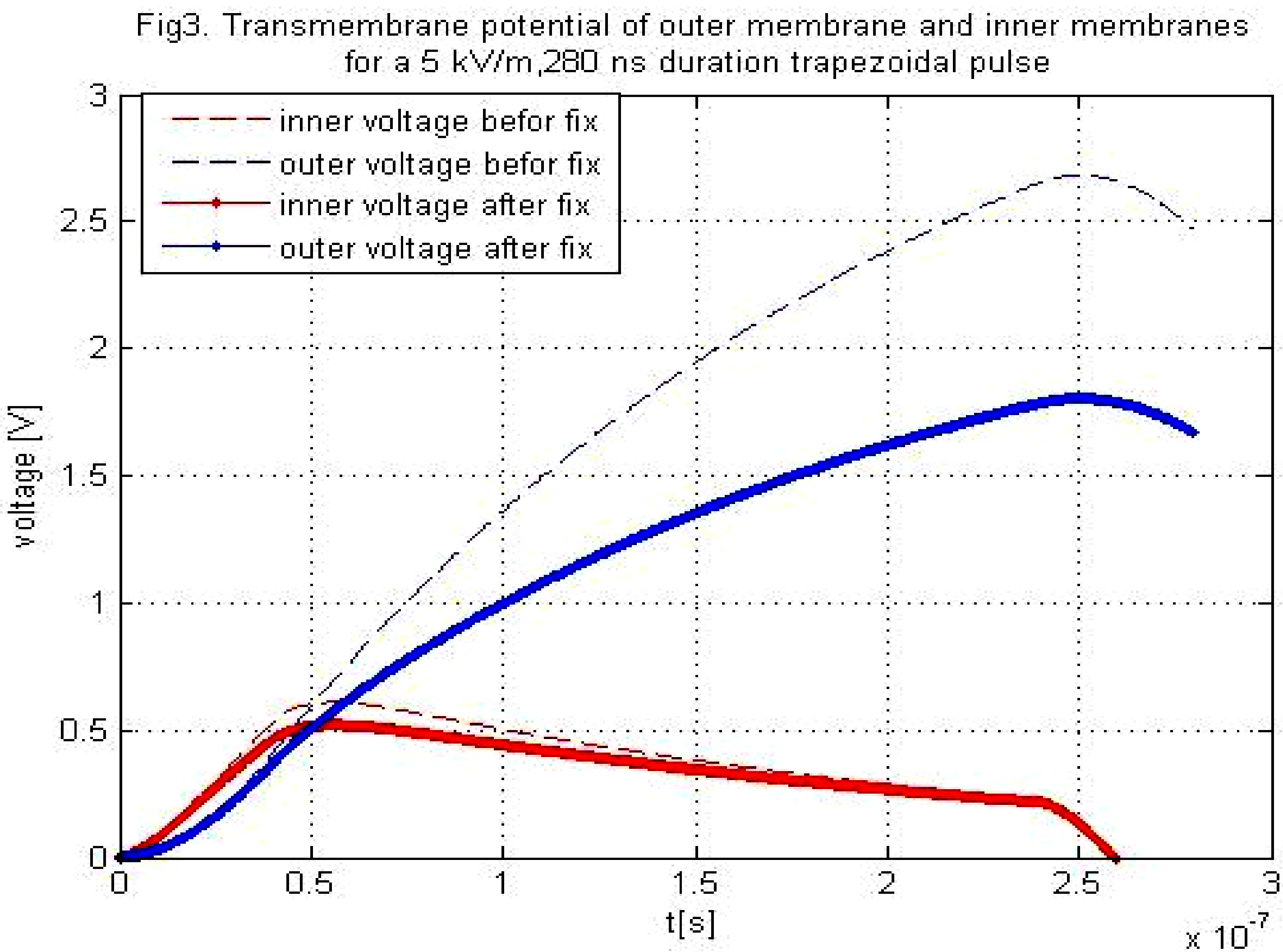
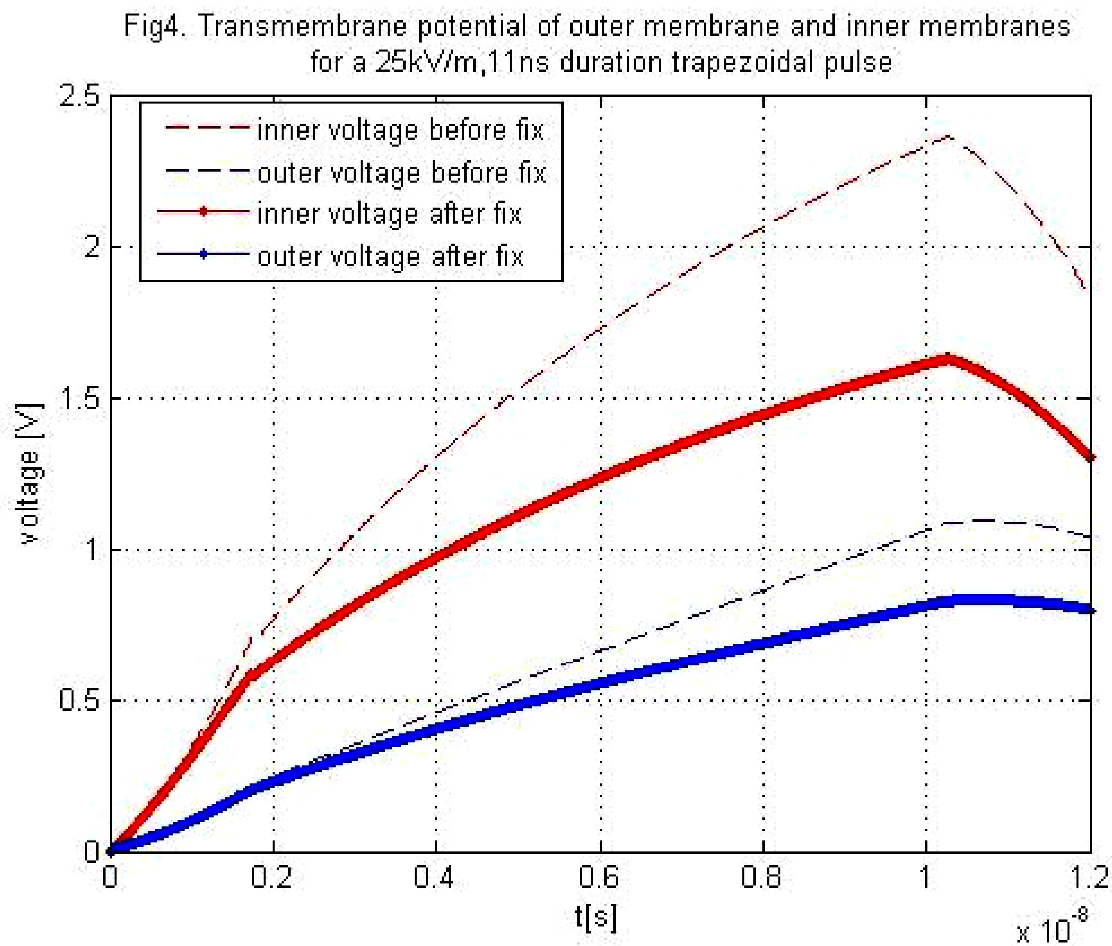


Fig2.the time course of cellular membrane and organelle membrane voltage induced by trapezoidal pulse with sigma1i=0.5 S/m, epsilon1m=3*10^-11 As/Vm, d1=10nm

- the manifestation of the membranes exposed to the long and the shorter trapezoidal pulses:

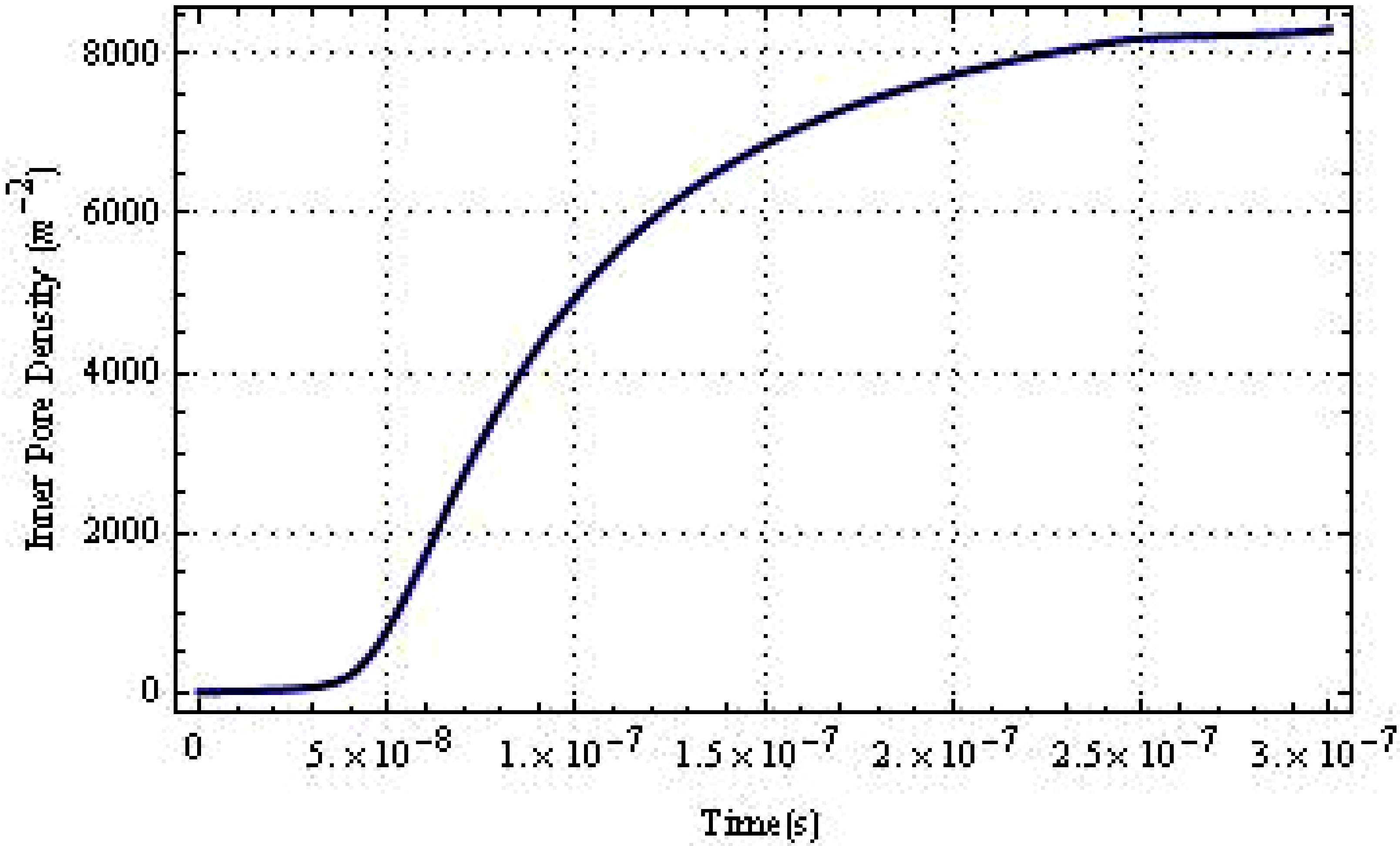




Inner potential easily surpasses the outer

- the pore density on inner membrane versus time of both pulses

Fig.5: Pore density versus time for long pulse



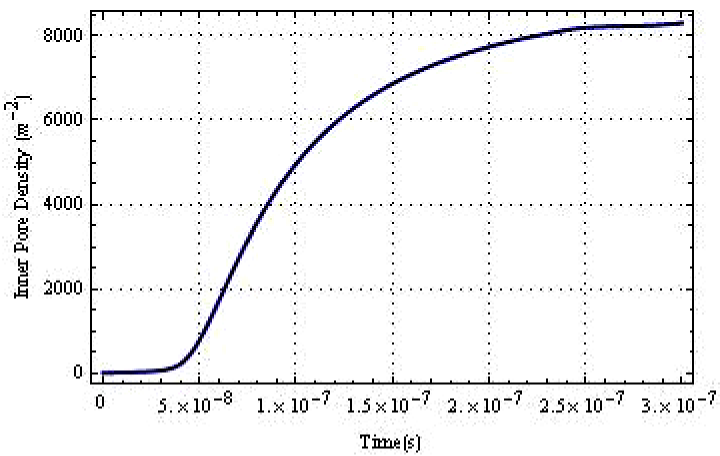
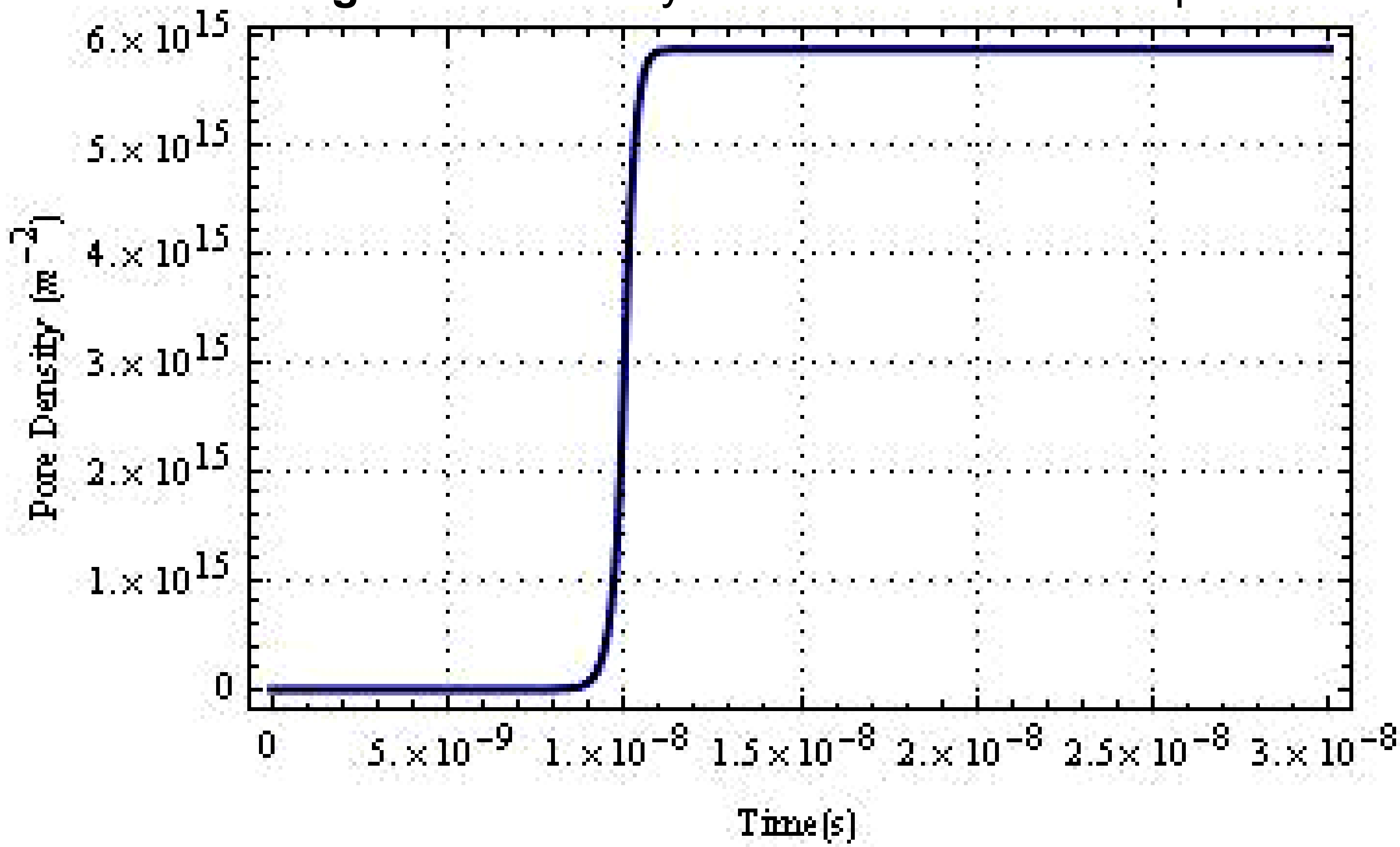


Fig.6: Pore density versus time for shorter pulse.



- ***Fig.5*** The equilibrium pore density is rather low, about *8000*, in according with the typical value of about *10^13 (cm^-2)*

- ***Fig.6*** : The peak value of the value of pore density is *10^16 (cm^-2)*, remarkably larger than in the long pulse case **=>** Electroporation!.

Conclusions

- We improve the model of cell membrane exposured to a *ns* ultrashort, high-intensity pulse.
- Basing on the analytical Laplace- transform method of pulses, we include the effect of dynamic conductivity of cell membranes to achieve better results

Thanks for your attention !

REFERENCES

- [1] Tadej Kotnik and Damijan Miklavcic, *Biophys J.* 2006, **90**(2), 480491.
- [2] Joshi, R.P., Qin Hu, Schoenbach, K.H., *Plasma Science, IEEE Transactions*,**32**, 4, 2004, 1677 - 1686.
- [3] John C. Neu and Wanda Krassowska, *Phys. Rev. E*, **59**, 3471 - 3482 (1999).
- [4] Katherine A. DeBruin, Wanda Krassowska, *Biophysical Journal*, **77**, 3, 1999,1213-1224.
- [5] Tadej Kotnik and Damijan Miklavcic, *Biophysical Journal*, **90**, 2, 480-491, 2006.

- **Electroporation:** a significant increase in the electrical conductivity
- and permeability of the cell plasma membrane caused by an externally applied electrical field. It is usually used in molecular biology as a way of
- introducing some substance into a cell , such as loading it with
- a molecular probe, a drug that can change the cell's function, or a piece of coding DNA

- **MODEL** a spherical cell with a concentric spherical organelle, both covered by bimembranes, interacting with a trapezoidal electric pulse