PLASMA JET INTERACTIONS WITH WET CELLS*

Seth A. Norberg[a), Eric Johnsen[a), and Mark J. Kushner[b)

[a)Department of Mechanical Engineering
University of Michigan, Ann Arbor, MI 48109, USA
norbergs@umich.edu, ejohnsen@umich.edu

[b)Department of Electrical Engineering and Computer Science
University of Michigan, Ann Arbor, MI 48109, USA
mjkush@umich.edu
http://uigelz.eecs.umich.edu

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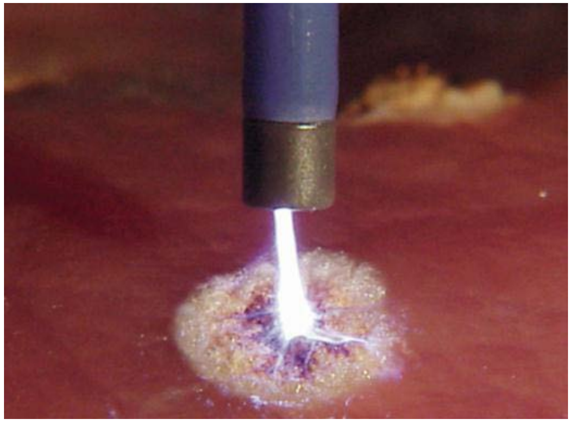
PLASMA MEDICINE

- **Treatment of biomedical surfaces and human tissue with atmospheric pressure plasma jets has been shown to:**
  - **Disinfect surfaces by killing bacteria**
  - **Sterilize medical equipment and implants**
  - **Sterilize food and food packaging**
  - **Induce blood coagulation**
  - **Kill cancer cells**
  - **Facilitate healing in chronic wounds**
  - **Sterilize acute wounds**



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- **In this poster, I will show the results of a 2-D model that investigated the interaction of the electric field produced by an atmospheric pressure plasma jet and wet cells and the potential for electroporation or intracellular electro-manipulation.**

ATMOSPHERIC PRESSURE PLASMA JETS (APPJ)

- Low-temperature non-equilibrium atmospheric pressure plasma jets provide therapeutic and sterilizing effects through:
  - Fluxes of charged and reactive species to surfaces
  - Ion and photon flux to cell structure
  - Intracellular and surface electric fields

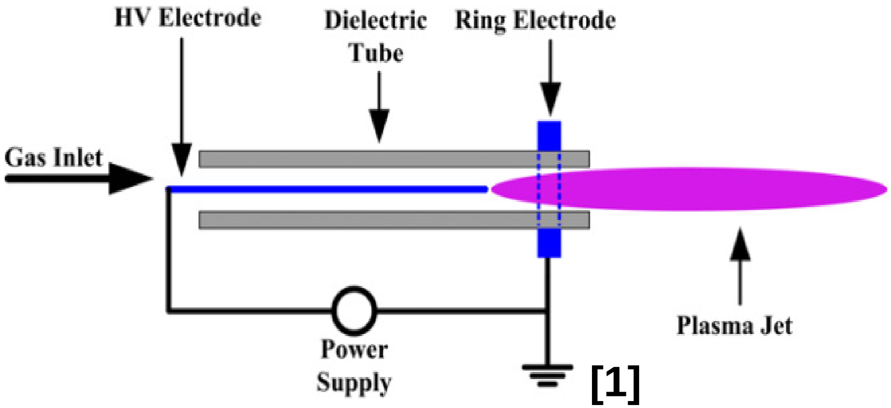

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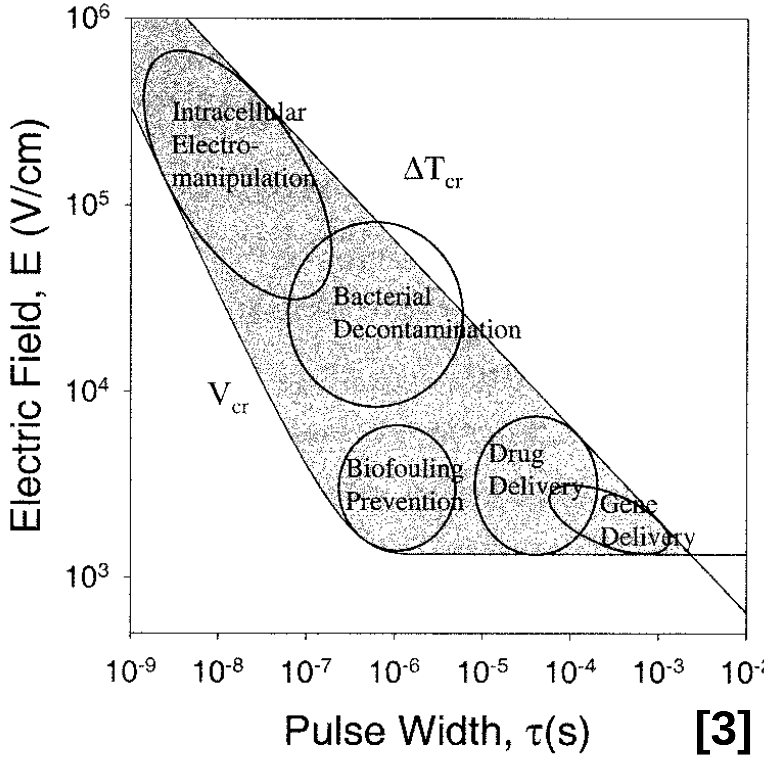
Figure from ZIK plasmatis at the INP Greifswald

BIOELECTRONICS REVIEW

- **Electroporation:**
  - **Transmembrane pore formation resulting from accumulation of electric charge at the cell membrane.**
  - **Threshold – membrane voltage drop of 0.1 – 1 V over pulses of 0.1 – 10 ms with electric fields of a few kV / cm.**
  - **Used for gene delivery and drug delivery.**

- **Intracellular Electro-manipulation (IEM):**
  - **Breaches subcellular vesicular membranes using short (10 – 100 ns) and high E-field pulses (10s of kV/cm) [2].**
  - **Does not reach the charging time of the plasma membrane – no pore formation.**
  - **ns pulsed electric field (nsPEF) induces apoptosis in mammalian cells by targeting intracellular structures.**



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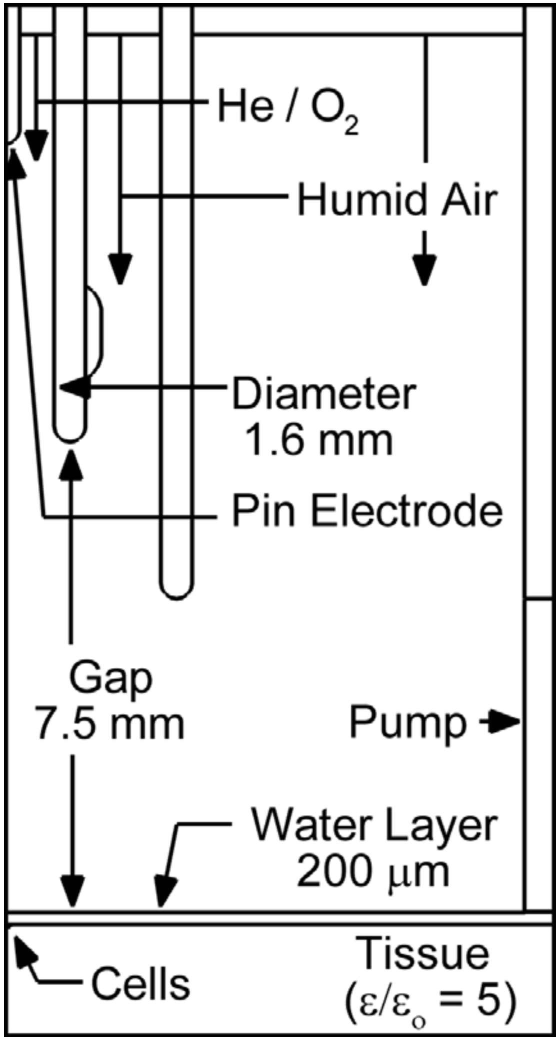
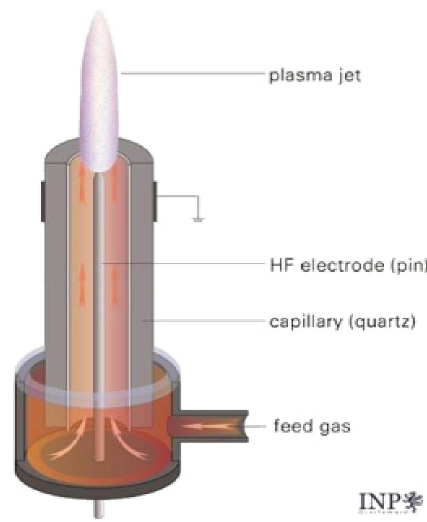
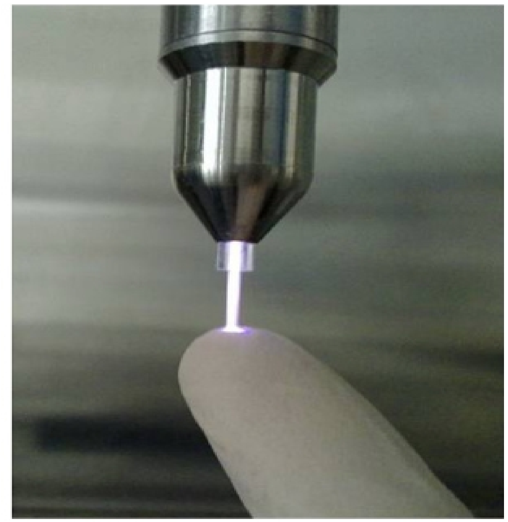
PLASMA JETS: TOUCHING OR NOT….



- **Context – Plasma medicine use of plasma jets in treating tissue with overlying liquid.**
- **There is intrinsic variability – does the plasma jet "touch" or "not-touch"?**
- **How important is variability?**
- **2D modeling study of He/O_2 plasma jet into humid air onto a thin water layer over tissue.**





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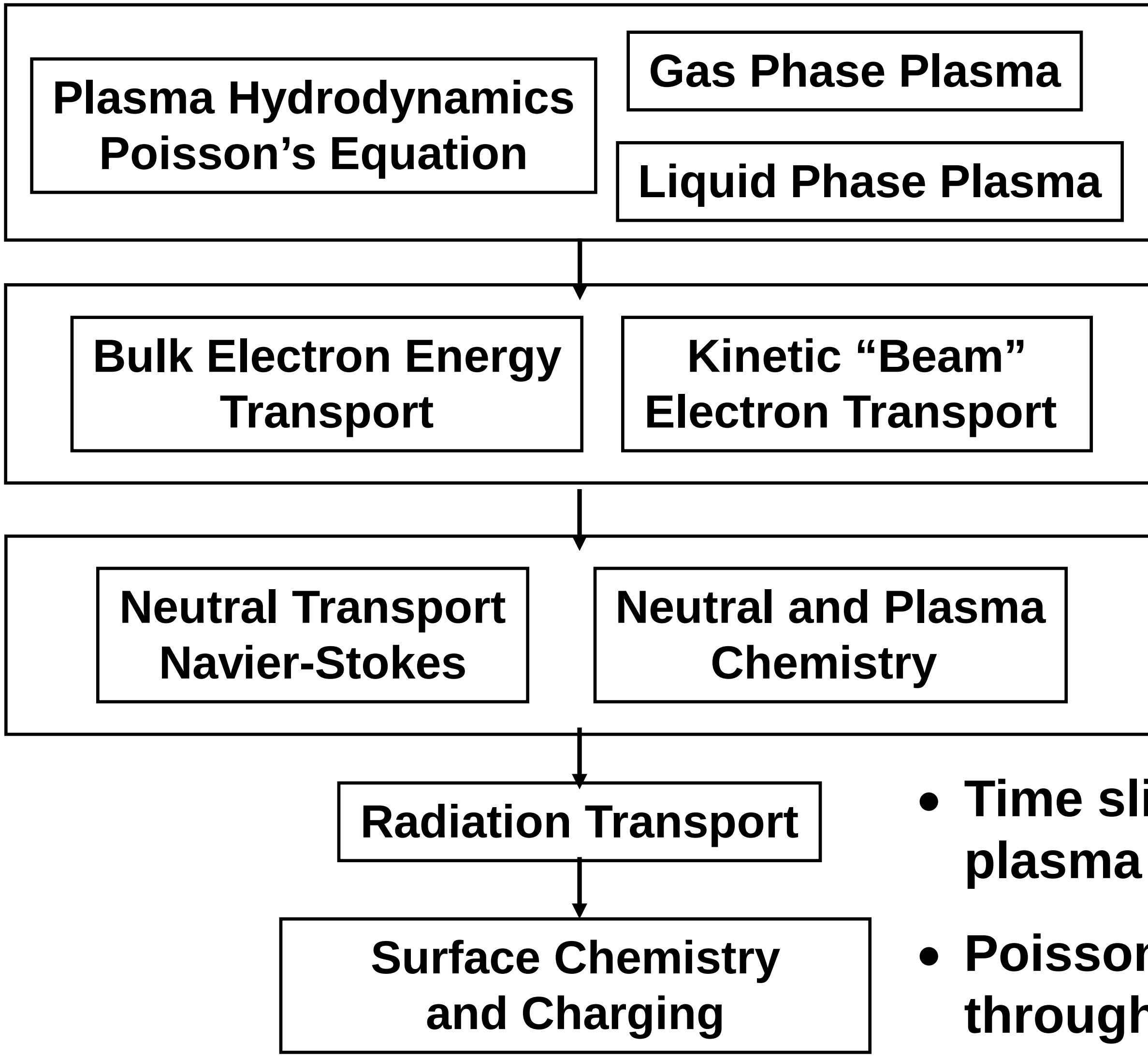
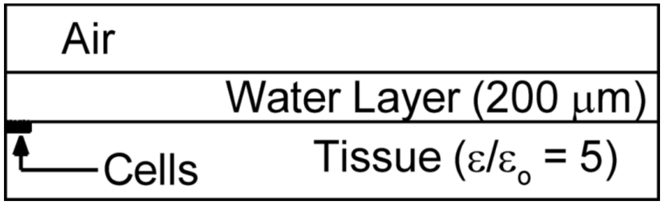
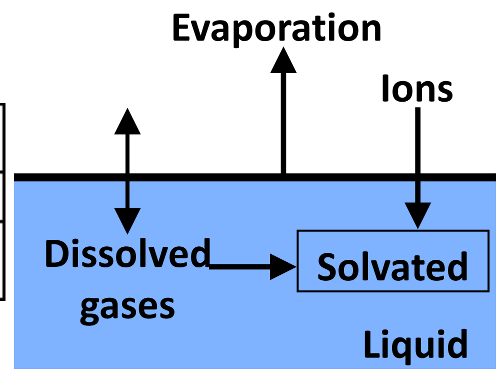
MODEL: *nonPDPSIM*



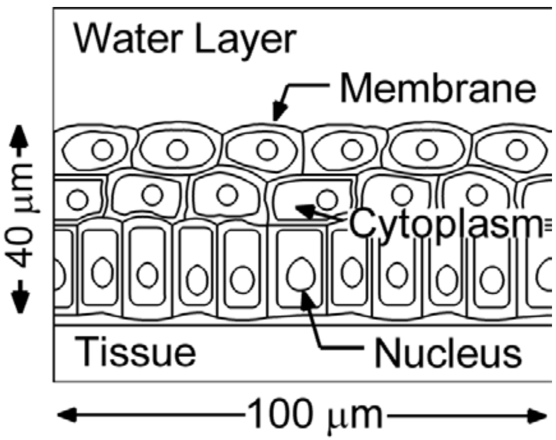
- **2-D unstructured mesh with spatial dynamic range of 10^4.**
- **Fully implicit plasma transport.**
- **Time slicing algorithms between plasma and fluid timescales.**
- **Poisson’s equation is solved throughout the computational domain.**

MODEL GEOMETRY





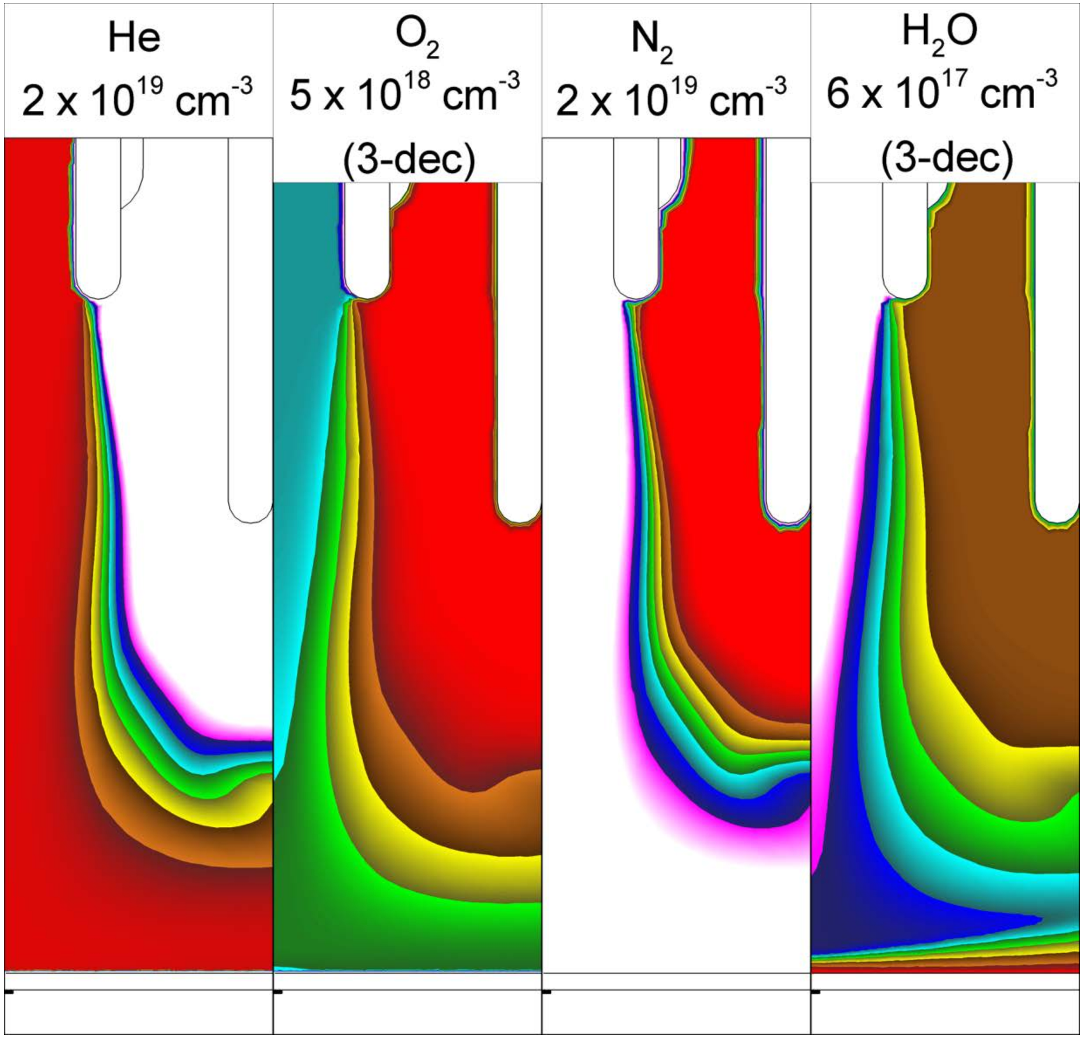
- **Liquid treated as a "dense plasma".**
- **Water evaporated above the water layer.**
- **The tissue acts as the counter electrode.**



	Permittivity ($\varepsilon/\varepsilon_o$)	Conductivity (Ω^{-1} cm^{-1})	Dielectric Relaxation Time (s)
Membrane	5.8	8.7×10^{-8}	5.9×10^{-6}
Cytoplasm	30	4.8×10^{-3}	5.5×10^{-10}
Nucleus	20	3.0×10^{-5}	5.9×10^{-8}
Tissue	5	1.0×10^{-6}	4.4×10^{-7}

- **Diffusion into water is limited by Henry's law equilibrium at the surface layer. O_2 is naturally dissolved in the liquid before plasma.**
- **Components of cell treated as dielectrics with permittivity, conductivity, and dielectric relaxation times listed.**

INITIAL FLOW CONDITIONS



- **Water evaporates from liquid layer at saturated vapor pressure.**
- **He jet displaces the evaporating water vapor.**
- **He/O_2 = 99.8/0.2 (4 slm) with humid air (N_2/O_2/H_2O = 79.5/20/0.5) flowing in the shielding gas (1 slm) for 13 ms to establish flow field.**
- **He jet alone effectively "blocks" the ambient air from the water layer.**

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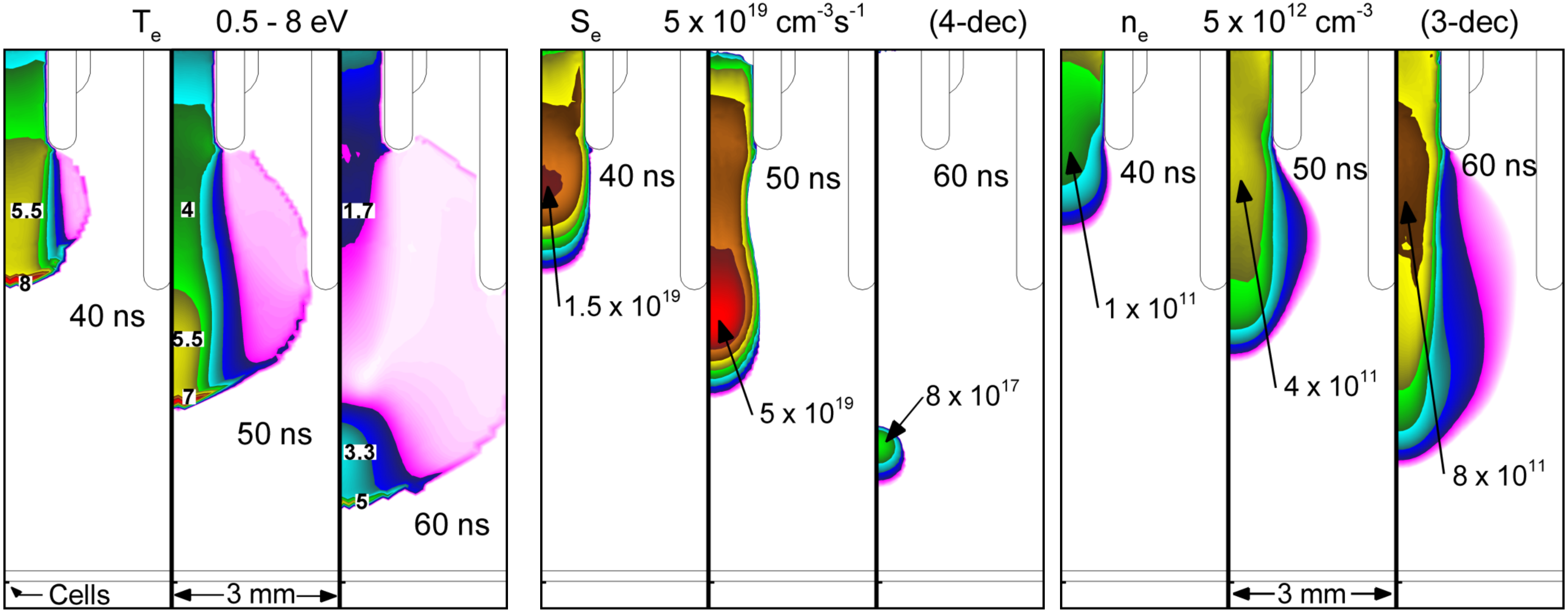
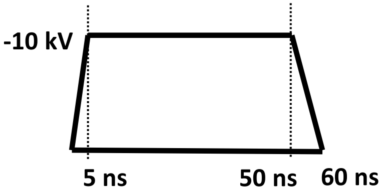
10 kV (NOT TOUCHING): e PROPERTIES





- **-10 kV, 60 ns pulse. Plasma bullet moves as an ionization wave (IW) propagating in He dominated channel at 2 x 10^7 cm/s.**
- **Electrons avalanche at tip of pin electrode, transition to "wall hugging" mode in tube, then transition to axis upon exit.**

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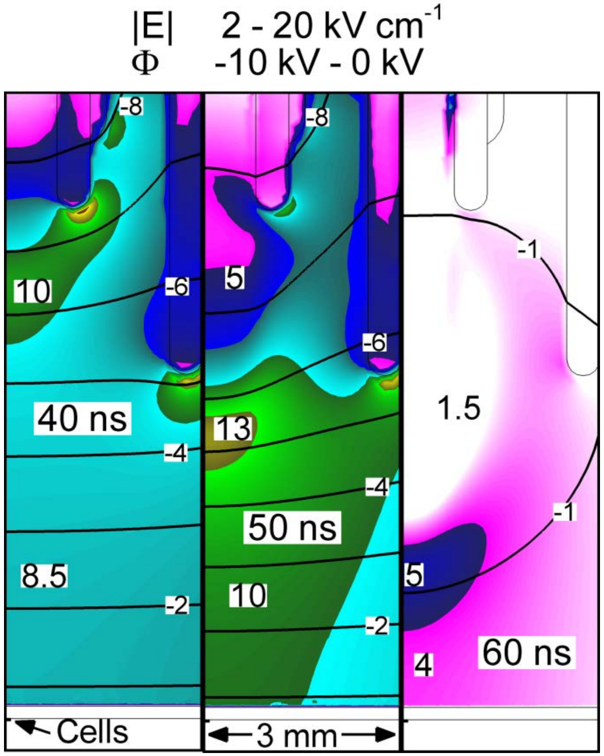
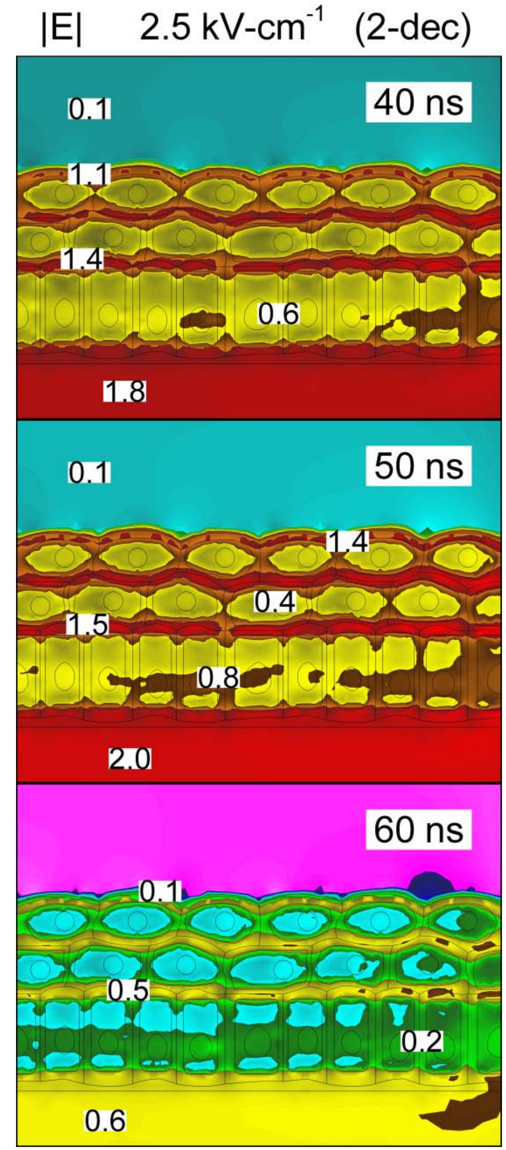
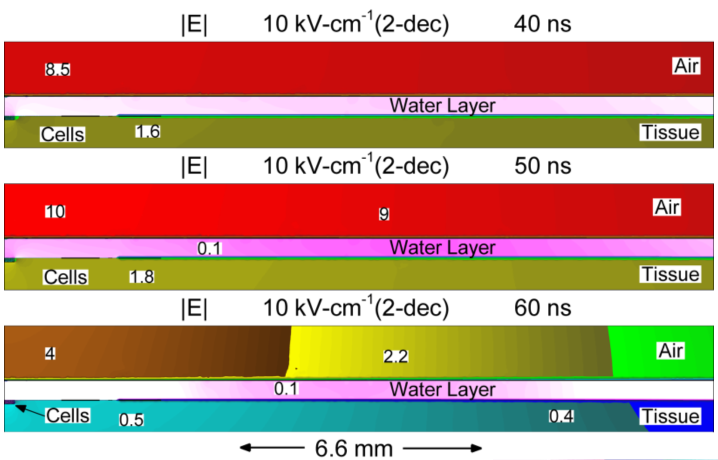
10 kV (NOT TOUCHING): E-FIELDS



- **-10 kV, 60 ns pulse.**
- **Ionization wave does not strike the water layer.**
- **E-fields to cells / tissue are not large enough to induce electroporation or intracellular effects.**
- **No surface charging on the water layer.**





- **E-field at peak voltage and end of the pulse.**

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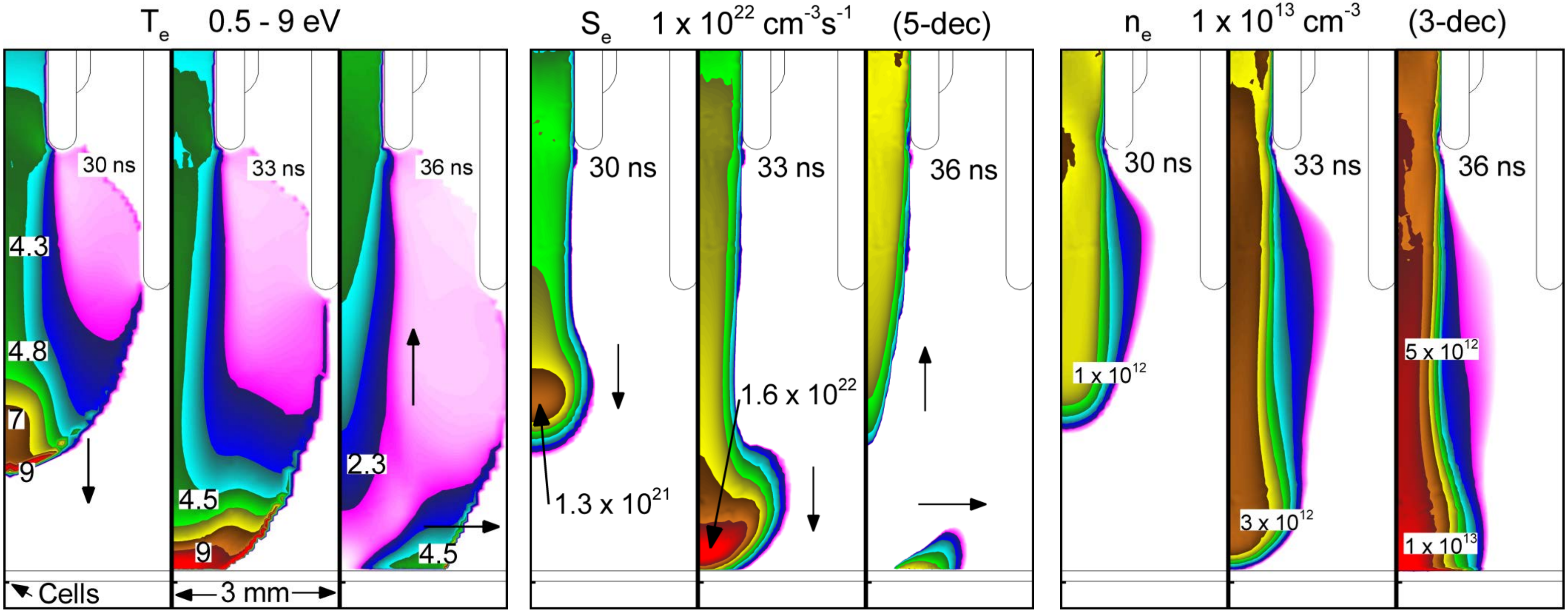
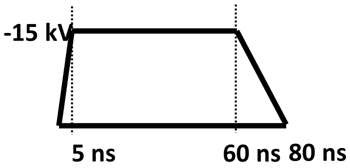
15 kV (TOUCHING): e PROPERTIES





- **-15 kV, 80 ns pulse. Ionization speed 8 x 10^7 cm/s, strikes water at 33 ns and continues as surface IW through H_2O vapor along the water surface.**
- **Upon striking the water layer, a restrike, positive IW propagates back up the plasma column.**
- **Electrons spread onto the water layer, accumulate and solvate.**

MIN **MAX**
Log scale

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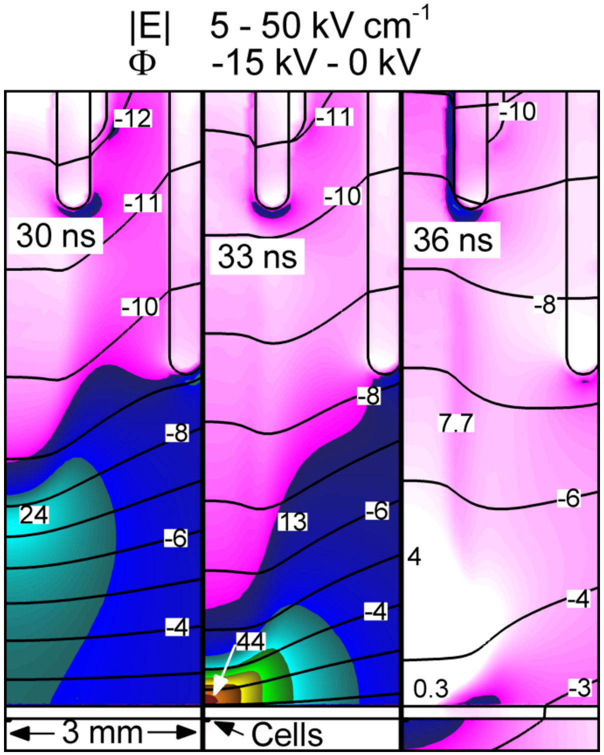
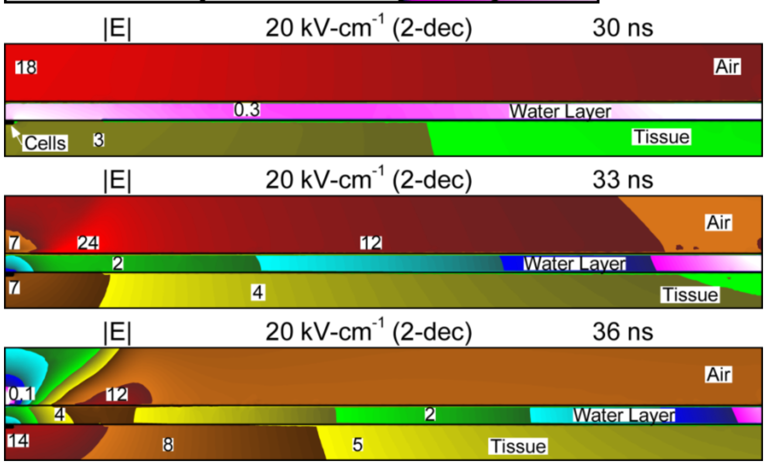
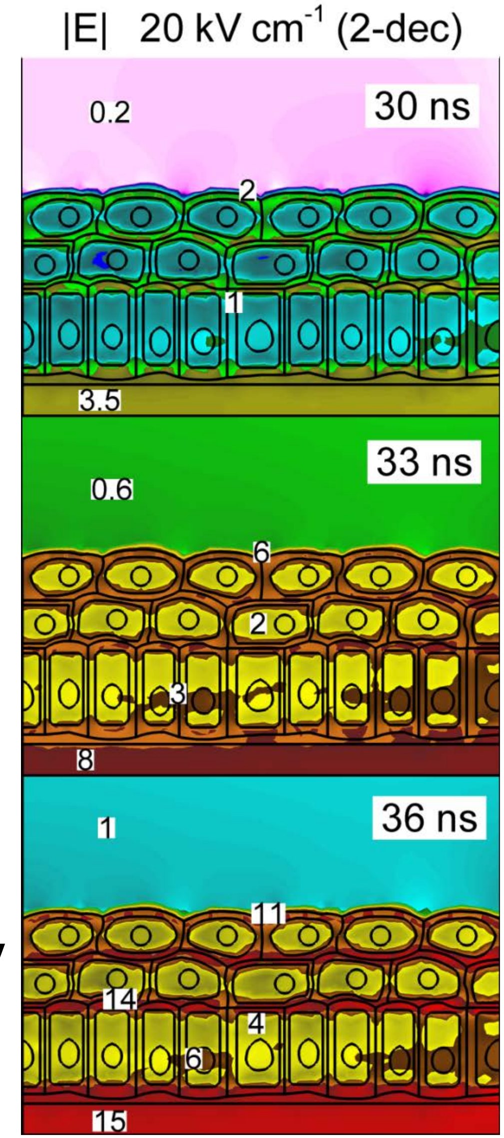
15 kV (TOUCHING): E-FIELDS



- **-15 kV, 80 ns pulse.**
- **IW strikes water at 33 ns.**
- **E-field rise from compression of voltage ahead of IW & charging of water surface.**
- **The E-field penetrates into the cell and tissue producing conduction currents.**



- **Max E-field at cell membrane produces voltage drop of 0.01 V – too low for pore formation.**



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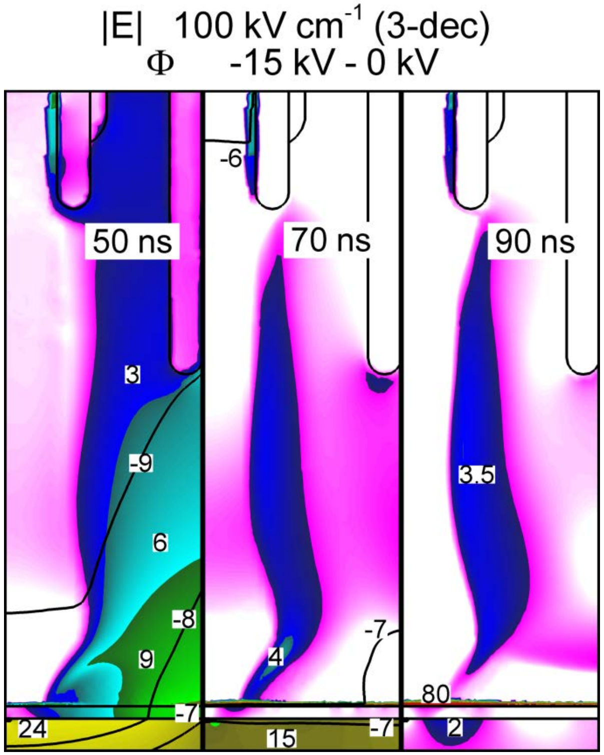
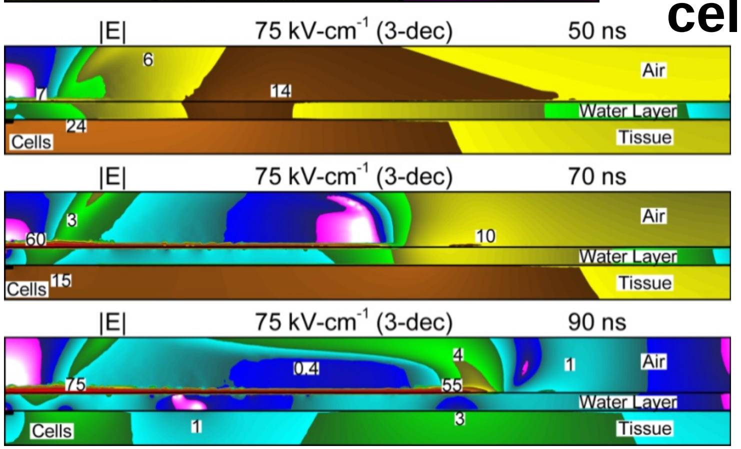
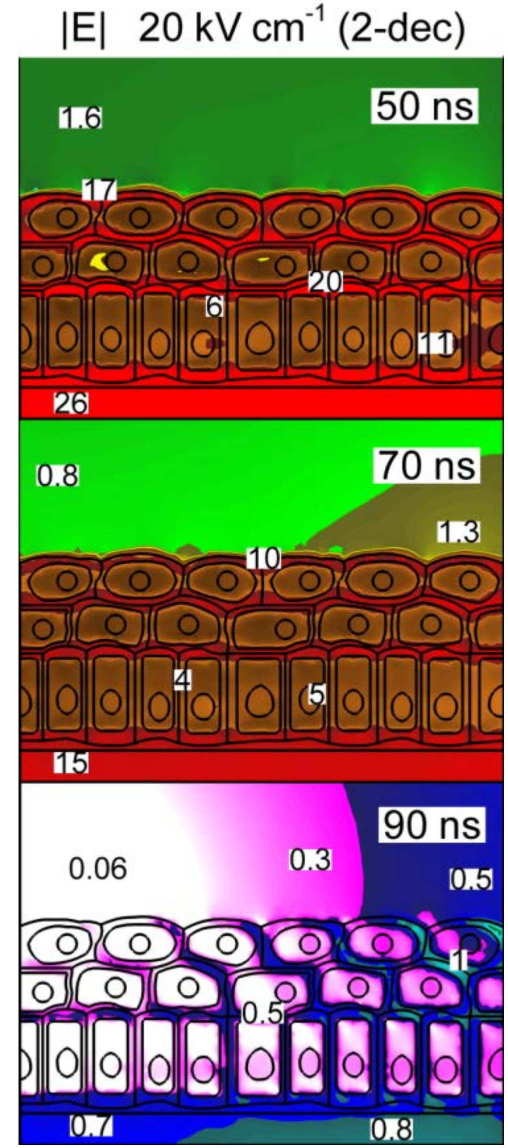
15 kV (TOUCHING): E-FIELDS





- **-15 kV, 80 ns pulse – end of pulse.**
- **E-field from surface charging (80 kV/cm) at water layer does not influence cells.**
- **Max E-field at membrane is too low for pore formation.**
- **Limited residual E-field in cells in afterglow.**
  - **Intracellular field is below predicted IEM range.**



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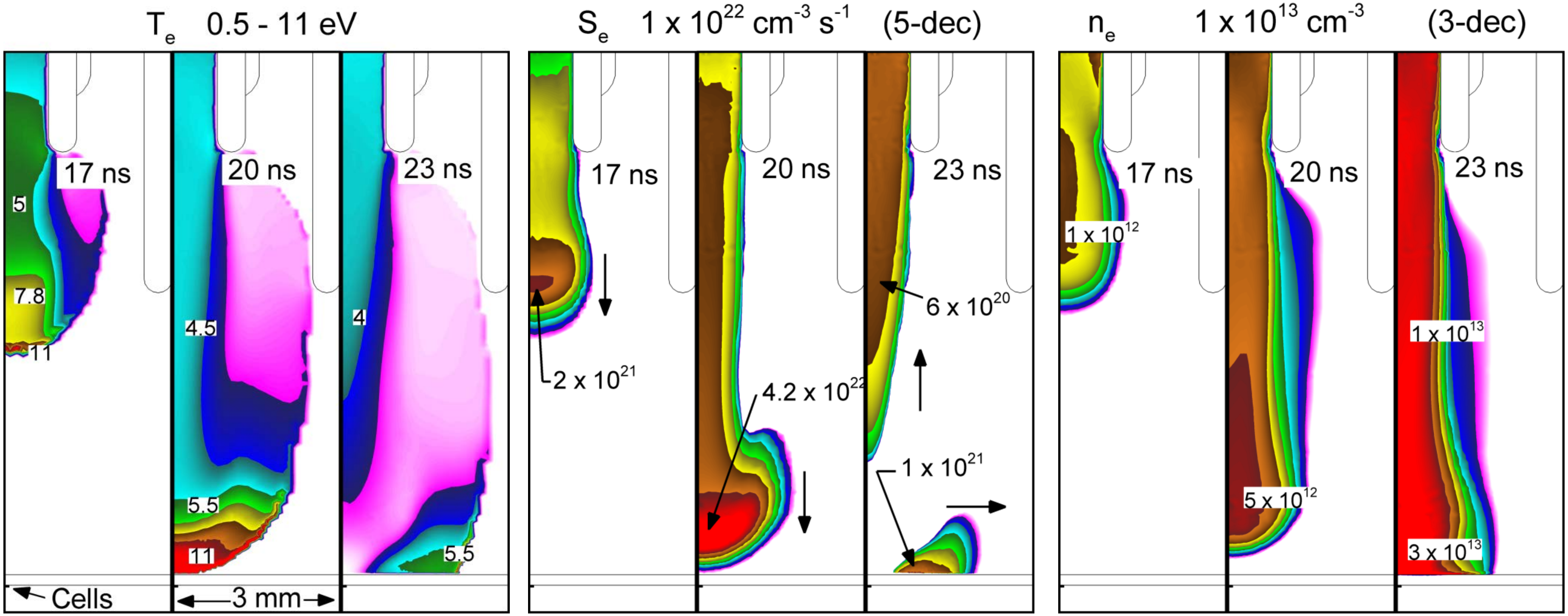
20 kV (TOUCHING): e PROPERTIES



- -20 kV pulse. Plasma bullet moves as an ionization wave (IW) at 1.4 x 10^8 cm/s.
- IW strikes water at 20 ns – 13 ns earlier than 15 kV case and with higher electron temperature, and source ionization levels.
- Electron density is 3-5 times higher in conduction channel and at surface than 15 kV case.

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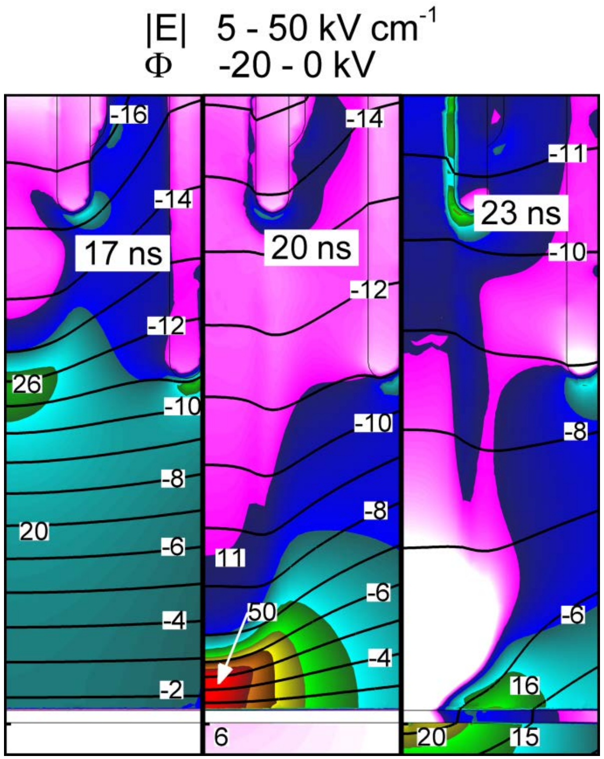
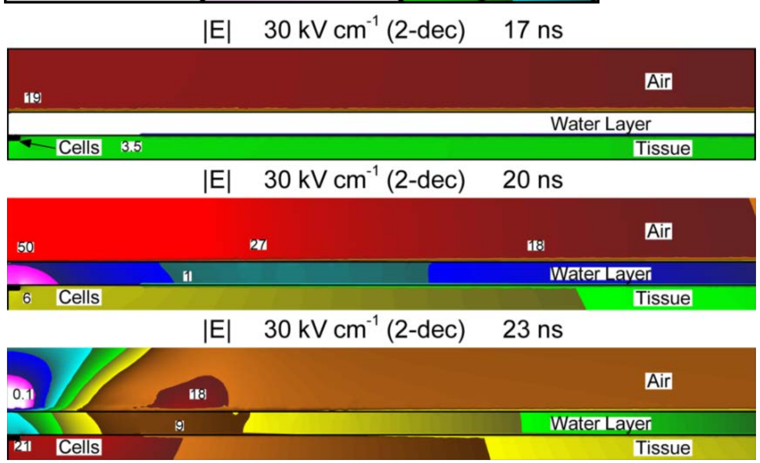
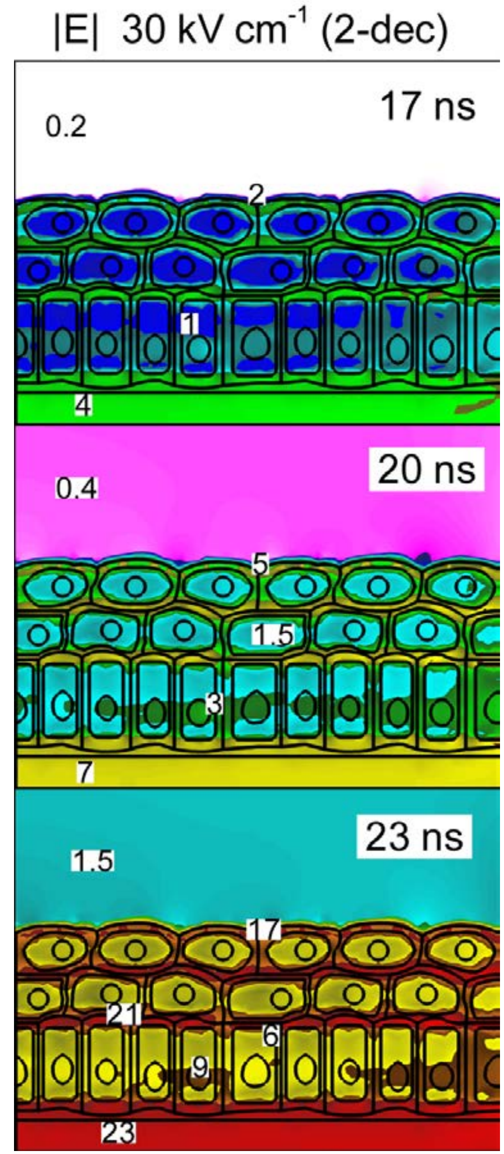
20 kV (TOUCHING): E-FIELDS



- **-20 kV pulse.**
- **Higher voltage creates higher E-field in all regions.**
- **Max E-field in cytoplasm is 9 kV/cm; membrane 21 kV/cm – still below predicted thresholds.**
- **Dielectric relaxation time for membrane 6 μs; cytoplasm 0.5 ns.**



- **Formation of conduction channel following the IW drops E-field behind the IW in air.**



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CONCLUDING REMARKS

- Plasma jets touching (-15 kV, -20 kV) and not-touching (-10 kV) a 200 μm water layer were computationally investigated.
- The spreading of the plasma over the liquid surface when touching cases enables photolysis, direct charge exchange reactions and direct solvation of the electrons.
- Also creates a surface electric field at a maximum of 80 kV/cm for the -15 kV case.
- Not-touching jet will not produce electroporation or intracellular electro-manipulation as the e-fields are much too low for either.
- The touching cases are influenced by the absence of surface charging effects on the cells which decreases the likelihood of electroporation and intracellular electro-manipulation.

REFERENCES

[1] X. Lu, M. Laroussi, V. Puech, “On atmospheric-pressure non-equilibrium plasma jets and plasma bullets”, *Plasma Sources Sci. Technol.*, vol. 21, no. 3, p. 034005, (2012).

[2] K. Schoenbach, S. Beebe, E. Buescher, “Intracellular Effect of Ultrashort Electric Pulses”, *Bioelectromagnetics*, vol. 22, pp. 440-448, (2001).

[3] K. Schoenbach, S. Katsuki, R. Stark, E. Buescher, S. Beebe, “Bioelectrics – New Applications for Pulsed Power Technology”, *IEEE Transactions on Plasma Science*, vol. 30, no. 1, pp. 293 – 300, (2002).

[4] M. Hoentsch, T. von Woedtke, K-D Weltmann, and J.B. Nebe, “Time-dependent effects of low-temperature atmospheric-pressure argon plasma on epithelial cell attachment, viability and tight junction formation in vitro”, *J. Phys. D: Appl. Phys.*, vol. 45, no. 2, p. 025206, (2012).