

What is Electroporation?

How do tumour therapies based on electroporation work?

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Background – tumor therapies

Standard tumor therapies

- Resection, Radiation, Chemotherapy

Minimally invasive therapies (MIC)

- Radiofrequency ablation (RFA) → hyperthermia
- Microwave ablation (MWA) → hyperthermia
- Cryoablation → hypothermia

New non-thermal therapies based on electroporation

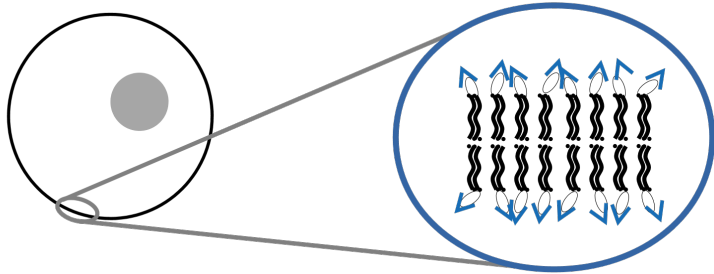
- IRE – Irreversible Electroporation
- ECT – Electrochemotherapy

WHO 2014:
14 mio / year
new cases
8.2 mio / year
cases of death



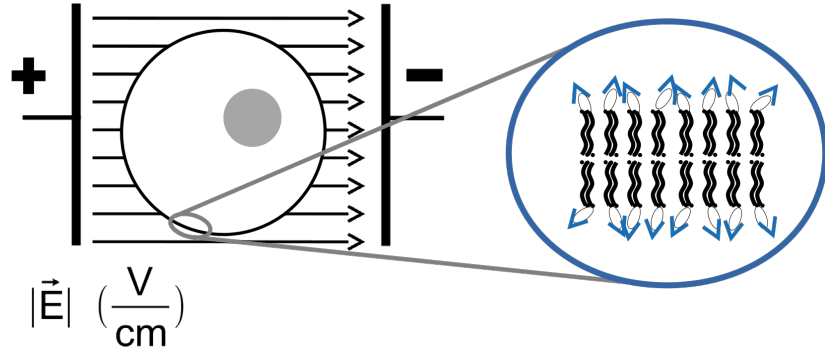
hepatic cancer
≈ 30 %

Background – What is Electroporation (EP)



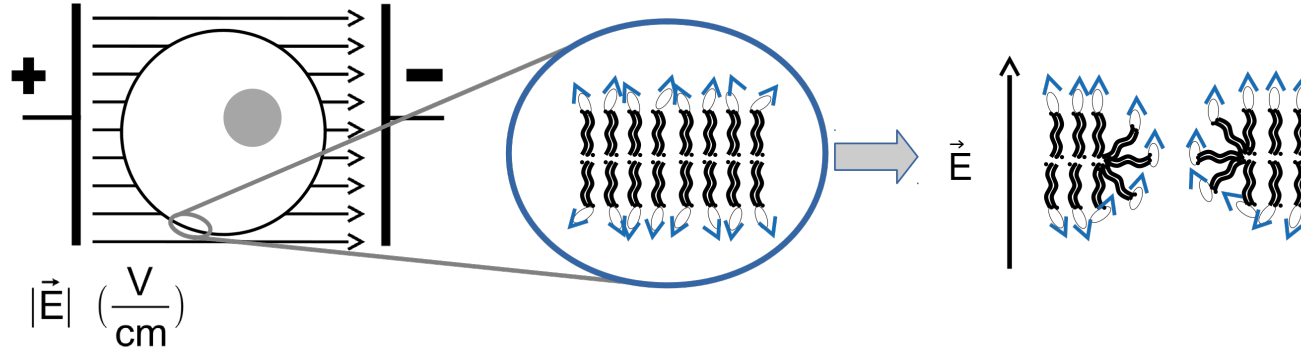
- Local destruction of the lipid bilayer

Background – What is Electroporation (EP)



- Local destruction of the lipid bilayer
- Cell in electric field

Background – What is Electroporation (EP)

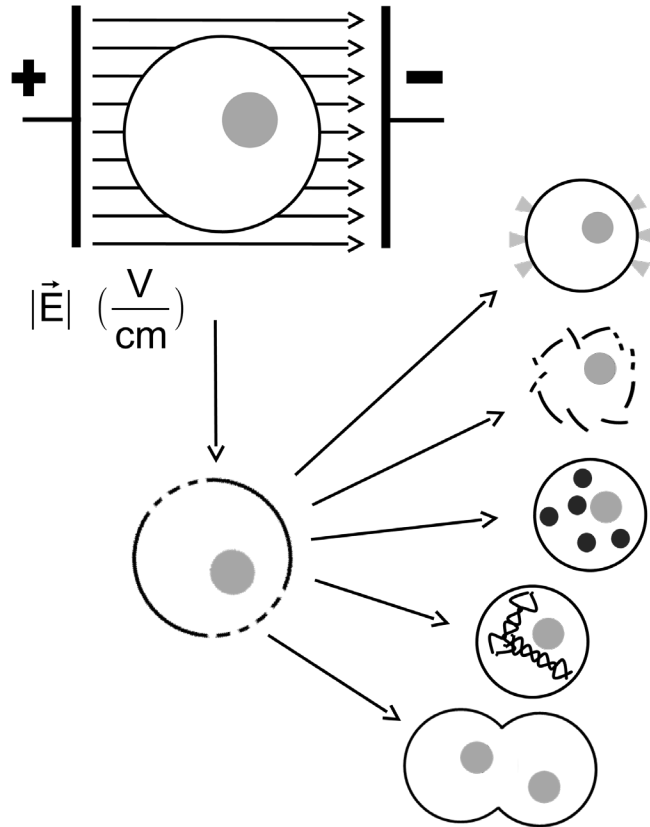


- Local destruction of the lipid bilayer
- Cell in electric field
 - Inducing “nanopores” ($\varnothing \approx 6,2$ [1] - 186 nm [2])
 - Increase membrane permeability (σ / w)
 - Increase transmembrane passage of hydrophilic substances

[1] Characteristics of the osmotically induced membrane rupture, Baumann, Grebe 1998

[2] Electroporation of unilamellar vesicles studied by using a pore-mediated electron-transfer reaction, Correa, Schelly 1998

Background – EP in medical usage



Usage of EP in **biology**

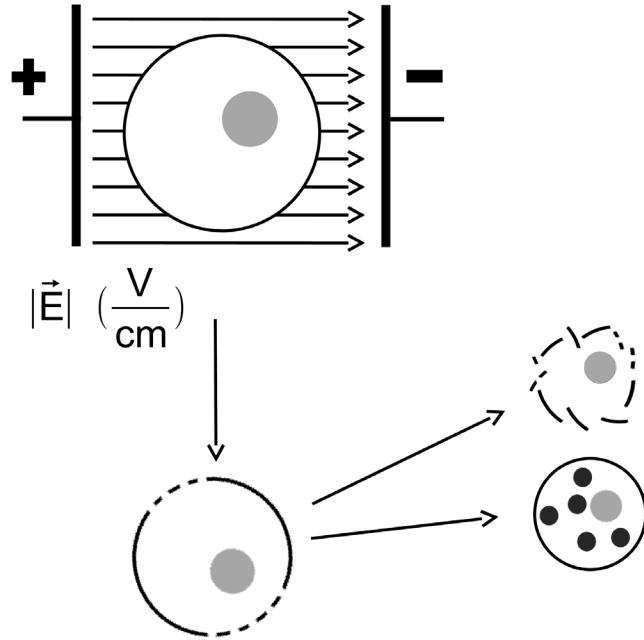
Delivering proteins into cells

Irreversible, permanent destruction of cell membrane

Insert small molecules: drugs

Insert big molecules: genes

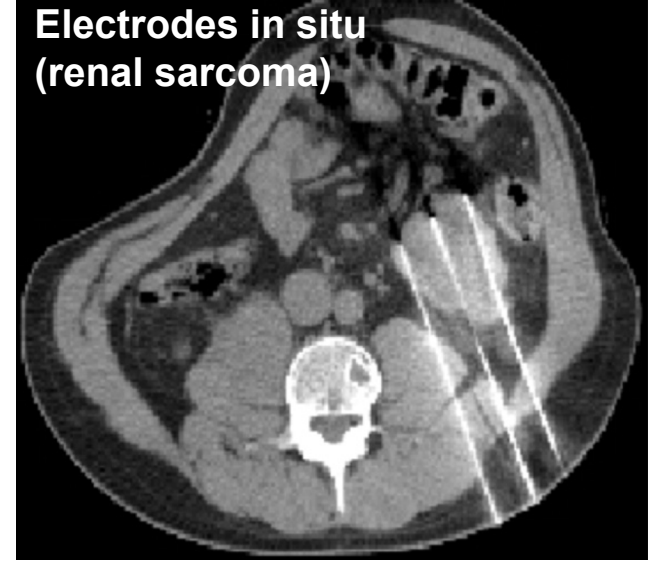
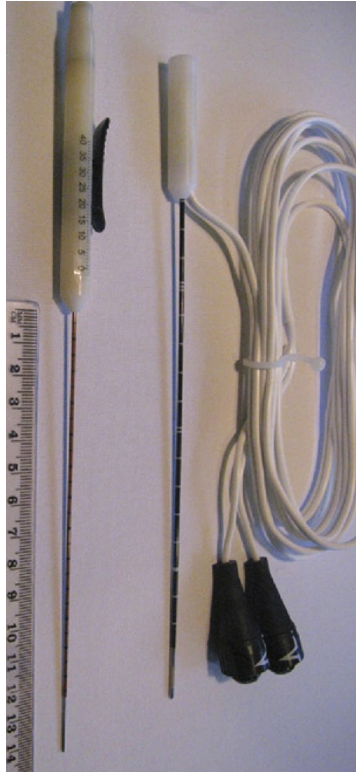
Cell fusion



Usage of EP in **medicine**

- 1) Irreversible, permanent destruction
 - Irrecoverable defects form (\approx s) [1]
 - Cells continue to die (\approx h) [1]
 - **IRE** – Irreversible Electroporation

Background – EP in medical usage

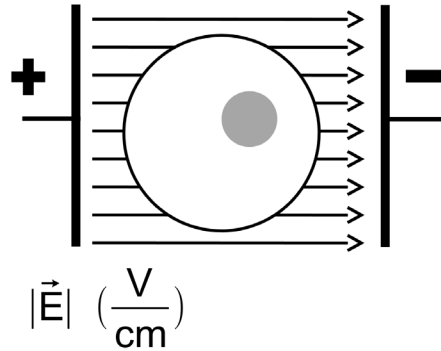


IRE with Nanoknife

- CT guided intervention
- Up to 6 electrodes, but EP with 2 electrodes only

Investigation of the Safety of Irreversible
Electroporation in Humans, KR Thomson 2011

Background – EP in medical usage

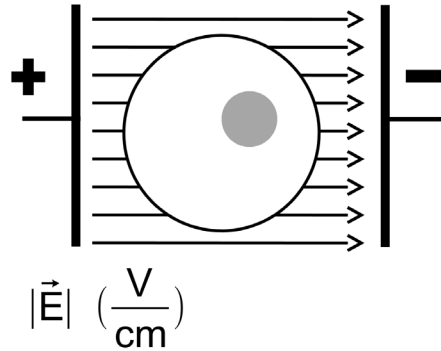


Advantages IRE vs. RFA

- Non-thermal mechanism
 - No heat sink effect
 - No harms to vessels
- More apoptosis than necrosis
- Pulsed electrical field instead of joule heating
 - Easier to simulate the physics
 - Better plannable Intervention



Background – EP in medical usage



Advantages IRE vs. RFA

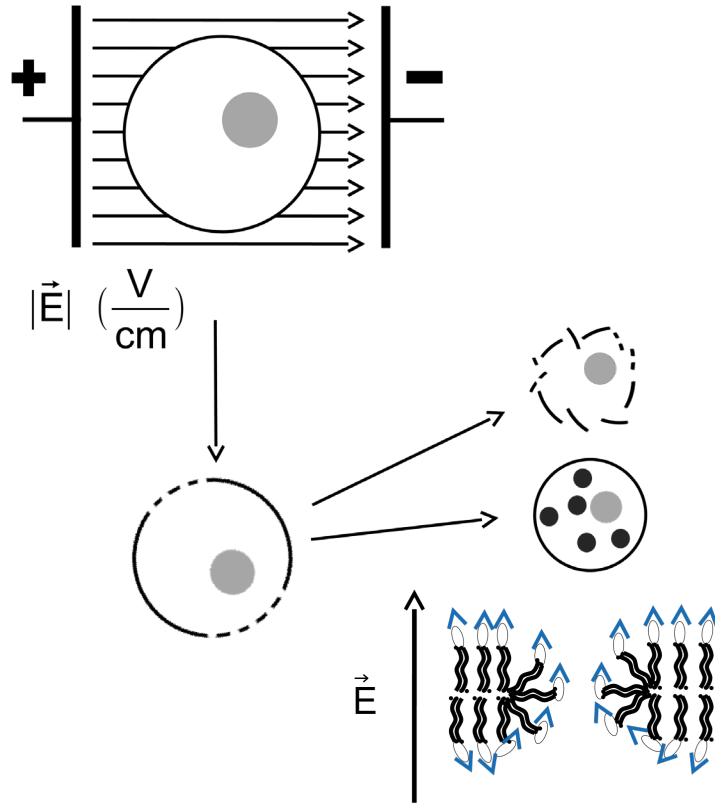
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Disadvantages IRE vs. RFA

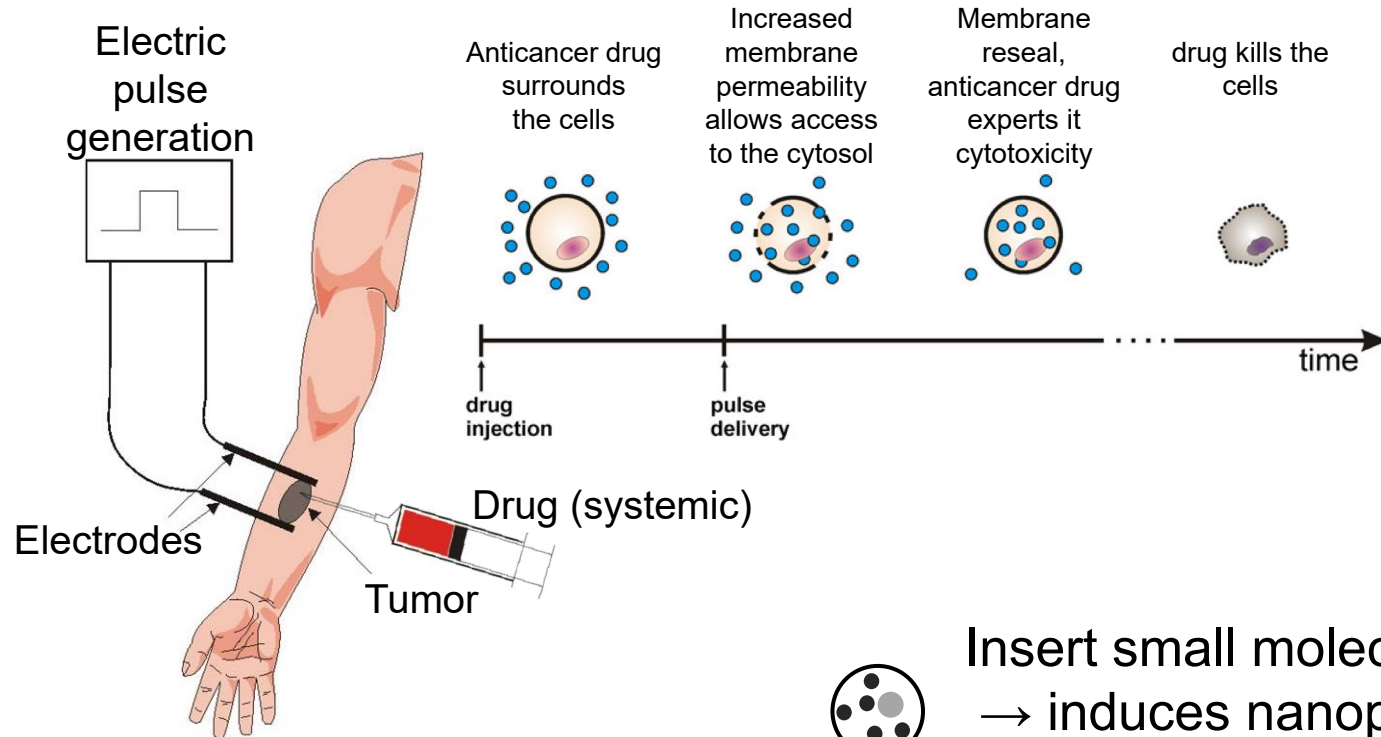
- More Electrodes
 - longer preparation time
- More needle tracts
 - increased risk tract seeding [1]

Background – EP for tumor therapies



- 1) Irreversible, permanent destruction
→ Irrecoverable defects ($\approx s$), cell death ($\approx h$) [1]
→ **IRE – Irreversible Electroporation**
- 2) Temporary destabilize of cell membrane
→ induces nanopores $\varnothing \approx 20-120$ nm [2]
→ Insert small molecules: drugs
→ Recovering, membrane still permeabilized ($\approx s$)
→ Defects recovered, membrane resealed ($\approx h$) [1]
→ **ECT – Electrochemotherapy**

Background – EP in medical usage



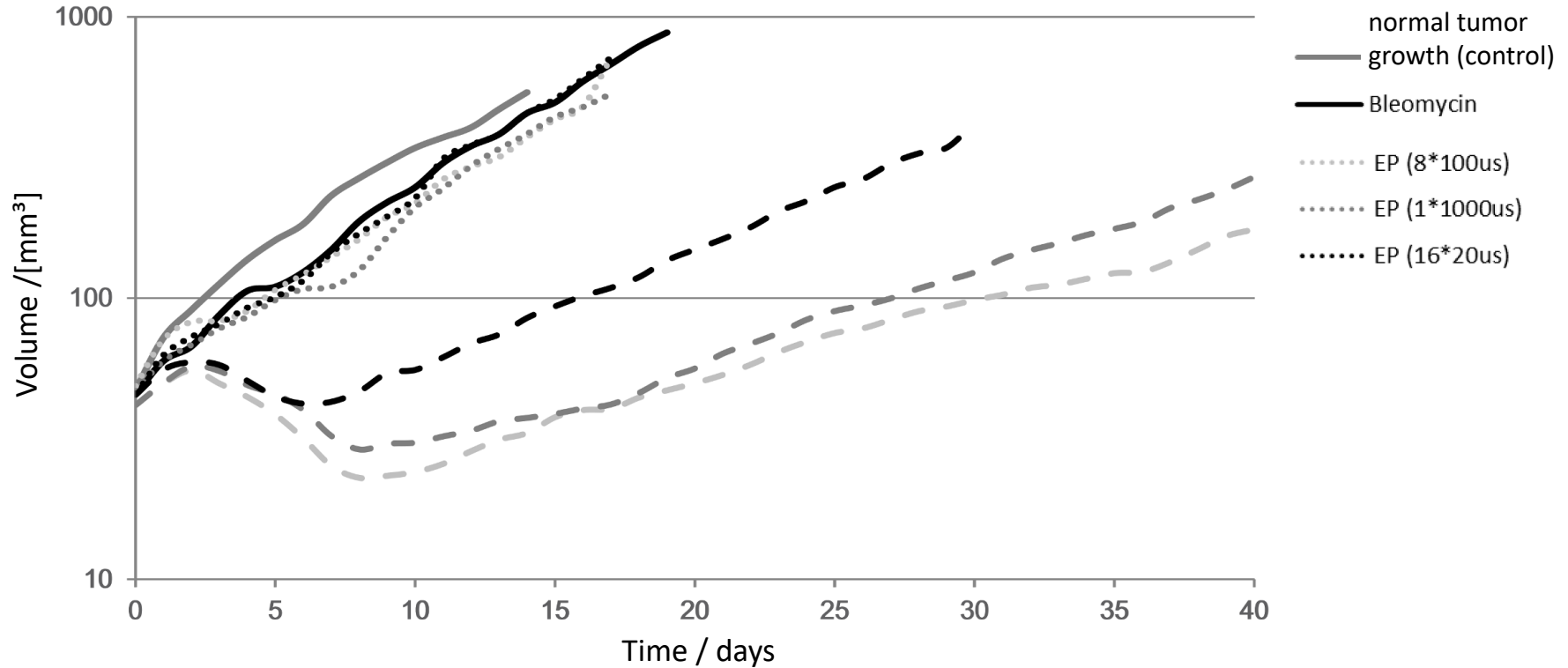
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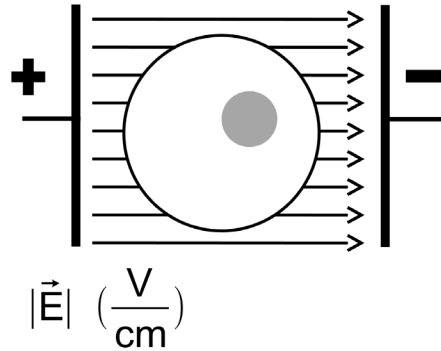
Electrochemotherapy in treatment of tumours
Serša, Snoj, 2008

Background – EP in medical usage



Based on: Optimisation of Pulse Parameters In Vitro for In Vivo Electrochemotherapy, Lebar, Miklavčič, 2002

Background – EP in medical usage



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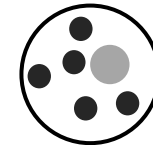


Disadvantages IRE vs. RFA

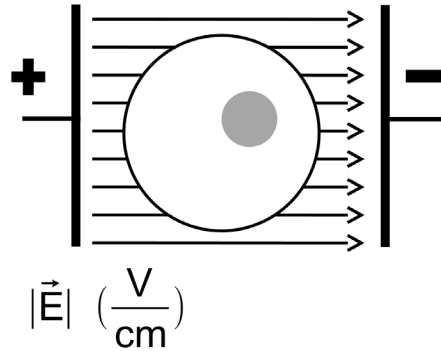
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Advantages ECT vs. IRE

- Apoptosis
- More tumor-specific
- Reduced field strength / bigger ablation area



Background – EP in medical usage



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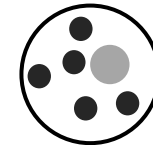


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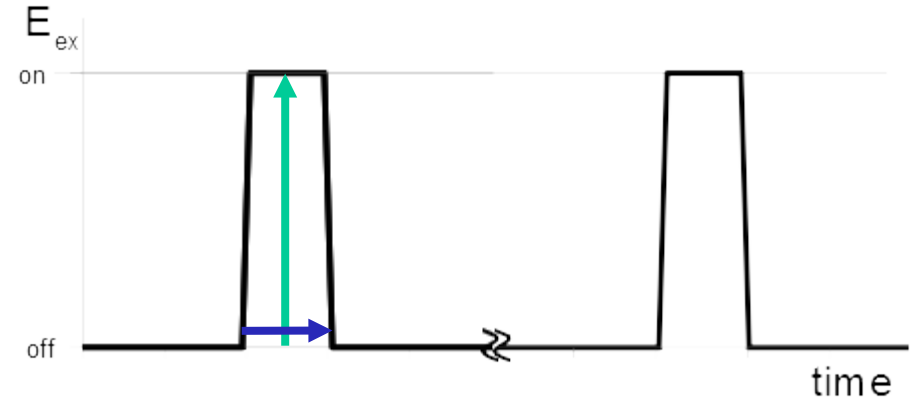
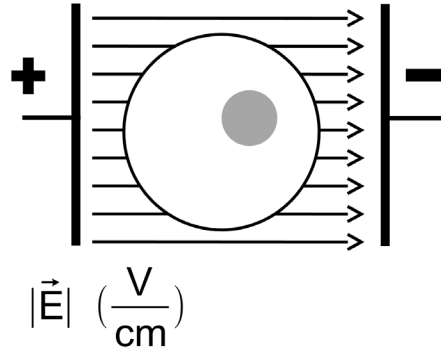
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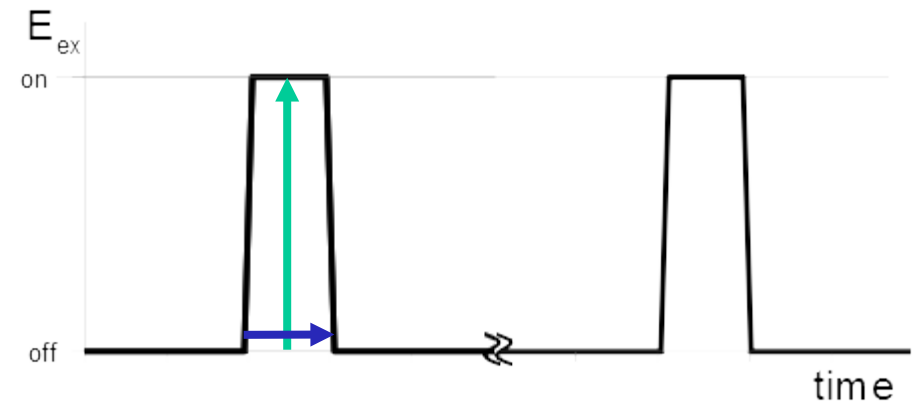
Background – EP in medical usage



Main parameters: field strength E (Volt / distance), puls width, shape (rect), distance, # of pulses, frequency

Background – EP in medical usage

Field strength E



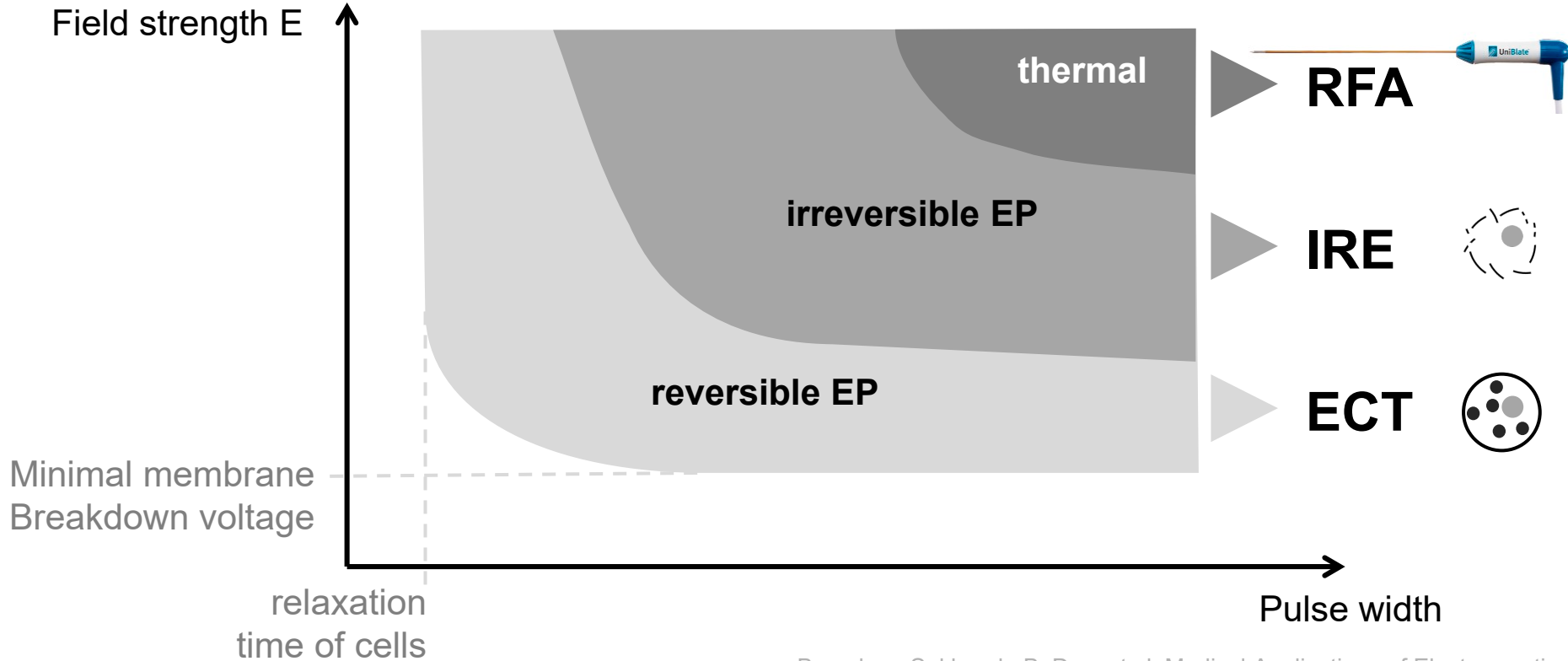
Minimal membrane
Breakdown voltage

relaxation
time of cells

Pulse width

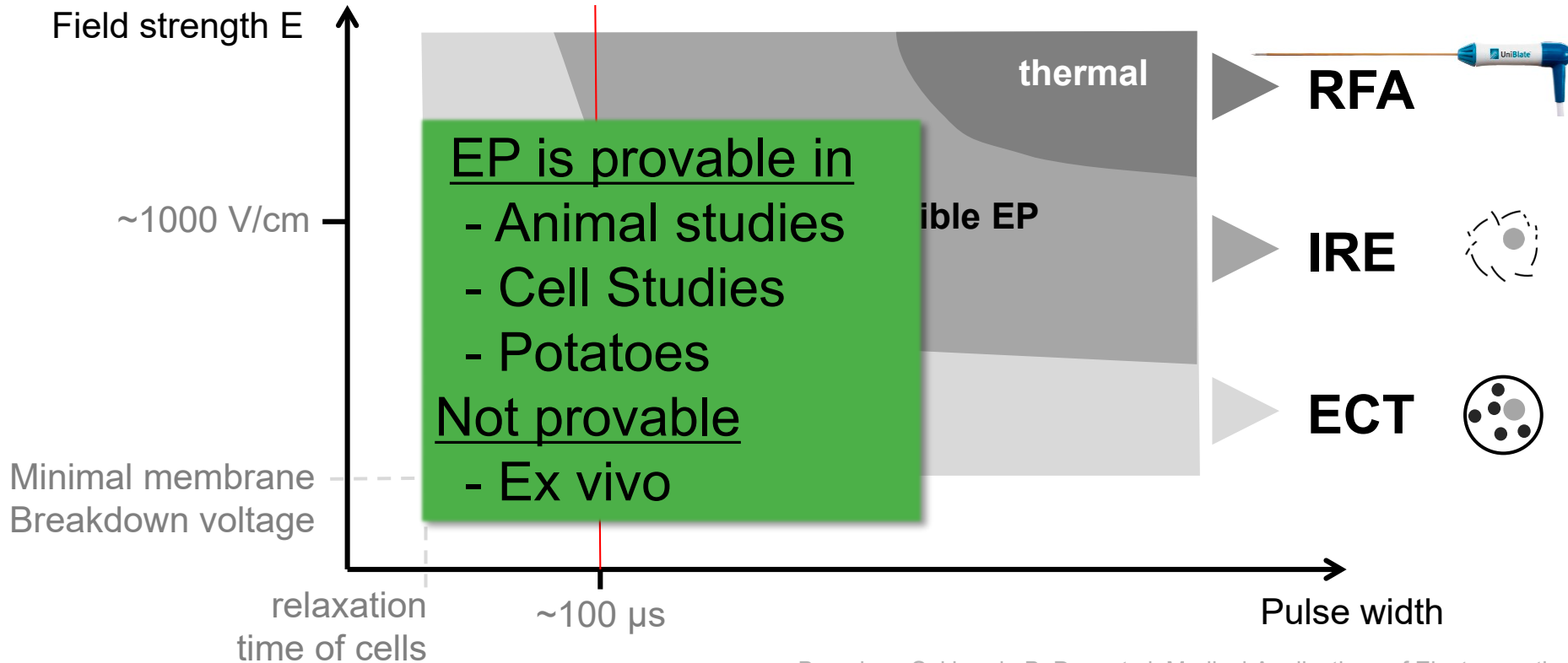
Based on: Sukhendu B. Dev, et al. Medical Applications of Electroporation“
IEEE transactions on Plasma Science 28/1, 2000

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