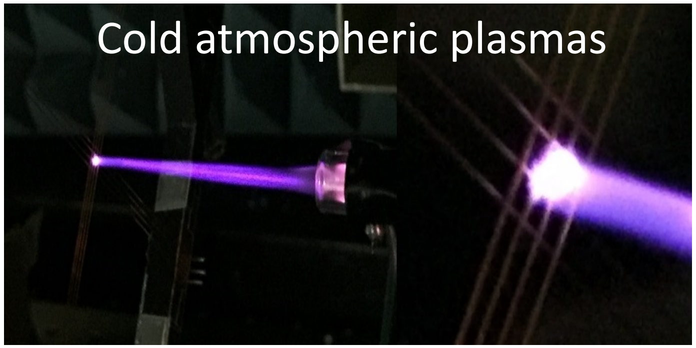
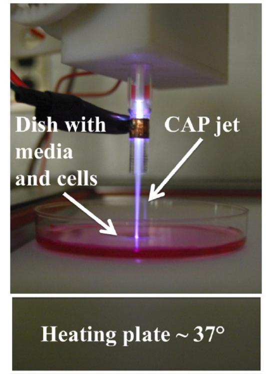
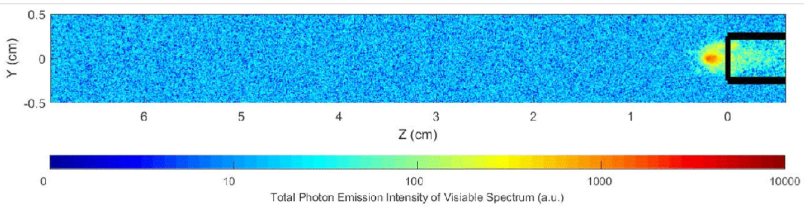
Project GWU # 1

- **Title:** Adaptive Plasmas and Plasma Medicine Mechanism
- **PI(s):** Michael Keidar and Taeyoung Lee, George Washington University
- **Need and Relevance:** medical application of plasmas require understanding mechanism of plasma action and higher control over plasma application
- **Goals:** to develop novel adaptive plasma devices and to understand the mechanism of plasma interaction with cells and tissue
- **Approach:** develop new diagnostics, hypothesis and validation
- **Outcomes/Deliverables:** new plasma devices, diagnostics
- **Project Duration, Budget:** 3 years / $50k/year

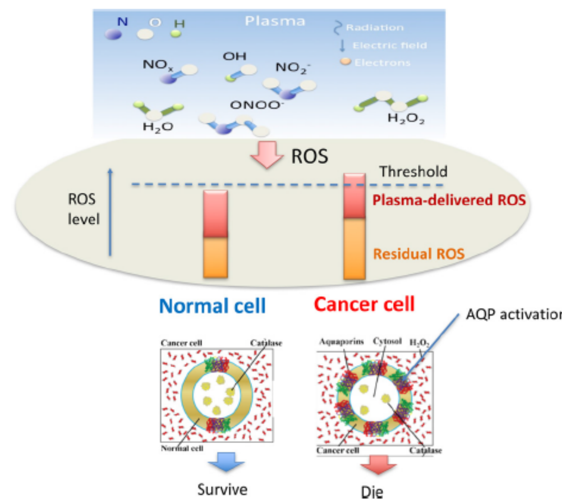
Need and Relevance



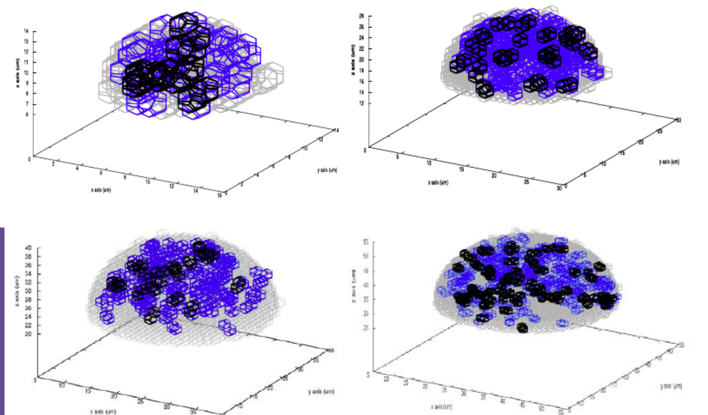




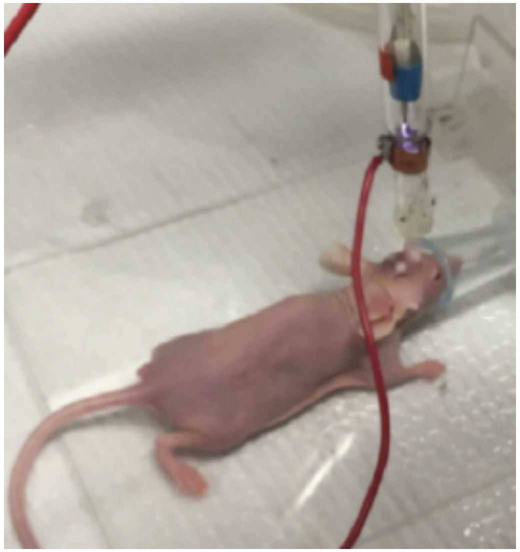
Mechanism

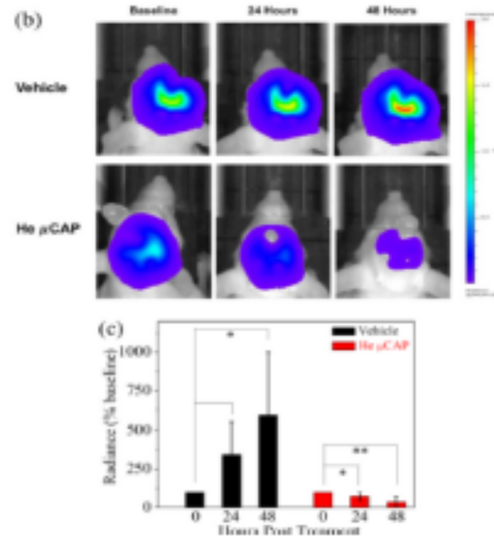


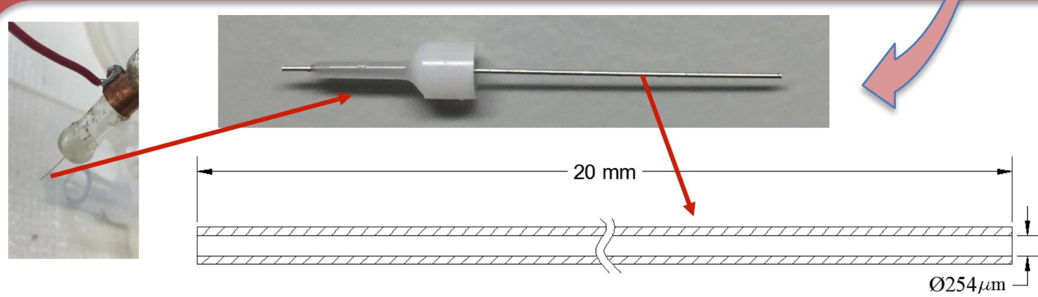
Simulation of plasma interaction with solid tumor



Recent results, brain tumor







Chen et al, *Cancers*, 2017
Keidar, Phys. Plasmas , 2018

Clinical study

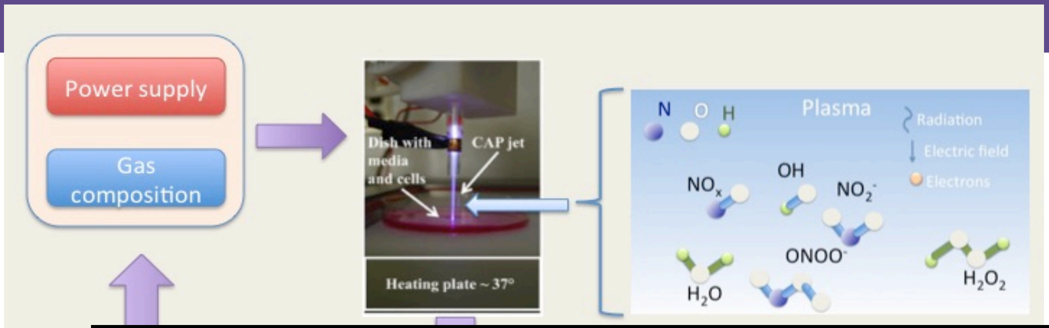
Treatment of surgical margins was performed

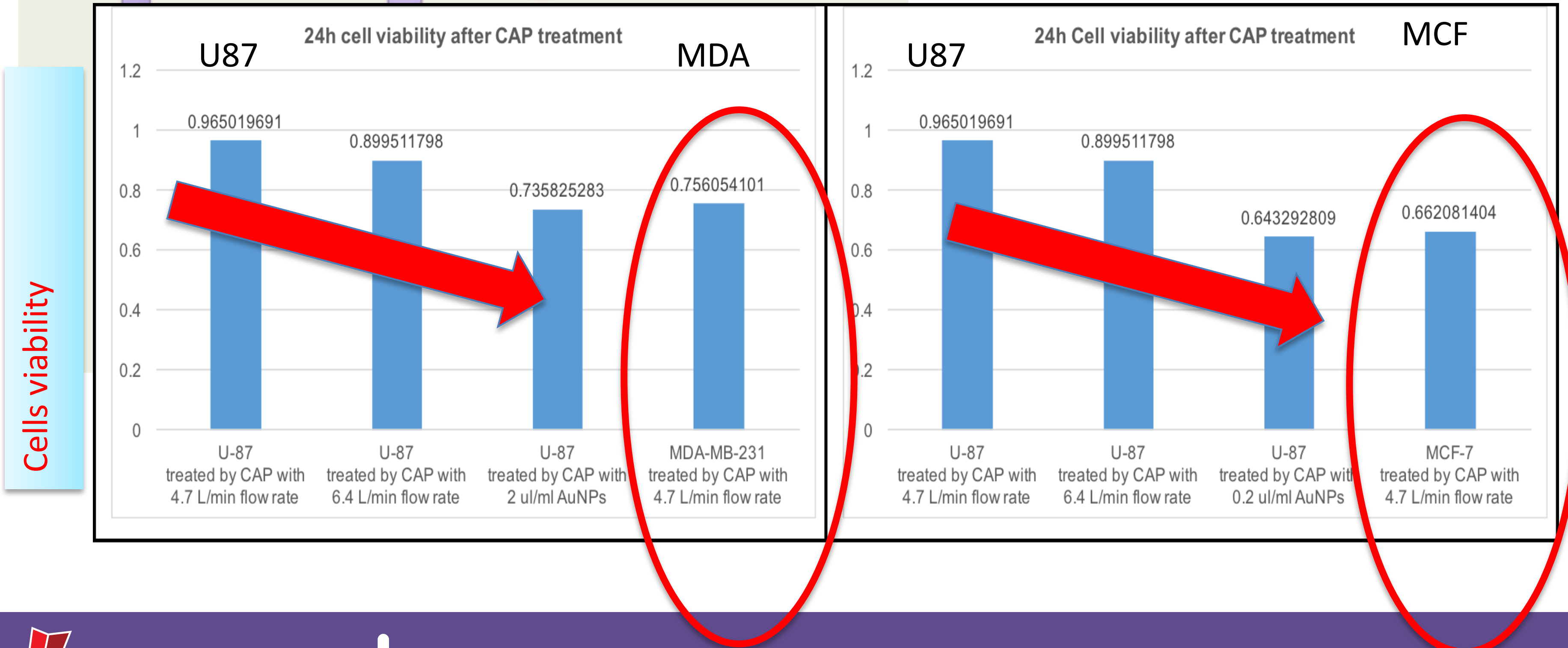
Rush University Medical Center applied USMI/GWU CAP device for treatment for pancreatic cancer, April 2017

Goals

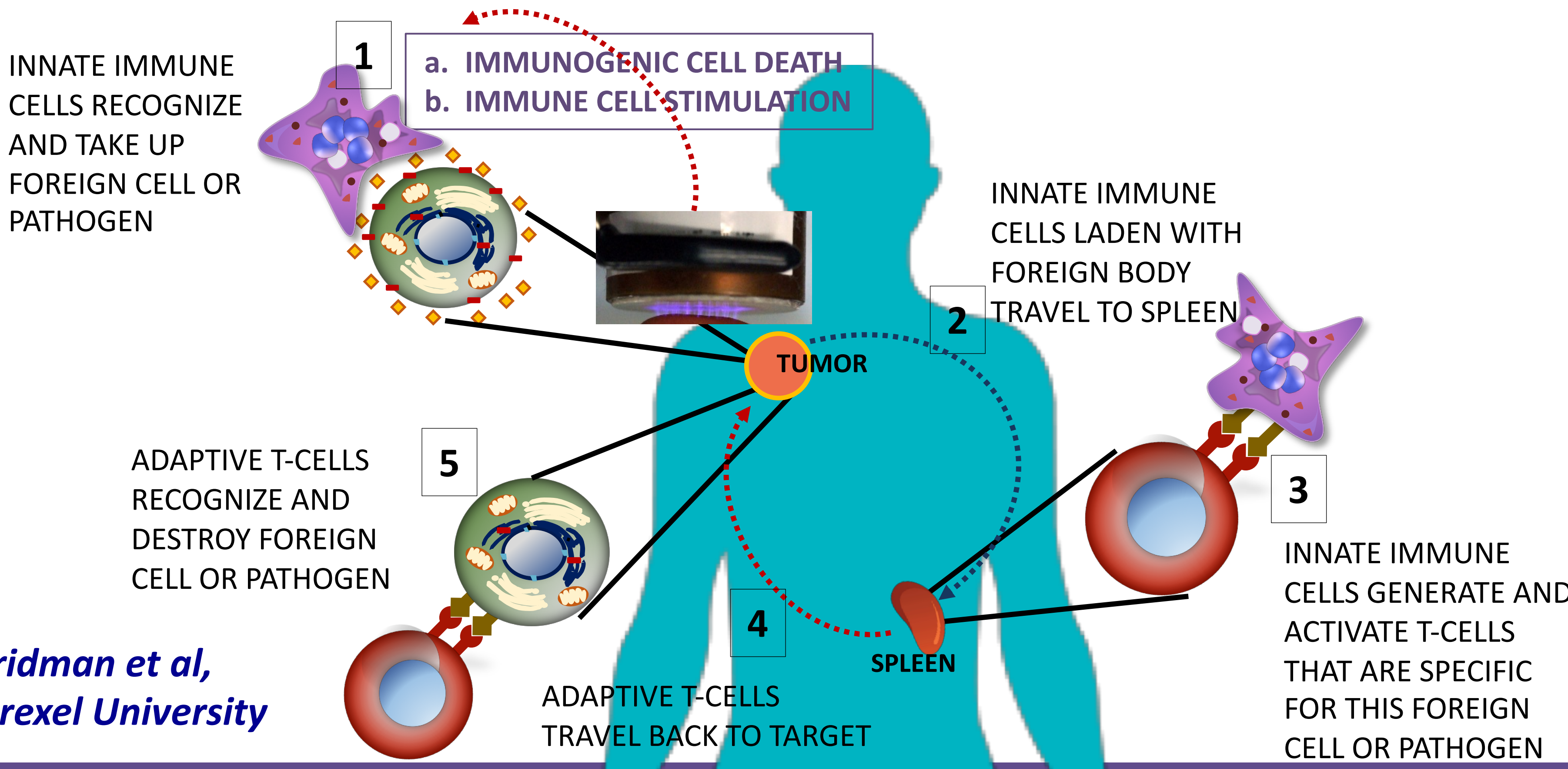
Adaptive plasma platform

M. Keidar, J. Nanomed Res, 2016
M. Keidar, Trends in Biotechnology, 2017



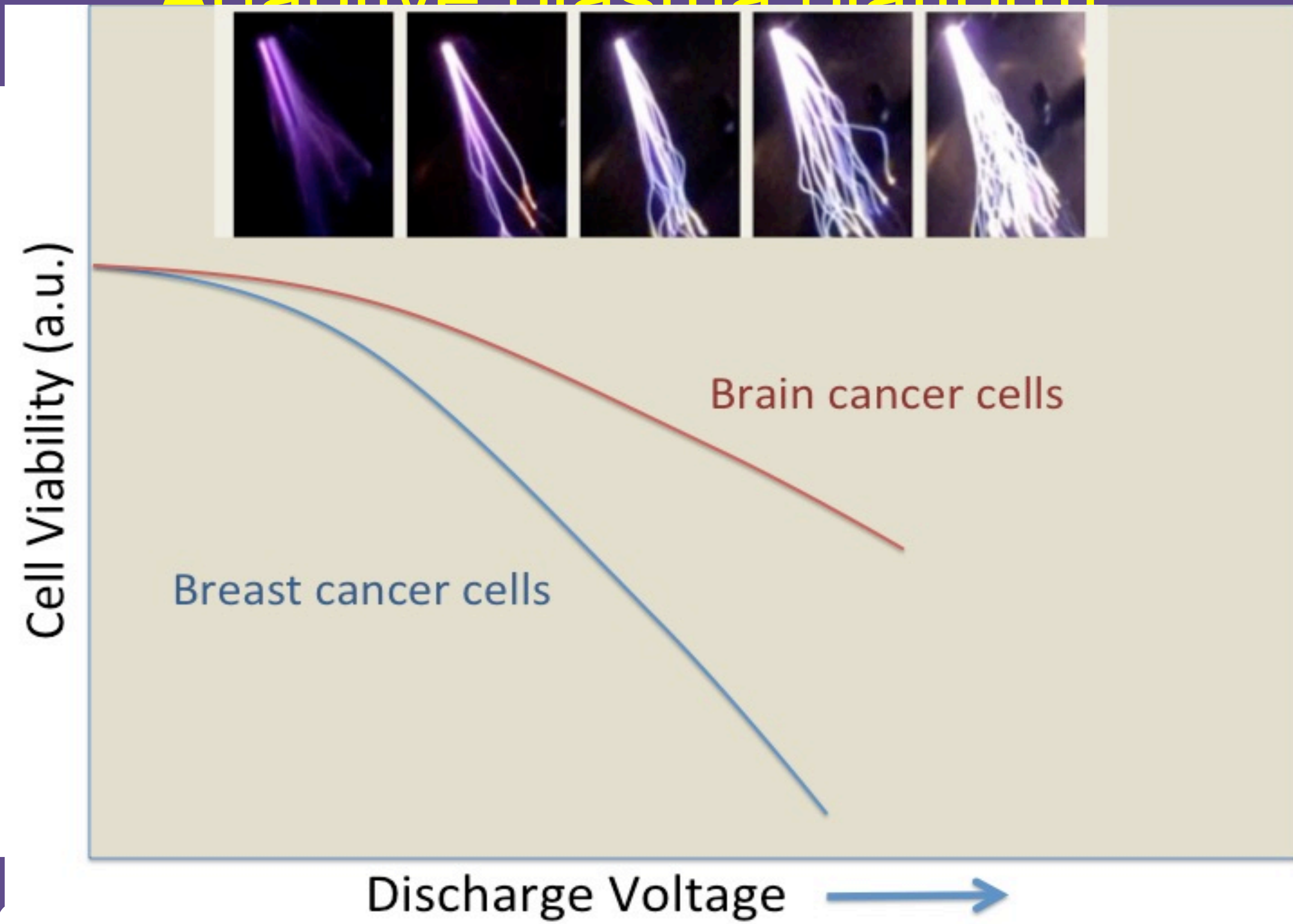


Plasma Immunotherapy

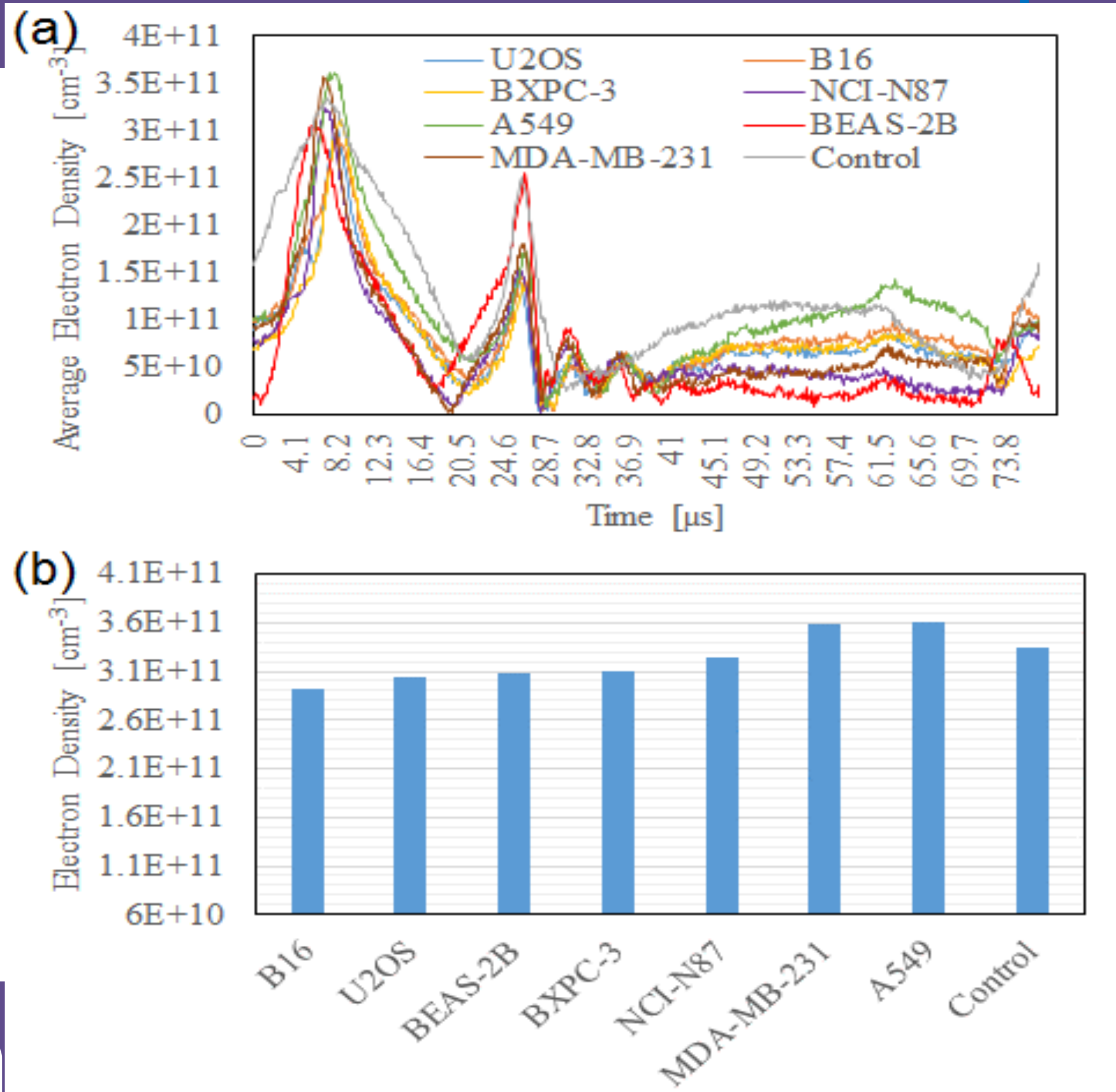


Fridman et al, Drexel University

Adaptive plasma platform



Medium & cells effect on plasma



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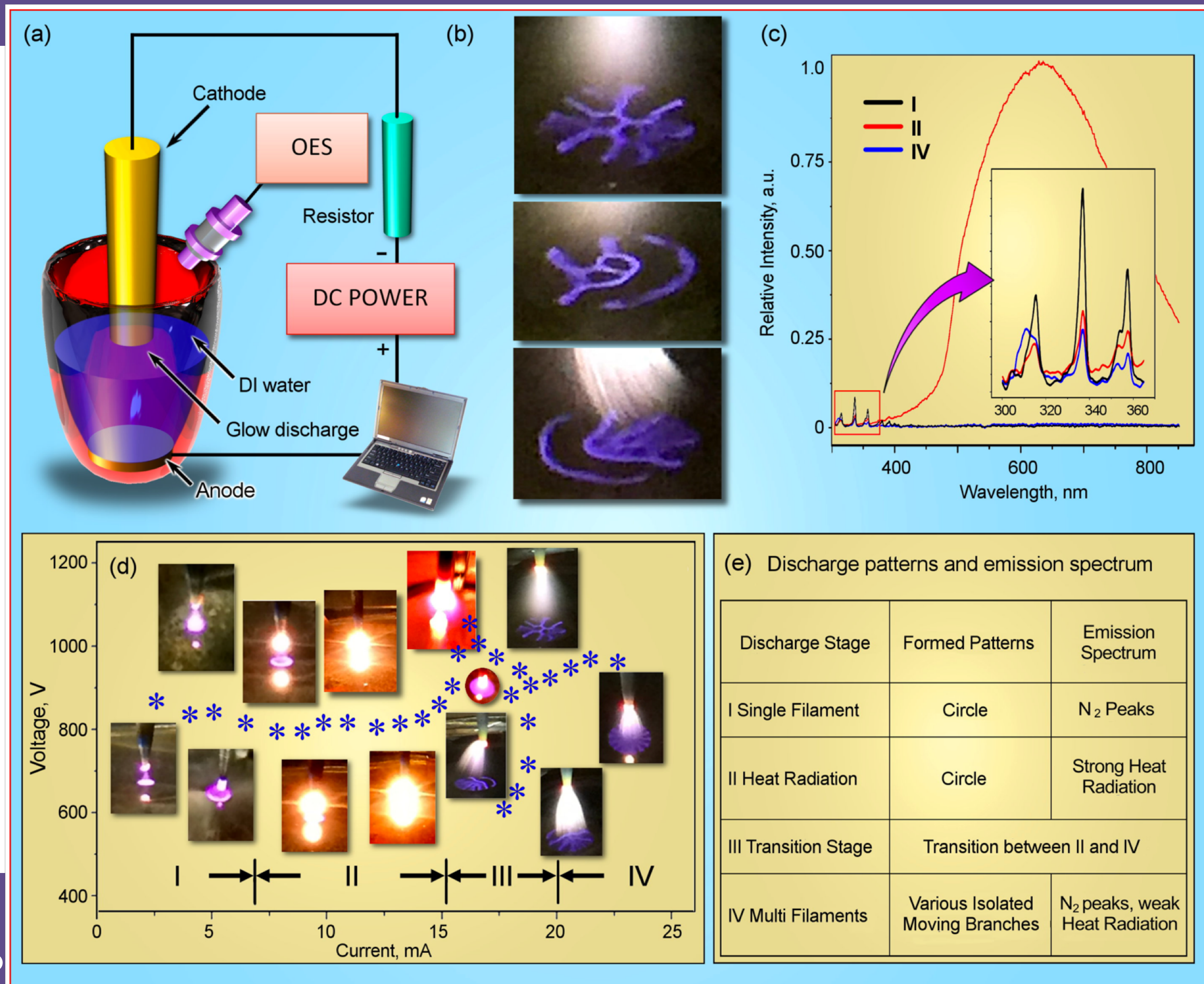
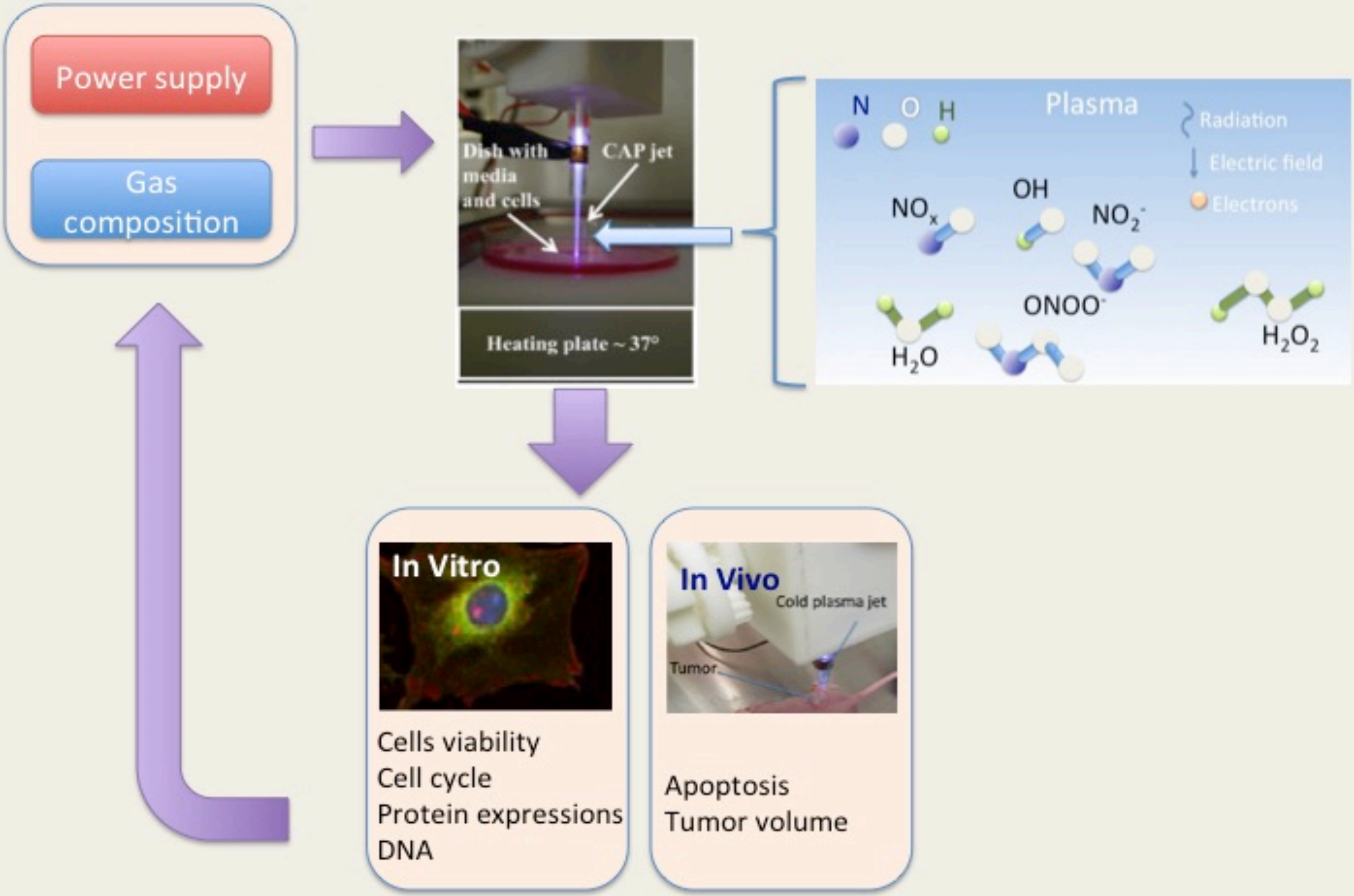


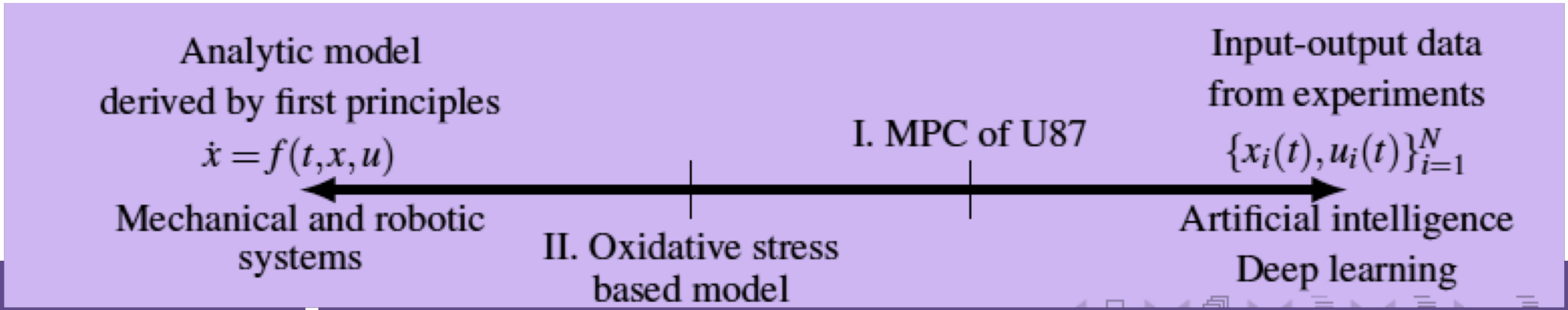
Discharge Stage	Formed Patterns	Emission Spectrum
I Single Filament	Circle	N_2 Peaks
II Heat Radiation	Circle	Strong Heat Radiation
III Transition Stage	Transition between II and IV	
IV Multi Filaments	Various Isolated Moving Branches	N_2 peaks, weak Heat Radiation



Power supply
Gas composition
Dish with media and cells
CAP jet
Heating plate ~ 37°
N
O
H
Plasma
Radiation
Electric field
Electrons
NOx
OH
NO2-
ONOO-
H2O
H2O2
In Vitro
Cells viability
Cell cycle
Protein expressions
DNA
In Vivo
Cold plasma jet
Tumor
Apoptosis
Tumor volume

Approach

- Interdisciplinary Research Toward Autonomous Cancer Therapy
  - Interplay between plasma physics, mathematical oncology, control system engineering for the development of intelligent biomedical system for oncology
  - Adaptivity: treatment tailored to the particular cancer cell response
  - Optimality: treatment schedule optimized for cancer viability, selectivity, etc
  - Robustness: reject undesired behavior caused by modeling errors and uncertainties
  - Autonomy: autonomous scheduling for dose and frequency



Model Predictive Control

Motivation

- Cancer cell response to CAP treatments depends on various intrinsic and extrinsic factors;
- Mathematical model may not represent the actual response of the specific cancer cells treated;
- Adjust the treatment parameters adaptive based on the actual cell response.

Problem Formulation

- CAP treatment is repeated four times at the interval of 48 hours;
- At the end of each 48 hour period, cell viability is measured;
- After completion of the treatments, cell viability should reduced to 10%

Model Predictive Control

Treating Control using MPC

- Adjust the desired relative cell viability based on the actual response of the previous treatment

$$r_{desired} = 0.1^{\frac{1}{4}} \quad \text{at the first treatment}$$

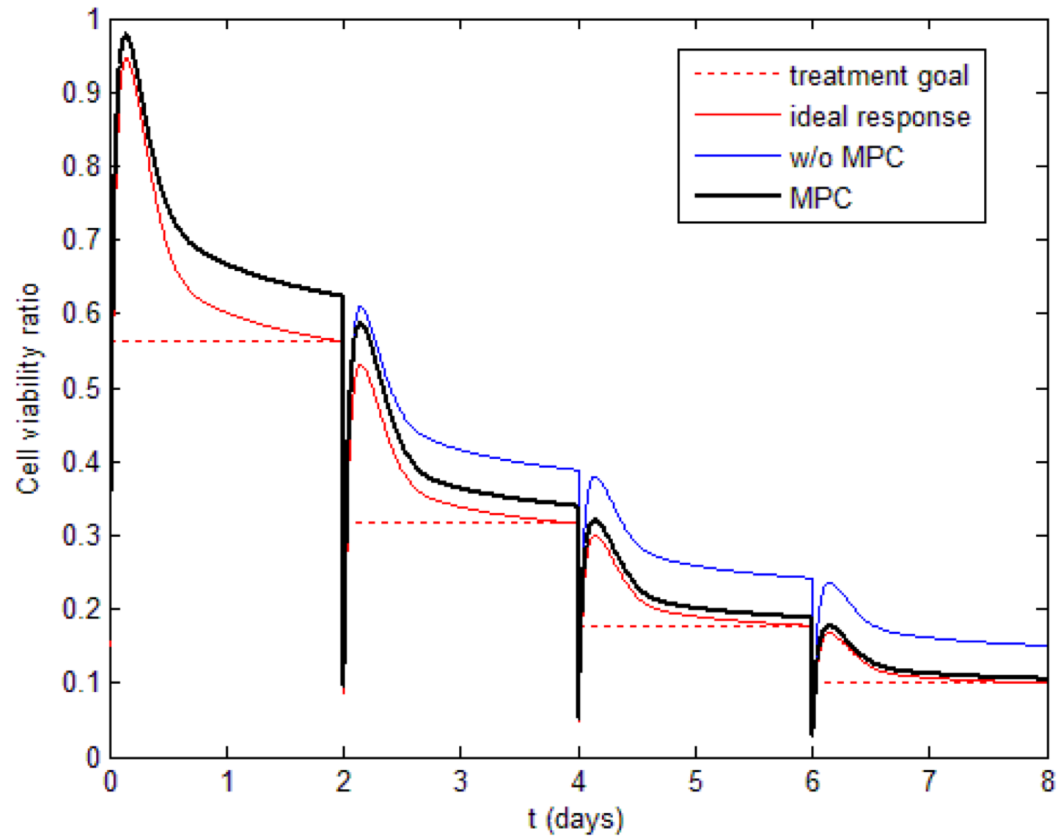
- (0.1)^(1/4) * expected cell viability / actual cell viability during the remaining treatments.

Numerical Simulation

- The preceding mathematical model is considered as the actual cancer response;
- The parameters of the mathematical model is altered to represent a mathematical model available to MPC.

Outcomes/Deliverables

Model Predictive Control

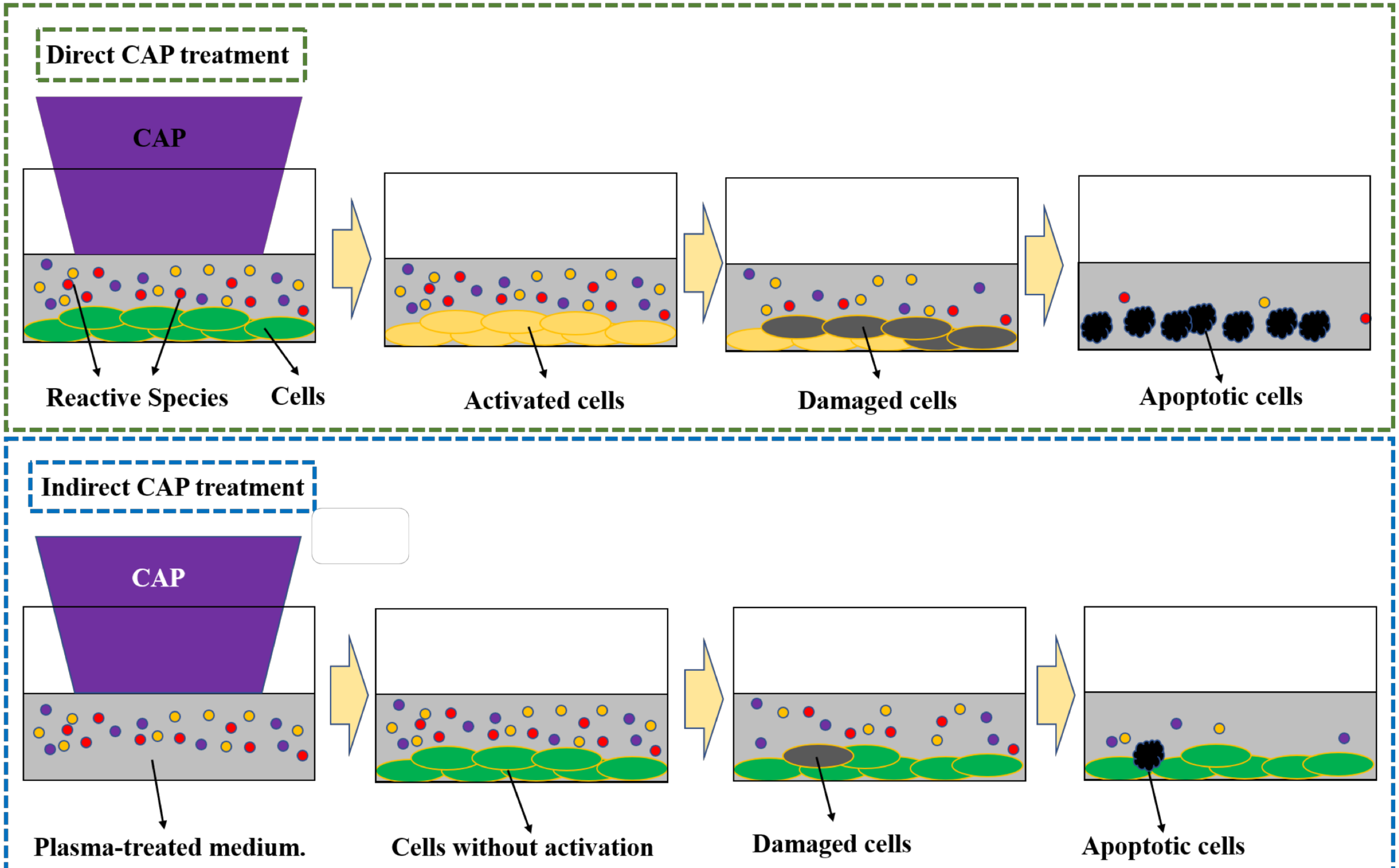


Red line: ideal case when the actual cancer dynamics is available

Blue line : optimal control without MPC scheme;

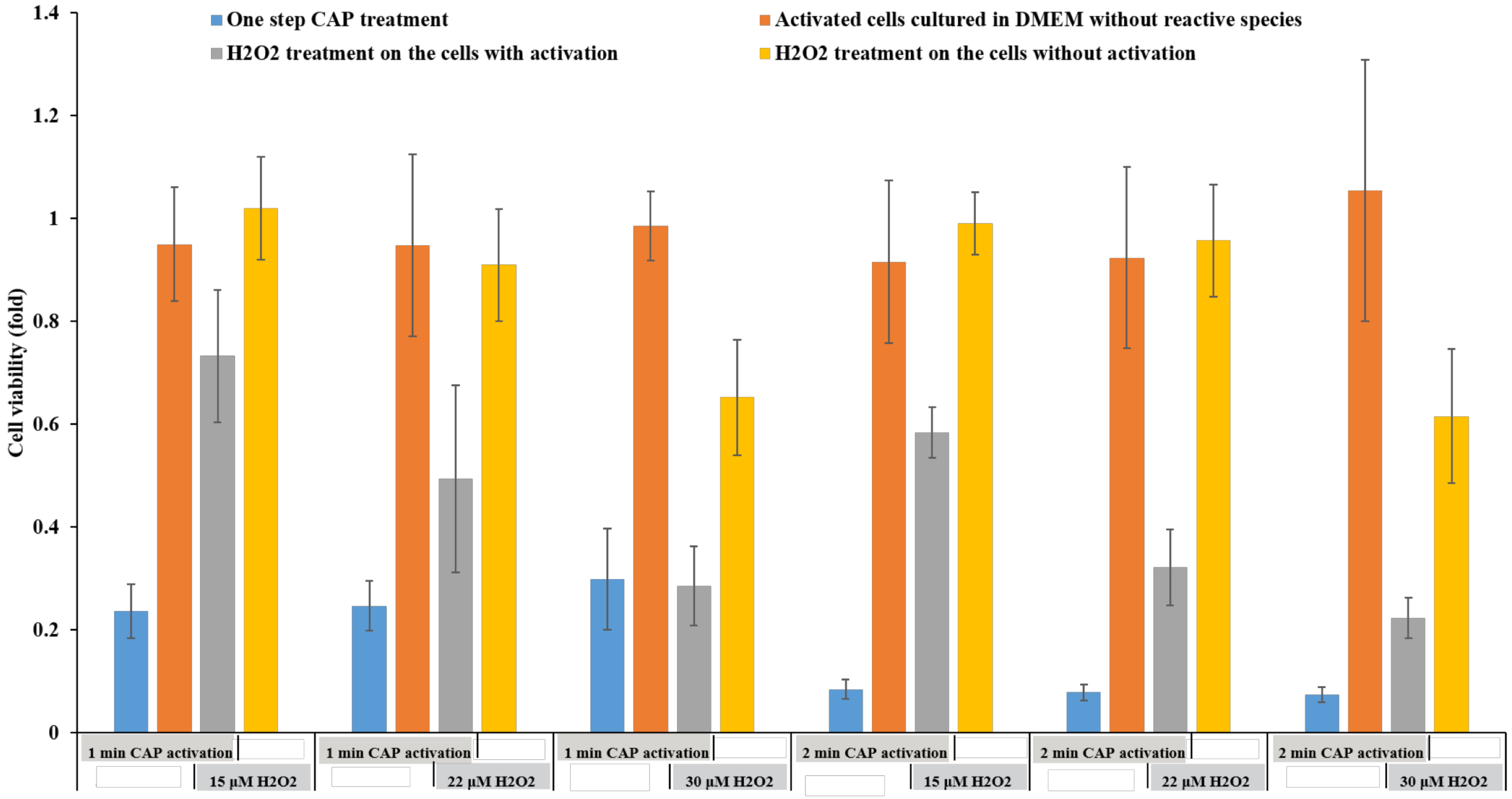
Black line : Model predictive control.

New evidence: the activation state of the CAP-treated cancer cells



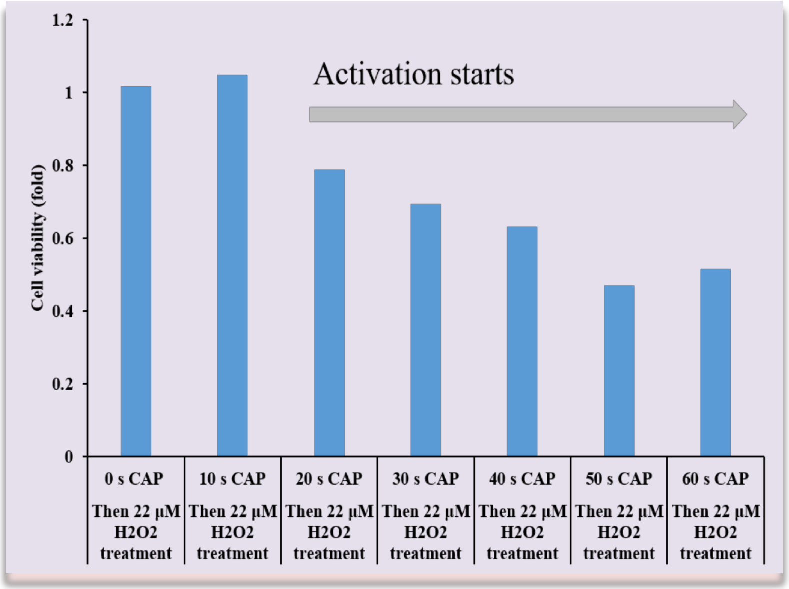
Dayun Yan, et al, just submitted.

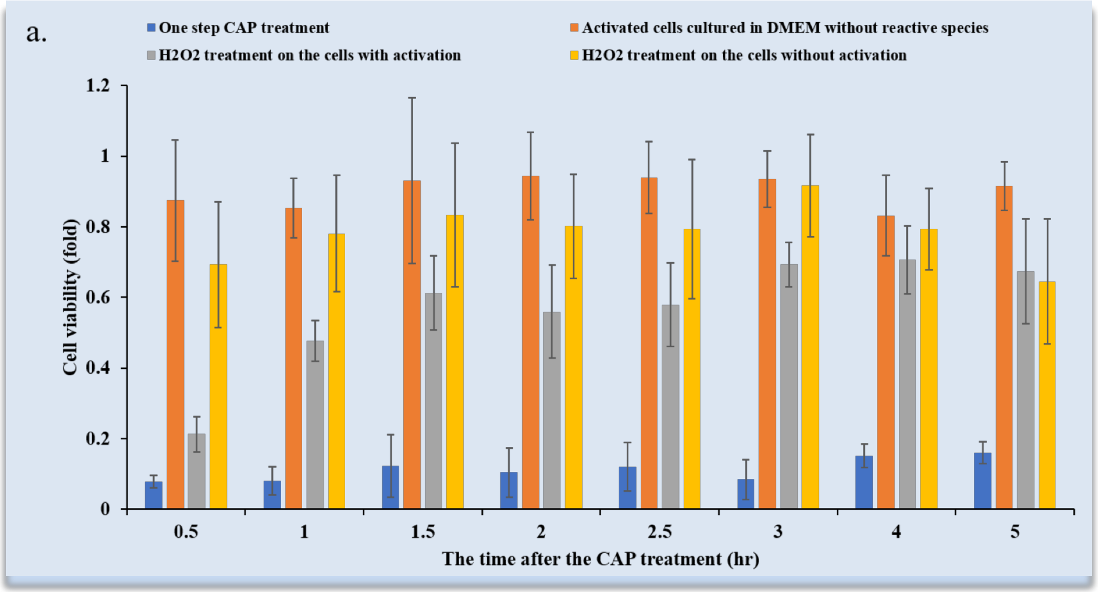
Activation state of the CAP-treated cells



Sensitization

The slow de-sensitization





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Project Timeline and Duration

Task / month	1	2	3	4	5	6	7	8	9	10	11	12
Plasma activation	x	x	x	x								
MPC software				x	x	x	x					
Feedback hardware							x	x	x	x		
First demo of adaptive device									x	x	x	x

Project Budget

Item	Cost
Student stipend + tuition	$ 35,000.00
Supplies	$ 7,000.00
Purchased services	$ 0.00
Equipment	$ 0.00
Travel	$ 3,000.00
Project total*	**$ 45,000**