SPATIAL PHARMACOKINETIC-TOXICOKINETIC MODELLING

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STOCHASTIC-REACTION DIFFUSION SYSTEMS

- **The mathematical core of Redi**

- Generalized Fick's first and second laws with state dependent diffusion coefficients.

- Stochastic selection of diffusion and chemical reaction events.

Inputs

- Molecular mass of diffusing particle

- Chemical reactions eventually involved in the system and their kinetic rates

- Initial local concentrations of the species.

GEMCITABINE DIFFUSION AND TUMOR SHRINKAGE

The reaction-diffusion system involves two compents drug (D), i.e. gemcitabine, and tumor cell (T) and the following events:

- gemcitabine diffusion (molecular weight of 299.66)
- gemcitabine degradation
- effective interaction of gemcitabine and death of tumor cell
- uneffective interaction of gemcitabine: the tumor cell survives
- tumor growth

Tumor size model:

- irregular 2D spheroidal tumor of 3 mm

Interaction	Rate constants
R1 : $D \xrightarrow{k_1} \emptyset$	$k_1 = 0.1 \text{ hours}^{-1}$
R2 : $D + T \xrightarrow{k_2} \emptyset$	$k_2 = 0.0001 \text{ (cm} \cdot \text{hours)}^{-1}$
R3 : $D + T \xrightarrow{k_3} T$	$k_3 = 0.001 \text{ (cm} \cdot \text{hours)}^{-1}$
R4 : $T \xrightarrow{k_4} T + T$	$k_4 = 0.02 \text{ cm} \cdot \text{hours}^{-1}$

Category of patient	Median value of efficacy
Male	$0.03817219 \text{ (cm} \cdot \text{hours)}^{-1}$
Female	$0.03815441 \text{ (cm} \cdot \text{hours)}^{-1}$
Smoker	$0.02937583 \text{ (cm} \cdot \text{hours)}^{-1}$
Ex-smoker	$0.07753538 \text{ (cm} \cdot \text{hours)}^{-1}$
Non-Smoker	$0.03815441 \text{ (cm} \cdot \text{hours)}^{-1}$

Lecca, P., Kahramanğullari, O., Morpurgo, D., Priami, C., Soo, R.A., **Modelling and Estimating Dynamics of Tumor Shrinkage with BlenX and Kinfer,** UkSim 13th International Conference on Computer Modelling and Simulation (UKSim), 2011

TIME EVOLUTION OF THE TUMOR

Refer to P.Lecca (lecca@cosbi.eu) for a longer and higher-quality video of the simulation.
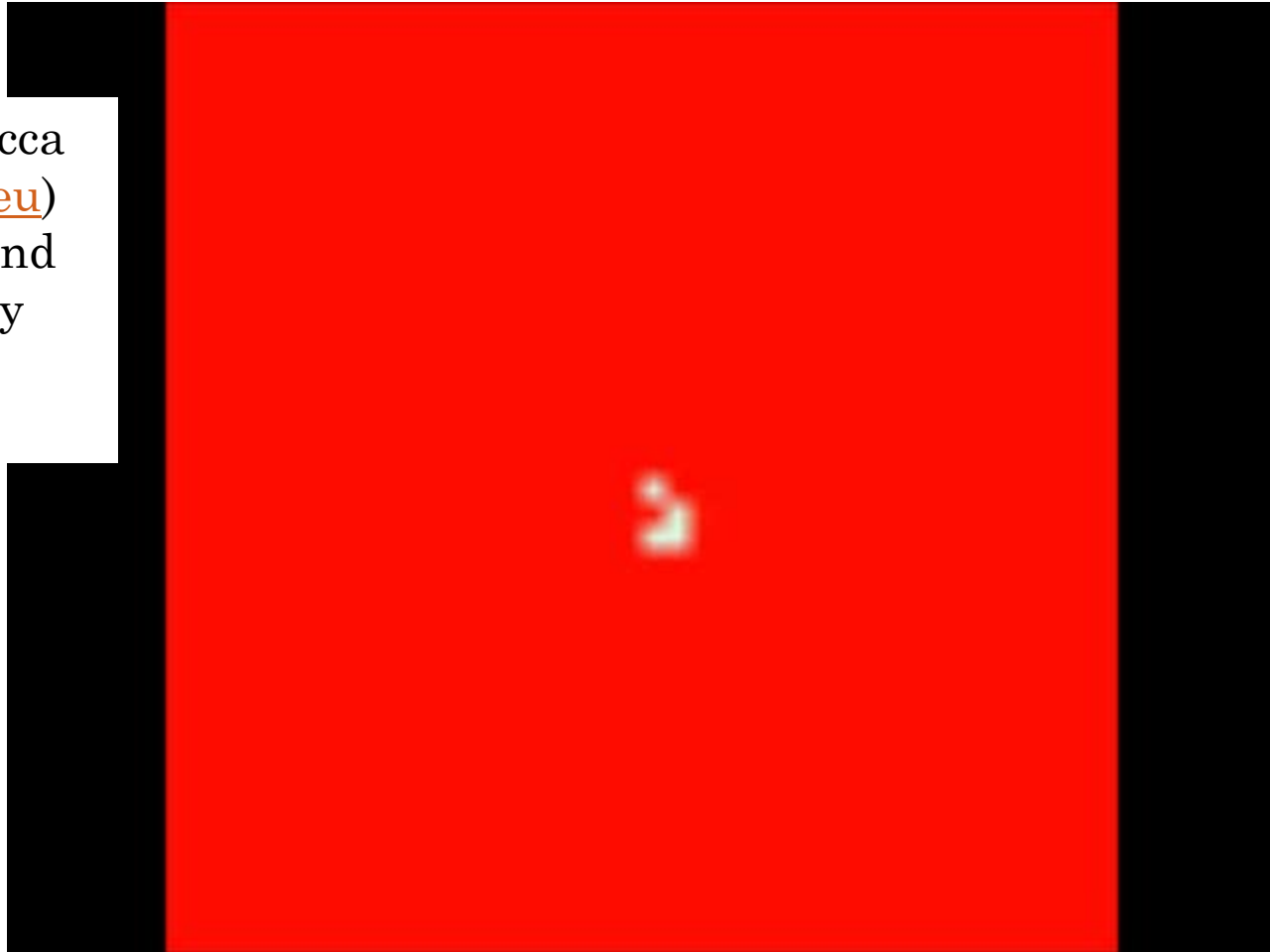
Duration of gemcitabine treatment: 14 weeks

REFERENCES

Redi: http://www.cosbi.eu/index.php/research/prototypes/redi

P. Lecca, O. Kahramanogullari, D. Morpurgo, C. Priami, R. Soo, Modelling and estimating dynamics of tumor shrinkage with BlenX and KInfer,, UKSim 2001 - 13th International Conference on Modelling and Simulation,2011

P. Lecca, L. Dematte', A. Ihekwaba, C. Priami, Redi: a simulator of stochastic biochemical reaction-diffusion systems, The Second International Conference on Advances in System Simulation (SIMUL 2010)