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Modelling cell response to cancer drug treatment identifies dynamic features of efficient cell death initiation, enabling prediction and control of therapeutic response heterogeneity

Marielle Péré, Madalena Chaves, Jérémie Roux

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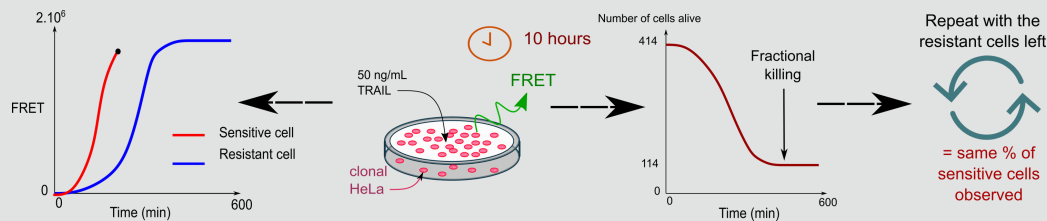
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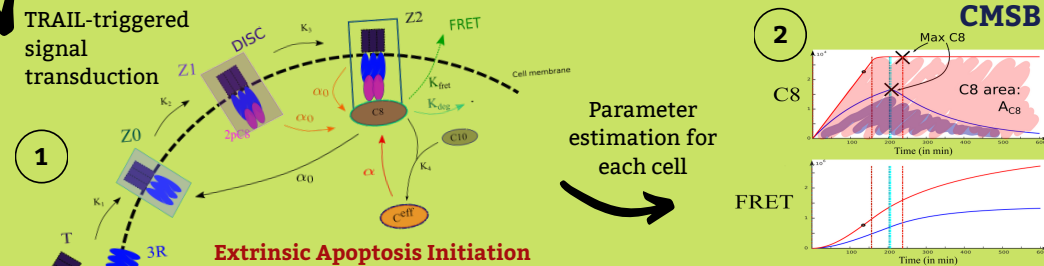


Marielle Péré, Madalena Chaves, Jérémie Roux - marielle.pere@inria.fr - Université Côte d'Azur, France

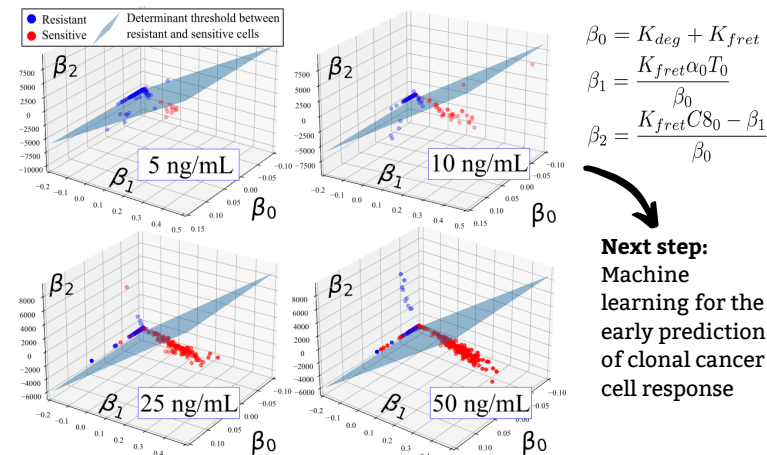
1 - Studying non-genetic resistance in cancer - Roux *et al.*, MSB 2015



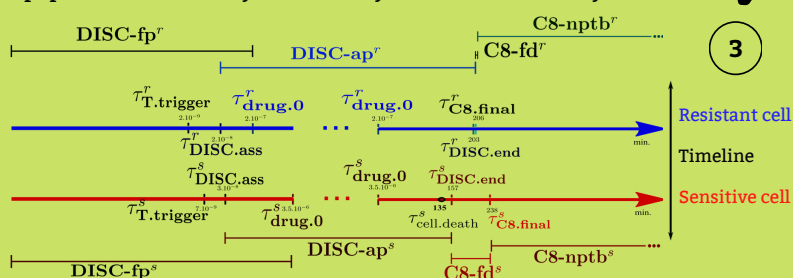
2 - Modeling pro-apoptotic drug response and timeline analysis - Péré *et al.*, CMSB 2021



3 - A cell decision threshold with potential predictive value - Péré *et al.*, FOSBE 2022



Apoptosis initiation key-times for dynamic solution analysis



4

Principal Process Analysis (PPA)

var.	All experience	$[0 \tau_{T.trigger}]$	$[\tau_{T.trigger}, \tau_{DISC.ass}]$	$[\tau_{DISC.ass}, \tau_{drug.0}]$	$[\tau_{drug.0}, \tau_{DISC.end}]$	$[\tau_{DISC.end}, \tau_{C8.final}]$	$[\tau_{C8.final}, \tau_{cell.death}]$
\dot{T}	$-K_1 TR^3$				$+K_1 Z_0$	$+K_1 Z_0$	$+K_1 Z_0$
\dot{R}	$-3K_1 TR^3$				$+3K_1 Z_0$	$+3K_1 Z_0$	$+3K_1 Z_0$
Z_0	$K_1 TR^3$ $-K_2 Z_0 p C_8^2$	$K_1 TR^3$	$K_1 TR^3 + \alpha_0 Z_1$ $-K_2 Z_0 p C_8^2$ $+K_2 Z_1$	$K_1 TR^3 + \alpha_0 Z_1$ $-K_2 Z_0 p C_8^2$ $+K_2 Z_1$	$+K_1 TR^3 + \alpha_0 Z_1$ $-K_2 Z_0 p C_8^2$ $+K_2 Z_1$	$K_1 TR^3 + \alpha_0 Z_1$ $-K_2 Z_0 p C_8^2 - K_1 Z_0$ $+K_2 Z_1$	$K_1 TR^3 + \alpha_0 Z_1$ $-K_2 Z_0 p C_8^2$ $-K_1 Z_0$ $+K_2 Z_1$
pC_8	$-K_2 Z_0 p C_8^2$			$2K_2 Z_1$	$+2K_2 Z_1$	$+2K_2 Z_1$	$+2K_2 Z_1$
Z_1	$K_2 Z_0 p C_8^2$		$-\alpha_0 Z_1 - K_2 Z_1$	$-\alpha_0 Z_1 - K_2 Z_1$	$-\alpha_0 Z_1 - K_2 Z_1$	$-\alpha_0 Z_1 - K_2 Z_1$	$-\alpha_0 Z_1 - K_2 Z_1$
Z_2	$K_3 Z_1 C_8$			$-\alpha_0 Z_1 - K_2 Z_1$	$-\alpha_0 Z_1 - K_2 Z_1$	$-\alpha_0 Z_1 - K_2 Z_1$	$-\alpha_0 Z_1 - K_2 Z_1$
C^{eff}	$K_4 C_{10} Z_2$			$-\alpha C^{eff}$	$-\alpha C^{eff}$	$-\alpha C^{eff}$	$-\alpha C^{eff}$
C_{10}	$-K_4 C_{10} Z_2$			αC^{eff}	αC^{eff}	αC^{eff}	αC^{eff}
C_8	$\alpha_0 Z_1$	$-K_{deg} C_8$		$-K_{deg} C_8$	$-K_{deg} C_8$	$-K_{deg} C_8$	$-K_{deg} C_8$
$FRET$	$K_{fret} C_8$						