MODELING OF THE METASTATIC VARIABILITY IN CANCER DISEASE

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PhD supported by the National Cancer Institute (France)
Project supported by ANR-09-BLAN-0217-01

Metastatic Index (MI)
We define the Metastatic Index at time $T$ by:

$$ M_{MI}(T) = \frac{dN_{c}}{dT} $$

- $dN_{c}$ is the total metastasis number when one cancer from $N_{c}$ appears
- $d$ is the number of days.

Illustration: The breast cancer
A cancer mass at the diagnosis of 1 gram (about 10^6 cells) corresponds to an origin time $T = 2943$ days (about 8 years). The parameter are:

- $a = 0.000471 \text{ day}^{-1}$
- $b = 10^6 \text{ cells}^{-1}$
- $c = 2.5 \times 10^6 \text{ cells}^{-1} \text{ day}^{-1}$
- $\alpha = 0.48$
- $M_{T}(0) = 5$

- The total MI is equal to 40 but we see that there is only one detectable metastases at time $T = 5$ years.
- We observe an exponential growth rate characterized by the Multihost parameter $\alpha$.

Variability of the MI with respect to the parameters $\alpha$ and $\mu$
- We present the variability of $\alpha$ and $\mu$ in the case of the breast cancer using the following parameters:

$$ \alpha = 0.000471 \text{ day}^{-1}, b = 10^6 \text{ cells}^{-1}, c = 2.5 \times 10^6 \text{ cells}^{-1} \text{ day}^{-1} $$

- $M_{T}(0) = 5$

- The parameter $\alpha$ is linked to the migration potential of the metastases.
- $\mu$ characterizes the angiogenic capacity of the tumor.
- $\mu_{T}(0) = 1$

- The parameter $\mu$ is linked to the aggressiveness of the tumor.
- $M_{T}(0) = 5$

- The total number of metastases at $T = 5$ years.

Optimization of the treatment taking into account the inter-individual variability
We consider here the “limit cases" in blue presented in the previous table. They represent the cases where the treatment is not adapted and the therapeutic response can be improved. We then choose the $M_{T}(0) + 5$ including 6 chemotherapy cycles for each patient.

- $M_{T}(0) = 5$
- $M_{T}(0) = 10$
- $M_{T}(0) = 15$
- $M_{T}(0) = 20$
- $M_{T}(0) = 25$
- $M_{T}(0) = 30$

- $\mu_{T}(0) = 1$
- $\mu_{T}(0) = 2$
- $\mu_{T}(0) = 3$
- $\mu_{T}(0) = 4$
- $\mu_{T}(0) = 5$
- $\mu_{T}(0) = 6$

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- $\alpha = 0.50$
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