Predictive modelling for personalized breast cancer treatment

SysBioCancer 2021, Institut Curie

Michal Kloc

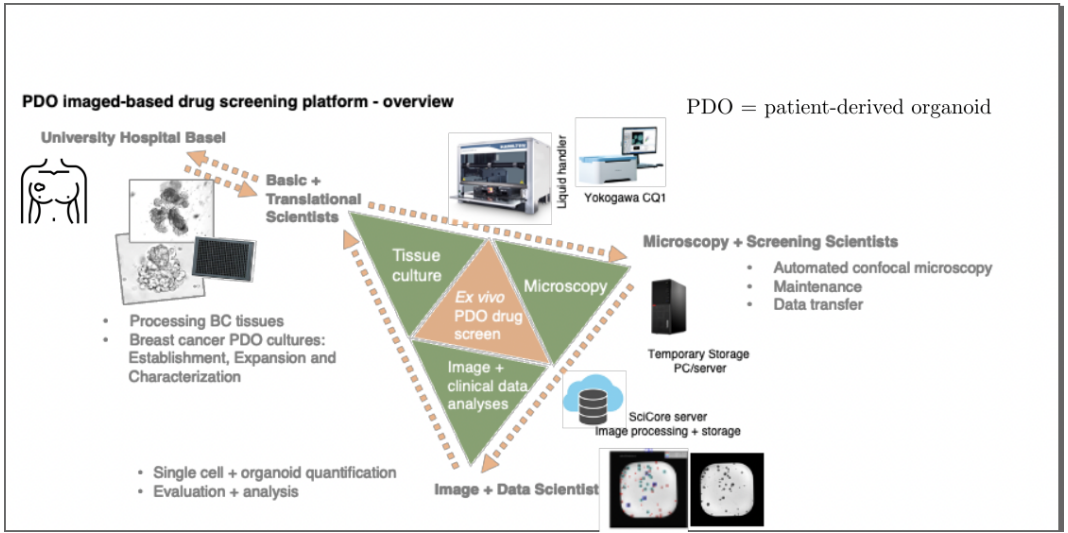
Bentires-Alj Lab, University Hospital Basel, Switzerland, September 27, 2021

Outline

Projects:

1. Drug sensitivity prediction for efficient screening
    a. Drug screening platform, pipeline
    b. PaccMann: open source model of cancer drug sensitivity by IBM
2. Optimizing a mathematical model of cancer therapy using differentiable programming
    a. Cancer therapy as dynamical system
    b. Optimal control problem

1 .Personalized treatment



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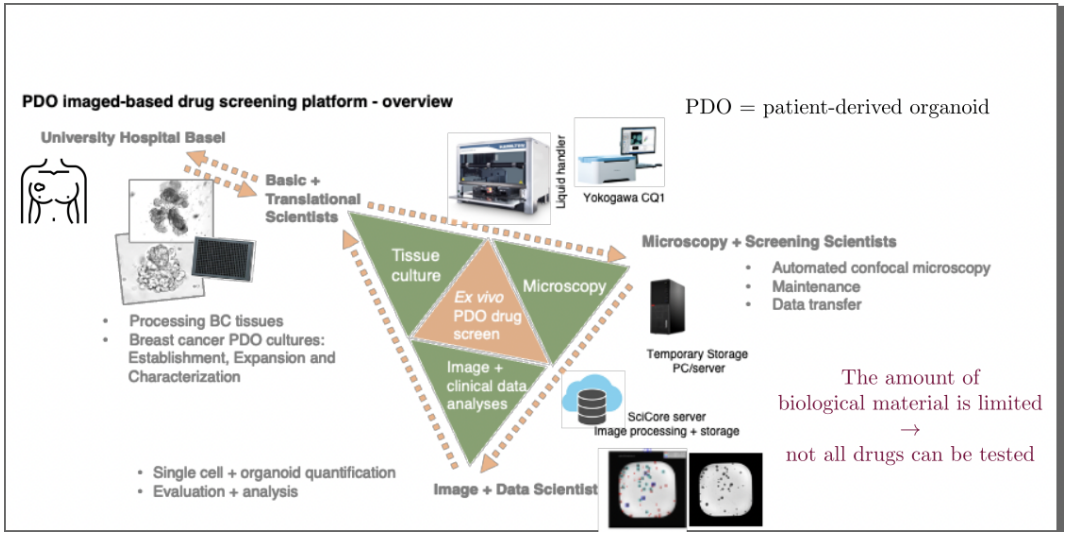

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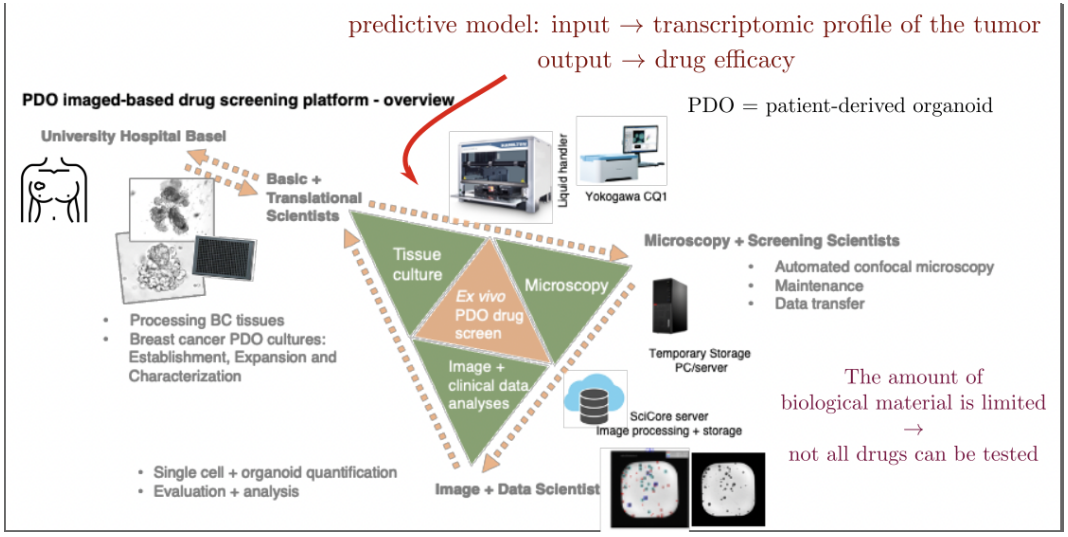

1. PaccMann: predictive model by IBM

- trained on GDSC data
  Genomics of Drug Sensitivity in Cancer

Drugs (ranked by cell line sensitivity)

Show 25 entries Filter: Export: CSV TSV

Drug	Targets	Z score
LCL161	XIAP, cIAP1, cIAP2	-3.83214
MCT4_1422	MCT4	-2.64526
FMK	RSK	-2.45049
LGK974	PORCN	-2.32604
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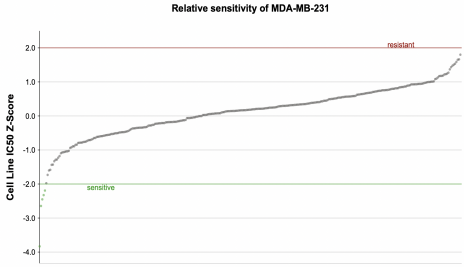

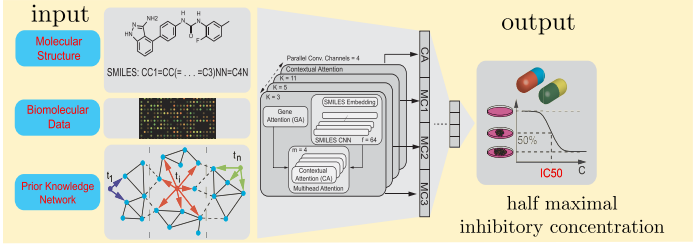

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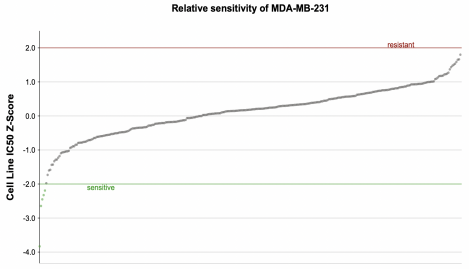
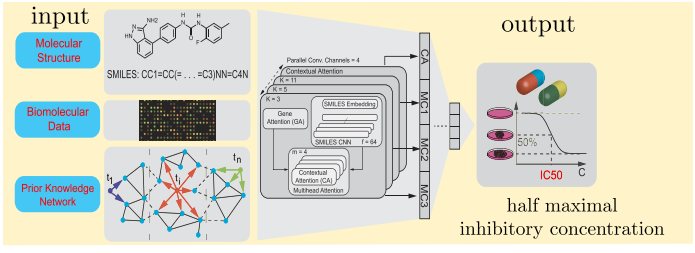




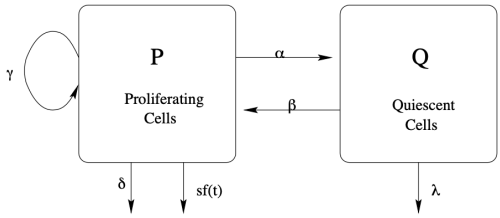
- Can 2D cell lines be a good training set for predictions for patients' samples?
- Perhaps a different source of the training data (TSGA database)?

2. Optimizing a model of cancer therapy

Cancer therapy as dynamical system

Model of bone marrow under chemotherapy

$$\begin{bmatrix} \frac{dP}{dt} \\ \frac{dQ}{dt} \end{bmatrix} = \begin{bmatrix} \gamma - \alpha - \delta - sf(t) & \beta \\ \alpha & -\beta - \lambda \end{bmatrix} \begin{bmatrix} P \\ Q \end{bmatrix}$$



- P: proliferating bone marrow cell mass, Q: quiescent bone marrow cell mass
- γ: growth rate of cycling cells
- α: transition rate from proliferating to resting
- β: transition rate from resting to proliferating
- δ: natural cell decay, λ: quiescent cell loss
- $0 \leq f(t) \leq 1$: time-dependent dosage of the chemotherapeutic treatment with amplitude s

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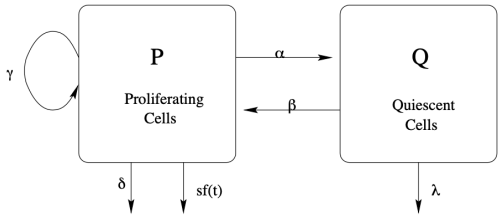

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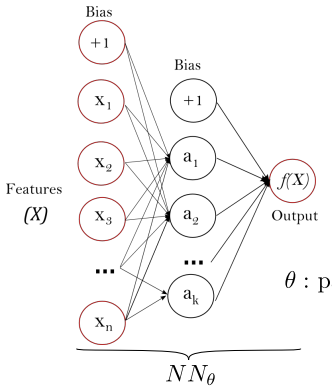
Optimal control problem:
Maximize the dose while maintaining bone marrow cell mass

2. Optimizing a model of cancer therapy

Let's employ the workhorse of machine learning:

automatic differentiation



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θ : parameters of the network

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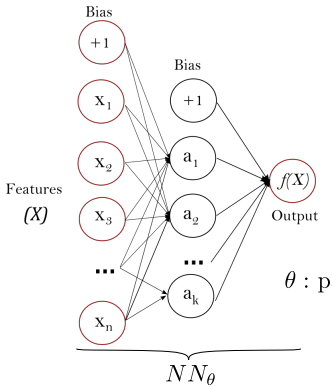

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Implement the task in a form of loss function $\mathcal{L}$ that needs to be minimized

$$\mathcal{L} = \sum_{i=1}^{N} \frac{c_1}{2}\,(1 - f(t_i)) - c_2\,(P(t_i) + Q(t_i))$$

maximize the dose

maximize the overall cell number

using AD compute gradients $\frac{\partial \mathcal{L}}{\partial \theta_i}$

Update parameters θ in direction given by the gradient

$$\theta_i \to \theta_i - \eta \frac{\partial \mathcal{L}}{\partial \theta_i}$$

2. Differentiable programming (∂P)

Not only the NNs but whole segments of the code (like ODE solver for example) are fully differentiable $\Rightarrow$ can get gradients with AD

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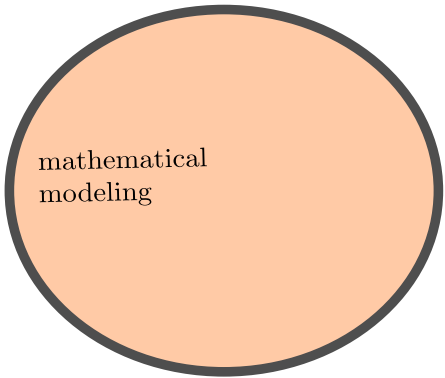

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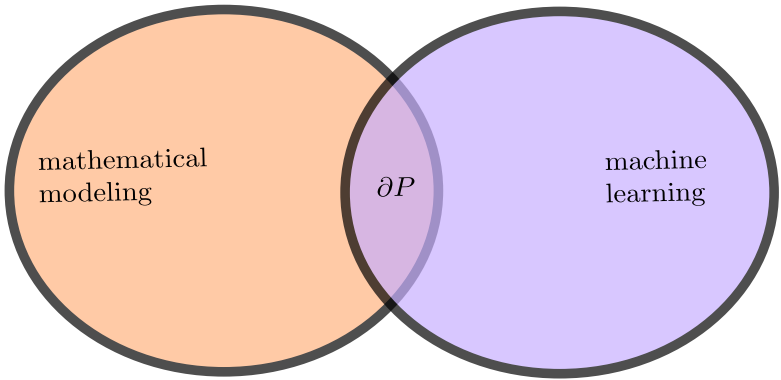

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- PaccMann (IBM)

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Thanks for your attention.