Potential predictors of type-2 diabetes risk: machine learning, synthetic data and wearable health devices

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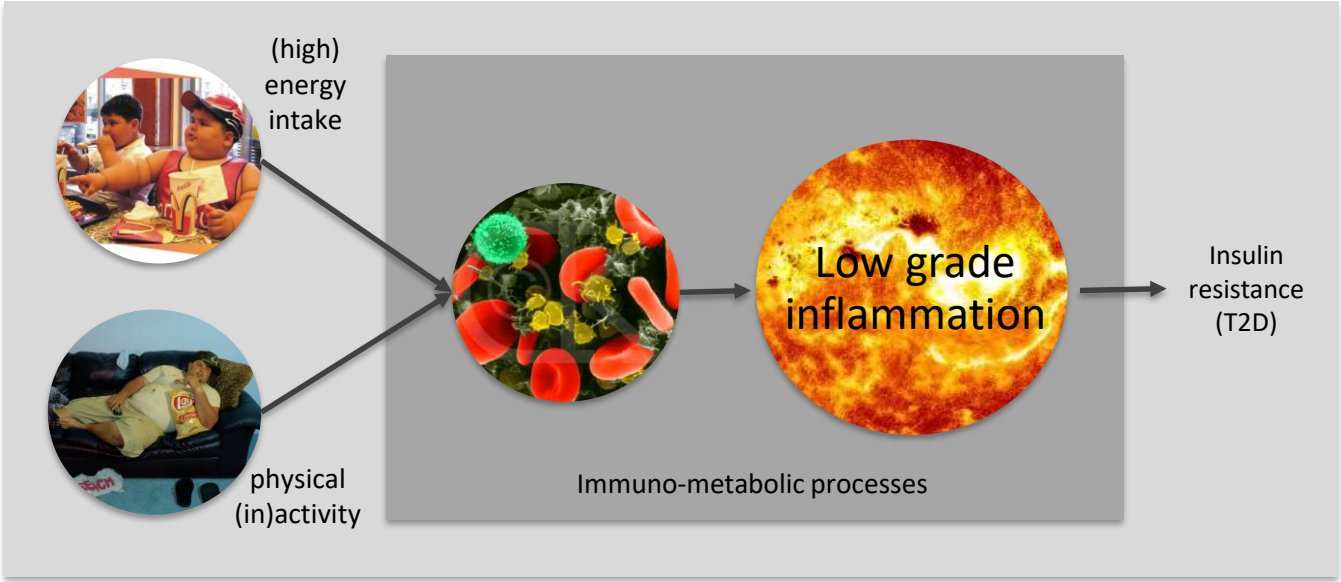
Workshop: the role of In Silico Medicine in diabetes
AIFA
Rome, May 26, 2022

T2D can be considered an auto-inflammatory disease

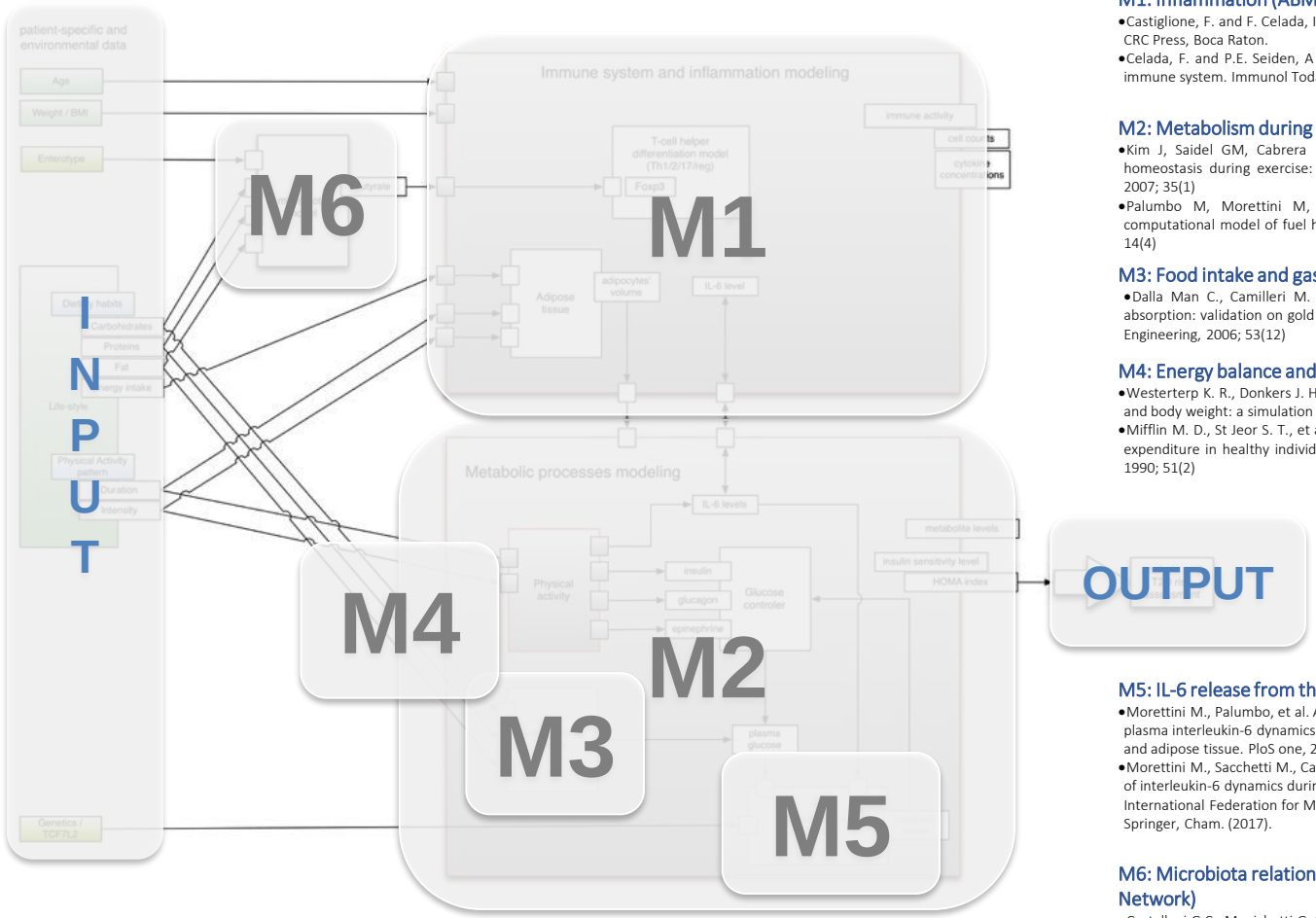
- evidence of inflammation markers in T2D (e.g., CRP, IL-6)
- clinical studies demonstrated the potential of use an anti-inflammatory drugs in T2D therapy

- Donath M., Shoelson S., Type 2 diabetes as an inflammatory disease, Nat. Rev. Immunol. 11: 98-107 (2011)
- Donath, M. Y., Boni-Schnetzler, M., Ellingsgaard, H. & Ehses, J. A. Islet inflammation impairs the pancreatic β-cell in type 2 diabetes. Physiology 24, 325–331 (2009)

Within the FP7-EU project MISSION-T2D we developed a **computational model** to study the emergence of T2D



Hotamisligil, G. S. Inflammation and metabolic disorders. Nature, 2006, 444, 860-867



M1: Inflammation (ABM)

- Castiglione, F. and F. Celada, Immune System Modeling and Simulation. 2015: CRC Press, Boca Raton.
- Celada, F. and P.E. Seiden, A computer model of cellular interactions in the immune system. Immunol Today, 1992; 13(2)

M2: Metabolism during exercise (ODEs)

- Kim J, Saidel GM, Cabrera ME. Multi-scale computational model of fuel homeostasis during exercise: effect of hormonal control. Ann Biomed Eng. 2007; 35(1)
- Palumbo M, Morettini M, et al. Personalizing physical exercise in a computational model of fuel homeostasis. PLoS computational biology. 2018; 14(4)

M3: Food intake and gastric emptying (ODEs)

- Dalla Man C., Camilleri M. & Cobelli C. A system model of oral glucose absorption: validation on gold standard data. IEEE Transactions on Biomedical Engineering, 2006; 53(12)

M4: Energy balance and fat gain/loss (ODEs)

- Westerterp K. R., Donkers J. H. & Fredrix E. W. Energy intake, physical activity and body weight: a simulation model. British Journal of Nutrition, 1995; 73(3)
- Mifflin M. D., St Jeor S. T., et al. A new predictive equation for resting energy expenditure in healthy individuals. The American journal of clinical nutrition, 1990; 51(2)

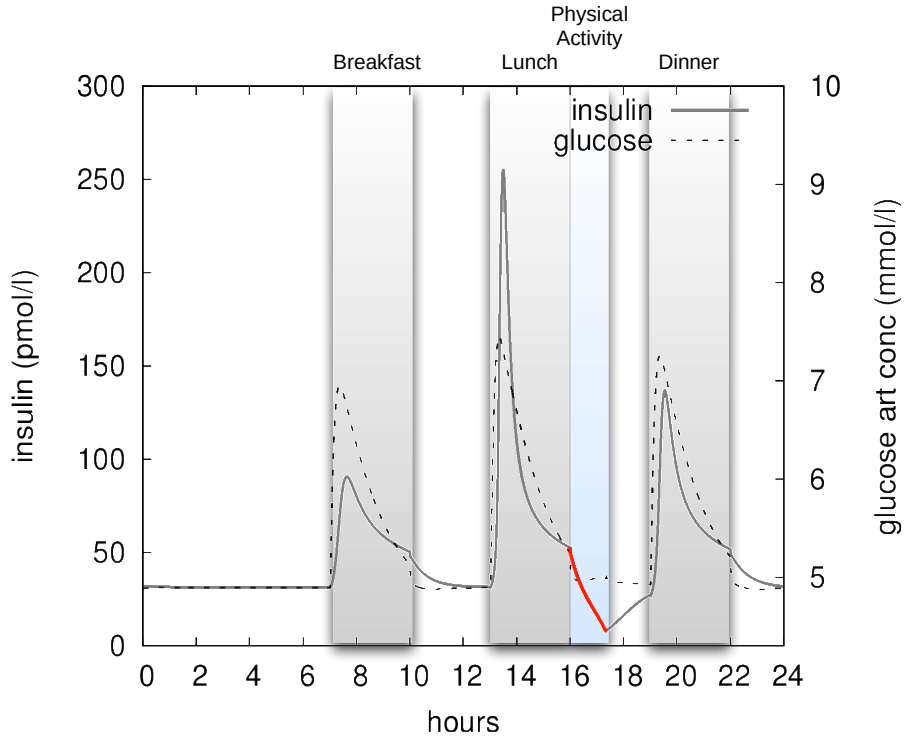
M5: IL-6 release from the skeletal muscle during PA (ODEs)

- Morettini M., Palumbo, et al. A system model of the effects of exercise on plasma interleukin-6 dynamics in healthy individuals: role of skeletal muscle and adipose tissue. PloS one, 2017; 12(7)
- Morettini M., Sacchetti M., Cappozzo, A., & Mazzà C. A mathematical model of interleukin-6 dynamics during exercise. In 6th European Conference of the International Federation for Medical and Biological Engineering (pp. 431-434). Springer, Cham. (2017).

M6: Microbiota relationship with inflammation (Multiplex Network)

- Castellani G C., Menichetti G, Garagnani P, et al. Systems medicine of inflammaging, *Briefings in Bioinformatics*, 2016; 17(32016)

One day


Physical Activity
Breakfast
Lunch
Dinner
insulin
glucose
insulin (pmol/l)
glucose art conc (mmol/l)
hours
0
50
100
150
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5
6
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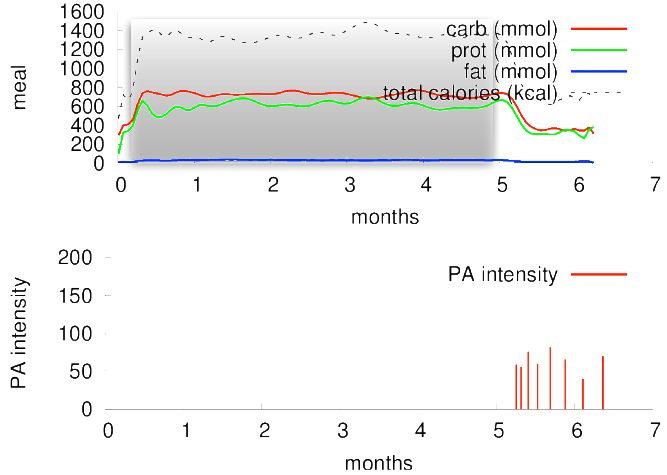
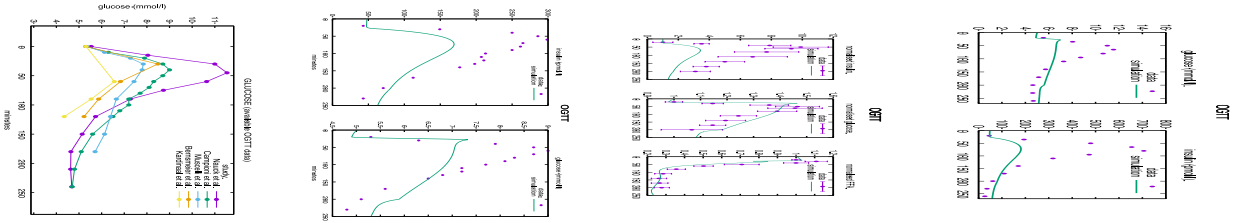
0 2 4 6 8 10 12 14 16 18 20 22 24

6 months

Long period of high caloric intake followed by diet and PA



input



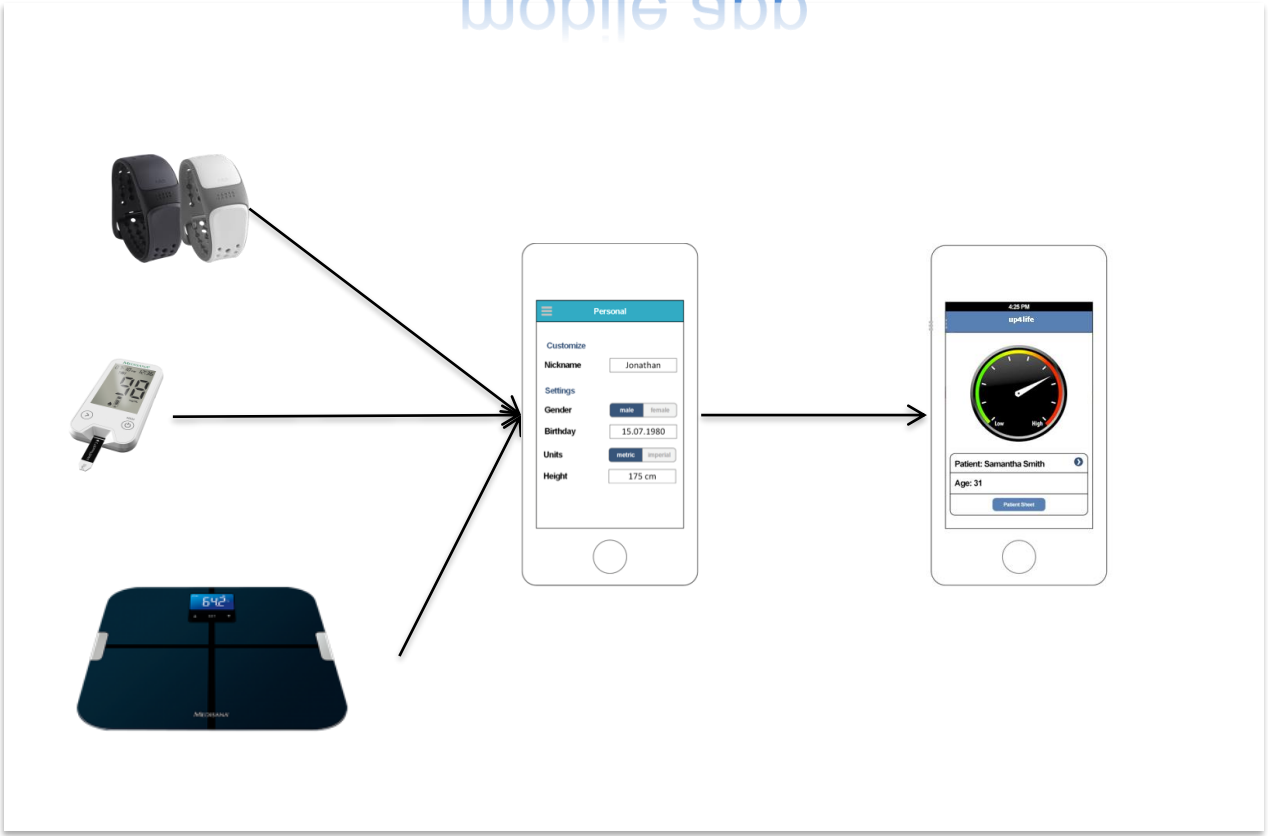
Validation

Physical activity

Lifestyle habits (diet + pa)

References	Input parameters	Output variables
Heilbronn [8]	age (37yr), weight (81.8kg), BMI ($27.5 kg \cdot m^{-2}$), CR diet (-25%kcal for 6 months), CREX diet (-12.5%kcal for 6 months, controllare pa), LCD diet (890kcal/day for 10 weeks)	weight, glucose, insulin
Kardinaal [7]	age (42.5yr), BMI ($24.1 kg \cdot m^{-2}$), weight (78.4kg), HFHC diet (+1300kcal/day)	weight, glucose, insulin
Wolfe [4]	weight (78kg), pa duration (60min), pa intensity (37%VO2max), VO2max ($40.5 mL^{-1} \cdot kg^{-1} \cdot min^{-1}$)	insulin, glucagon, epinephrine, FFA

mobile app


Personal
Customize
Nickname
Jonathan
Settings
Gender
male
female
Birthday
15.07.1980
Units
metric
imperial
Height
175 cm
up4life
Patient: Samantha Smith
Age: 31
Patient Sheet

MEDISANA

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Data synthesis for ML

ANTHROPOMETRIC MEASURES

Sex	$\boldsymbol{S} \in \{\text{female, male}\}$
Age	$\boldsymbol{A} \in \{28,38,48,58,68\}$
Weight	$\boldsymbol{W} \in \{\text{underweight, normal, overweight}\}$
Height	$\boldsymbol{H} \in \{\text{short, average, tall}\}$

$$BMI_0 = W_0/H^2$$

PHYSICAL ACTIVITY

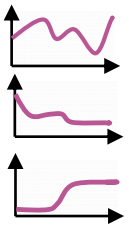
Number of sessions per week	$\boldsymbol{N_{PA}} \in \{0, 1, 2, 3\}$
Duration (mins)	$\boldsymbol{D_{PA}} \in \{\text{low} = 30, \text{medium} = 60, \text{high} = 90\}$
Intensity (% of VO_{2max})	$\boldsymbol{I_{PA}} \in \{\text{low} = 40, \text{high} = 60\}$

FOOD INTAKE (3 meals per day, breakfast, lunch, dinner)

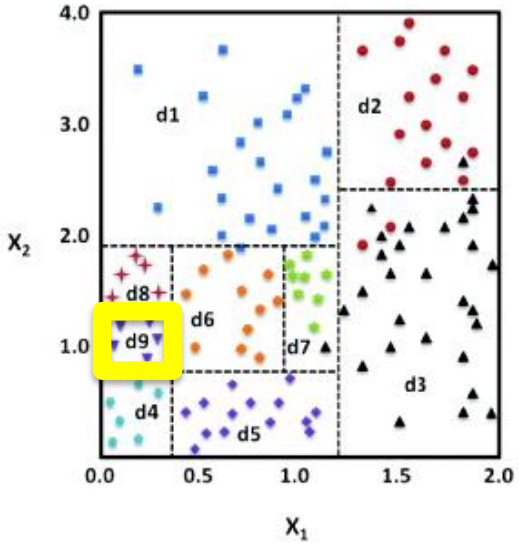
Carbohydrates (grams)	$\boldsymbol{C_{ME}} \in \{\text{low, med, high}\}$
Proteins (grams)	$\boldsymbol{P_{ME}} \in \{\text{low, med, high}\}$
Fats (grams)	$\boldsymbol{F_{ME}} \in \{\text{low, med, high}\}$

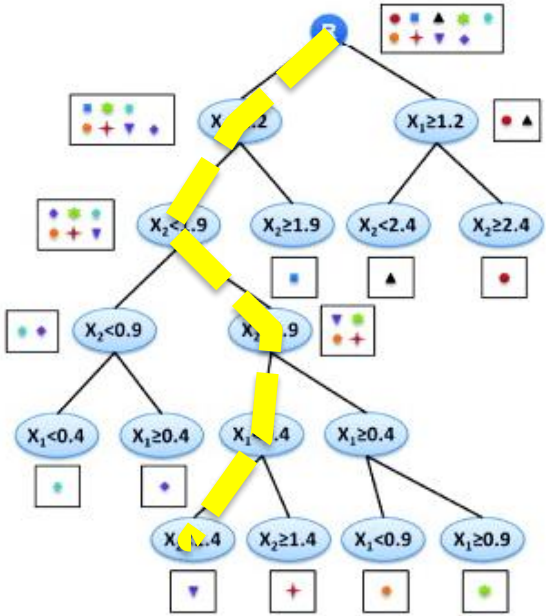
$$x = [S, A, BMI_0, (N_{PA}, D_{PA}, I_{PA}), (C_{ME}, P_{ME}, F_{ME})]$$
$$y = [BMI(t), GBL(t), TNF(t)]$$

$BMI(t)$ body mass index
$GBL(t)$ glucose base level (fasting glucose)
$TNF(t)$ inflammation level
t = six months



Decision tree

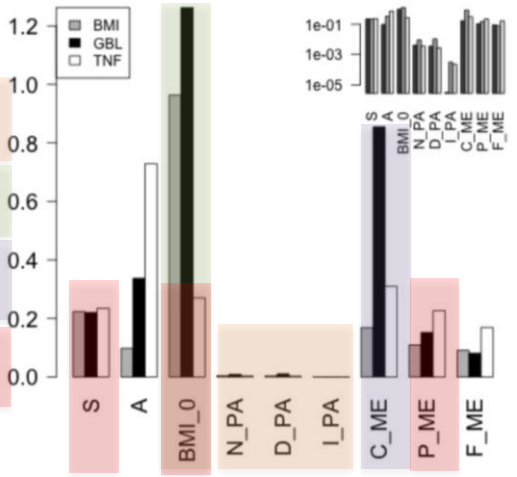




Variables' importance

Sensitivity analysis reveals that:

- the variables related to the physical activity (*i.e.*, N_{PA}, D_{PA} and I_{PA}) appear as the less important
- The most important variable for both the BMI and GBL is the initial value BMI_0
- GBL also strongly depends on the amount of carbohydrates in the diet (C_{ME})
- As for inflammation (TNF), the most important dependence is age (A) followed in order of importance by C_{ME} and then BMI_0



- H. Ishwaran, "Variable importance in binary regression trees and forests," Electron. J. Statist., vol. 1, pp. 519-537, Nov 2007.

Conclusions

- A tool which allows people's self-assessment based on lifestyle parameters remains the most powerful means to increase awareness of the risk of T2D

- The computational model can be used to feed a ML method which demonstrated to perform well to predict the risk of T2D using notably less computational resources, making it compliant for mobile devices

- The ML model can be used to compute optimal lifestyle patterns with respect to users' characteristics

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Thank you for your attention

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