Math Oncology
Hillen
starting soon.

Of course today: Computer problems.
Coming soon.

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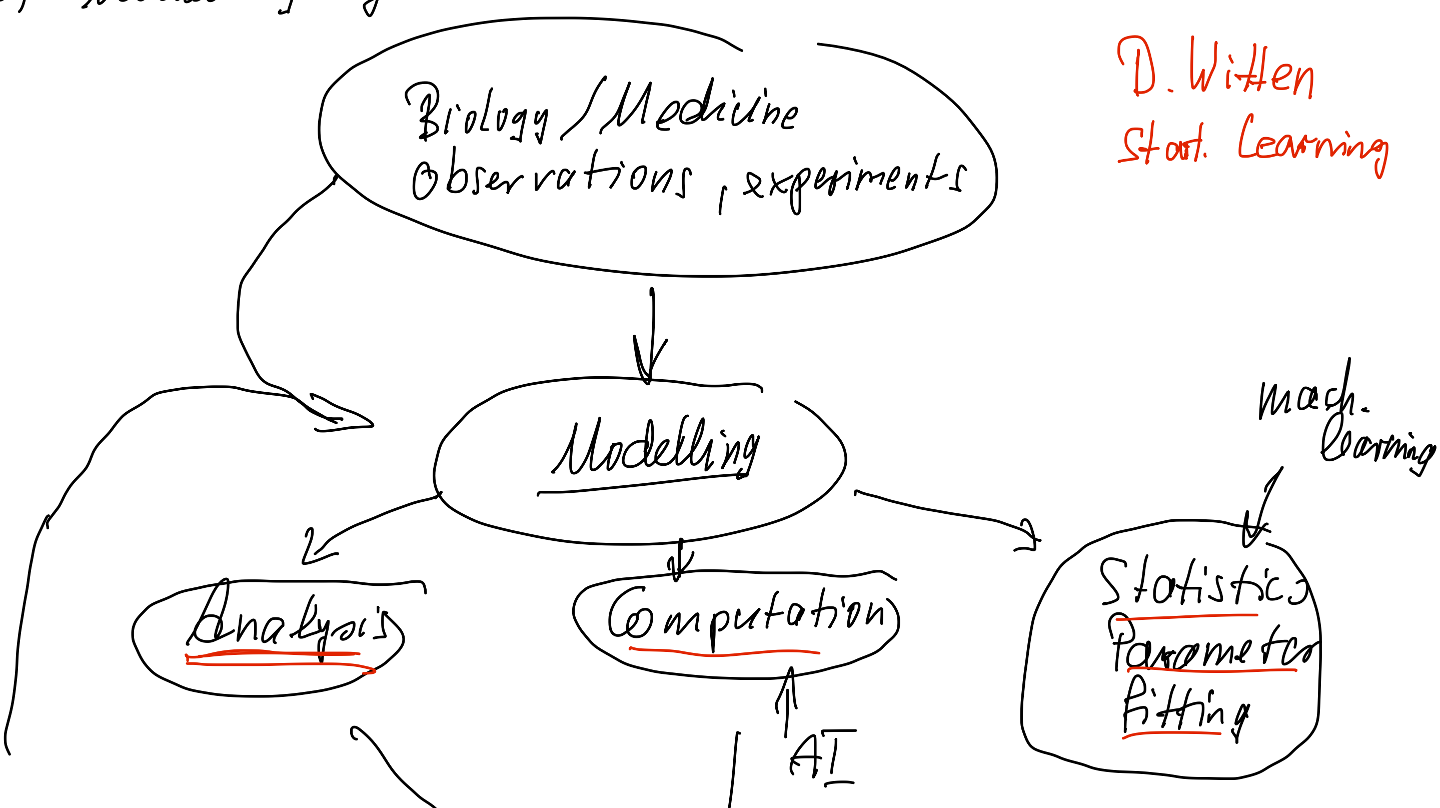
1) Introduction.

(1.1) Course outline

(1.2) Modelling cycle



Insight, Explanations
Control

(1.3) Probabilities and Rates

SIR: Susceptible $\to$ Infected

Recover

quantify transitions: Infected $\to$

recovery

- assume 2 out of 100 people recover per day.

  prob. of recovery $p_1 = \frac{2}{100} = \frac{1}{50}$

  $\alpha_1 = \text{rate} = \frac{\text{probability}}{\text{unit of time}} = \frac{1}{50}\,\frac{1}{\text{day}}$

- 2 days. prob. $p_2 = \frac{4}{100} = \frac{1}{25}$

  $\alpha_2 = \text{rate} = \frac{\text{prob}}{\text{unit of time}} = \frac{1}{25}\,\frac{1}{2\,\text{days}} = \frac{1}{50}\,\frac{1}{\text{day}}$ ✓

- $\frac{1}{2}$ day $p_{1/2} = \frac{1}{100}$

  $\alpha_{1/2} = \frac{1/100}{\frac{1}{2}\,\text{day}} = \frac{1}{50}\,\frac{1}{\text{day}}$

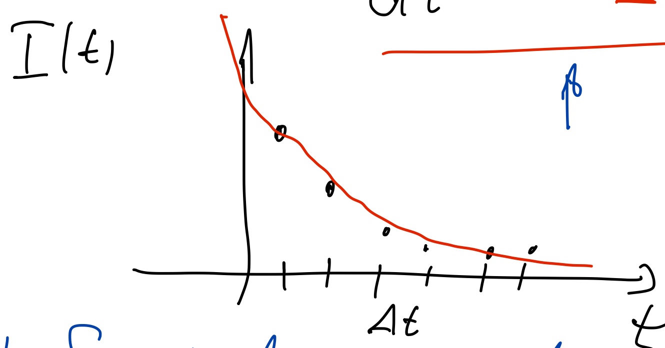
generalize Δt, $p_{\Delta t}$, $\boxed{\alpha_{\Delta t} = \frac{p_{\Delta t}}{\Delta t} = \alpha}$ (*)

Master equation: $I(t+\Delta t) = I(t) - p_{\Delta t}\, I(t)$

$$\frac{I(t+\Delta t)-I(t)}{\Delta t} = -\underbrace{\frac{p_{\Delta t}}{\Delta t}}_{\alpha} I(t)$$

$$\frac{dI}{dt} = -\alpha I$$

$I(t) = I_0 e^{-\alpha t}$



(1.4) Survival-Time Analysis

(Soujuorn time, Thieme book)

a: time an individual spends in a state

$F(a)$: prob. to still be in the state at time a.

$F(a)$ non-increasing $\quad F(0) = 1$

$$\lim_{a \to \infty} F(a) = 0$$

If $F(a) = 0 \;\; \forall\, a > c$, then c is a maximum duration in this state.

T: random time of stage exit.

$$F(a) = Pr(T > a)$$

$$G(a) = 1 - F(a) \quad \text{prob. of exit}$$
$$= \Pr(T \leq a)$$

Cond. probability to survive h time units longer, if survived already a time units is

$$F(h|a) = \frac{F(a+h)}{F(a)}.$$

prob. exit between a and $a+h$

$$1 - F(h|a) = \frac{F(a) - F(a+h)}{F(a)}$$

define <u>exit rate</u>

$$\mu(a) = \lim_{h \to 0} \frac{1}{h}\left(1 - F(h|a)\right)$$

$$= \lim_{h \to 0} \frac{F(a) - F(a+h)}{h\, F(a)}$$

$$\boxed{\mu(a) = -\frac{F'(a)}{F(a)}}$$

Example 1: (exponential distribution) Assume the survival time is exponentially distributed.

$$F(a) = e^{-\gamma a} \qquad \gamma > 0$$

$$\mu(a) = \frac{\gamma e^{-\gamma a}}{e^{-\gamma a}} = \gamma \quad \text{exit rate}$$

Conditional prob. $F(h|a) = e^{-\gamma h} = F(h)$

<u>Theorem</u> (Thieme book)

→ $F(h|a)$ is independent of <u>a</u> <u>iff</u> $F(a) = e^{-\gamma a}$ for some $\gamma \geq 0$.

If Δt is small we can write the prob. of leaving

$$G(\Delta t) = 1 - F(\Delta t | t) = \underline{1 - e^{-\gamma \Delta t}}$$

<u>more correct</u>

$$\approx 1 - (1 - \gamma \Delta t + \text{h.o.t.})$$

$$= \underline{\gamma \Delta t + o(\Delta t)}$$

approx for Δt small

$$\Rightarrow \boxed{\gamma = \frac{G(\Delta t)}{\Delta t}}$$ this is (∗)

Back to epidemic model

$$I(t + \Delta t) = I(t) - G(\Delta t) I(t)$$

$$\frac{I(t + \Delta t) - I(t)}{\Delta t} = - \frac{G(\Delta t)}{\Delta t} I(t)$$

$$\dot{I} = -\gamma I$$

<u>Important</u> 1) A relation of the form

$\dot{x} = -\gamma x$

assumes exponentially distr. survival times.

2) The prob. to leave a state in the time interval $[t, t+\Delta t]$ is often denoted as $p_{\Delta t} = \gamma \Delta t$

This is an approximation of

$$p_{\Delta t} = 1 - e^{-\gamma \Delta t}$$ for small Δt.

(1.5) Cancer

[→ Kulesza, et. al. Jo. Pharmacokinetics and Pharmacodynamics, 2024.]

Thoughts: – heterogeneous pop. of dynamic interactions.

– microenvironment (stroma, immune cells, blood supply, ECM, extracellular matrix)

Cancer Modelling

- multiple scales: genes, proteins, cell, tissue, body scale
- top-down: data inform models
- bottom-up: processes inform models
- need to strike a balance between complexity, data availability, and interpretability.