



The University of Manchester



**MANCHESTER CANCER
RESEARCH CENTRE**

Scientific reasoning in oncology at the age of Large Language Models (LLMs)

André Freitas & Neuro-Symbolic AI Group

AstraZeneca, October 2023





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**MANCHESTER CANCER
RESEARCH CENTRE**



Neuro-symbolic AI Group



Analytical limits in cancer research

Fundamental tensions

Abundance of reported
studies

vs.

Scarcity of quality, individual-level
patient data

Interventional (RCT)

vs.

Observational (RWD)

More data per patient
($p \gg n$)

vs.

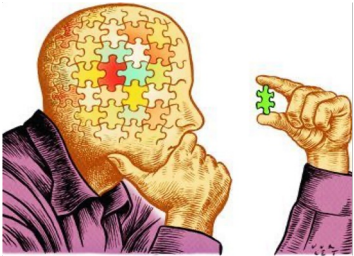
More specific phenomena
(personalised response, smaller cohorts)

Mechanistic phenomena

vs.

Statistical inference

Prototypical scientific workflow

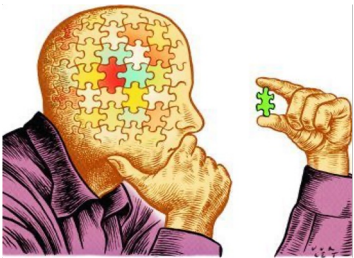


Hypotheses
Questions

New context

New data

Prototypical scientific workflow



Hypotheses
Questions

New context

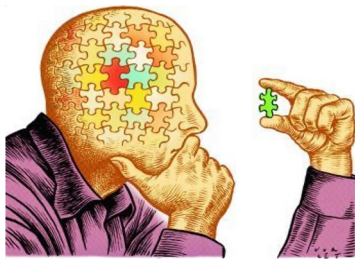
New data

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← Select
relevant
background
knowledge



Prototypical scientific workflow



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Select
relevant
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knowledge

Translate to a
computable expression

```
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```

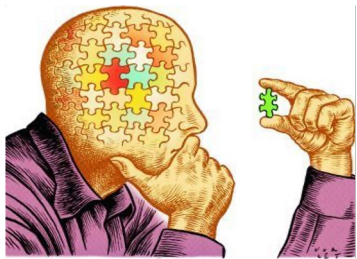
```
...  
end
```

Solve, Simulate

Data (phenomenal level)



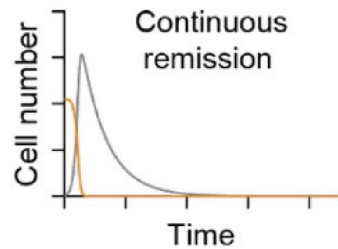
Prototypical scientific workflow



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Contrast
to new data

Elicit
relevant patterns

Data (phenomenal level)

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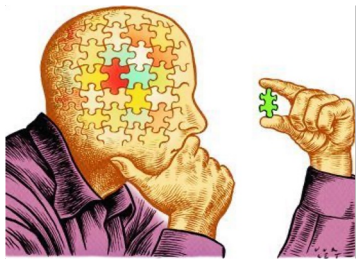
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Solve, Simulate



Prototypical scientific workflow

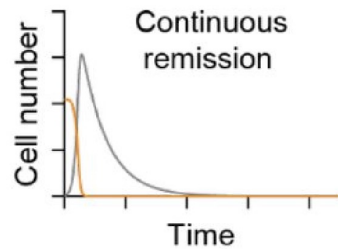


Hypotheses
Questions

New context

New data

Hypothesise
an explanation



Contrast
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Data (phenomenal level)

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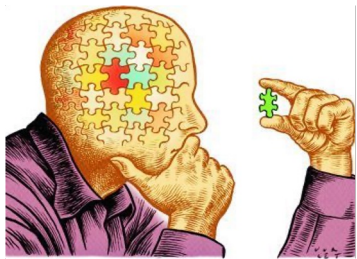
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...
`end`

Solve, Simulate



Prototypical scientific workflow

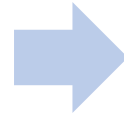


Hypotheses
Questions

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New data

Hypothesise
an explanation



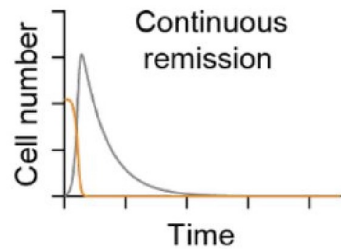
(Formally) Extend
existing model



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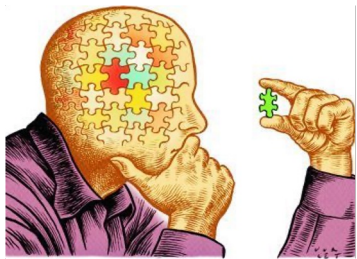
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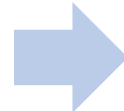


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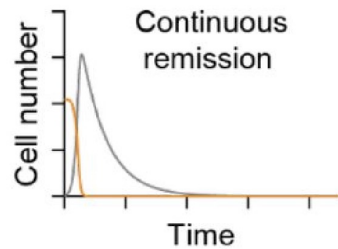
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Corroborate
with previous
evidence



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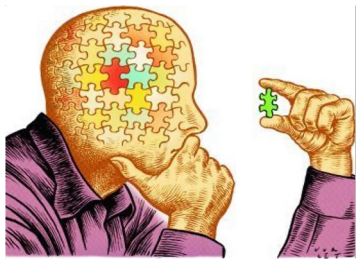


Resource-intensive.

Requires diverse and highly specialised skill sets beyond the core domain of expertise.

Implies: Compromises all over the pipeline.

Prototypical scientific workflow

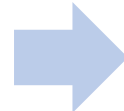


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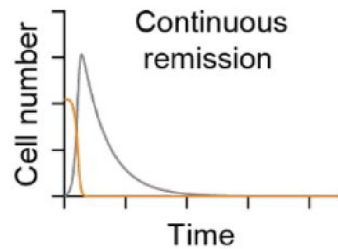
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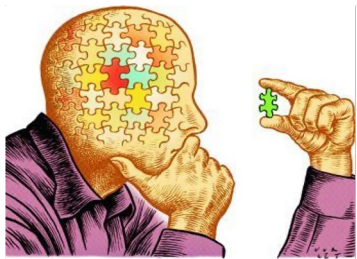
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Industrialising scientific discovery

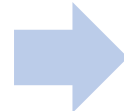


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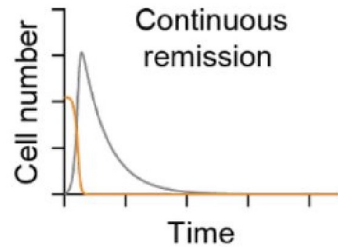
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Corroborate
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Abductive NLI
Evidence selection
Automating meta-analysis



Contrast
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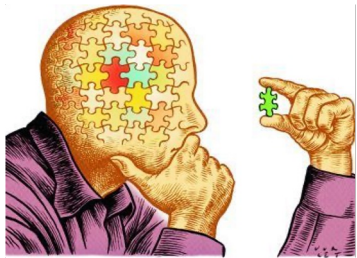
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Solve, Simulate

Data (phenomenal level)



Industrialising scientific discovery

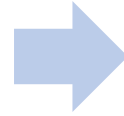


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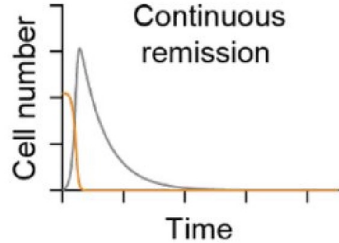


Abductive NLI
Evidence selection
Automating meta-analysis



Auto-coding
Auto-formalisation
function y = simulate
CRS(x1, x2, t)
...
end

Solve, Simulate



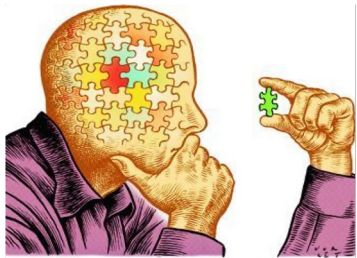
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Industrialising scientific discovery

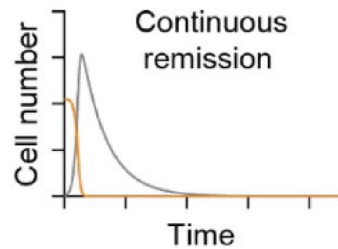


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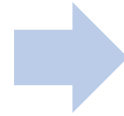
New context

New data

Hypothesise
an explanation



Auto-coding
Auto-formalisation
Abstraction models



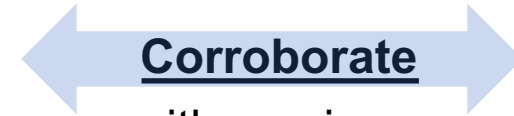
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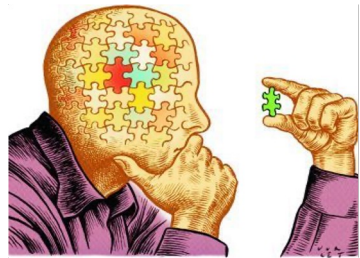


Abductive NLI
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Data (phenomenal level)

Industrialising scientific discovery



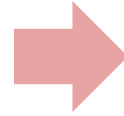
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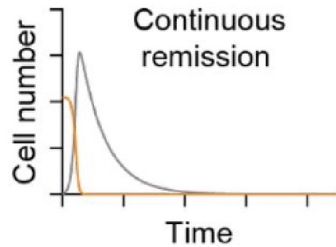
New data

Symbolic regression
Explanation generation

Hypothesise
an explanation



(Formally) Extend
existing model



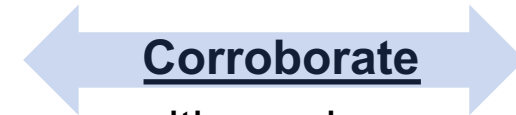
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Solve, Simulate



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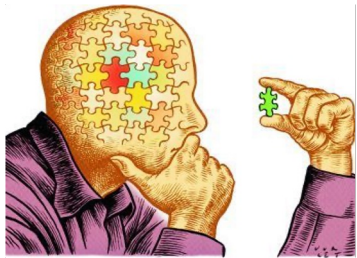


Abductive NLI
Evidence selection
Automating meta-analysis

Data (phenomenal level)



Industrialising scientific discovery



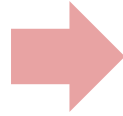
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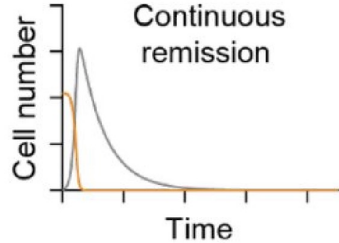


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Solve, Simulate



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Common denominator

“miR-155 Activates Cytokine Gene Expression in Th17 Cells by Regulating the DNA-Binding Protein Jarid2 to Relieve Polycomb-Mediated Repression.”

	Patients with SARS-Cov-2 confirmed by PCR	Patients without SARS-Cov-2 confirmed by PCR
Median age (IQR)—years	63 (53–72)	60 (49–73)
Male	787/1,309 (60.1%)	90/167 (53.9%)
Race/ethnicity—Hispanic	577/1,268 (45.5%)	62/167 (37.1%)
Race/ethnicity—African American	278/1,268 (21.9%)	46/167 (27.5%)
Race/ethnicity—White	277/1,268 (21.8%)	43/167 (25.7%)
Race/ethnicity—Asian	73/1,268 (5.8%)	5/167 (3.0%)
Race/ethnicity—Other	63/1,268 (5.0%)	11/167 (6.6%)
Obesity (BMI ≥30)	465/1,176 (39.5%)	34/149 (22.8%) ^a
Comorbidities—hypertension	420/1,268 (33.1%)	67/167 (40.1%)
Comorbidities—diabetes	293/1,268 (23.1%)	34/167 (20.4%)
Comorbidities—CKD	167/1,268 (13.2%)	27/167 (16.2%)
...

Del Valle et al. , *Nature Medicine* (2020)

$$\frac{dx_1(t)}{dt} = x_2(t)$$

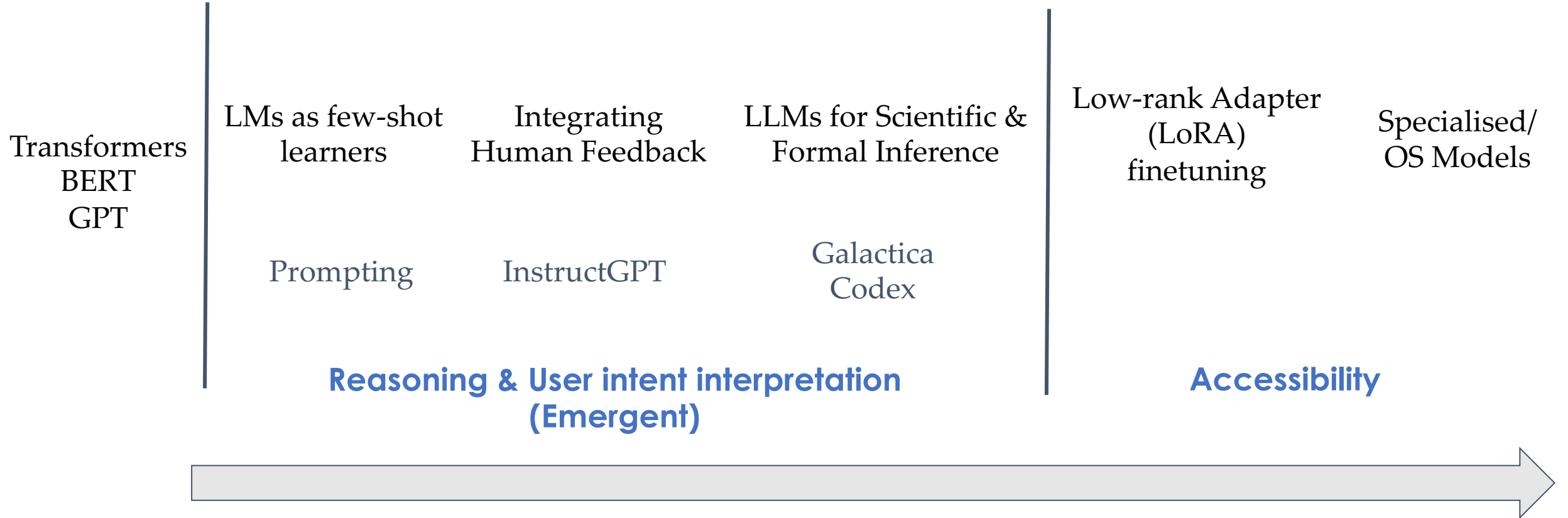
$$\frac{dx_2(t)}{dt} = ax_1(t) - bx_2(t)$$

$$\frac{d^2x_1(t)}{dt^2} = \frac{dx_2(t)}{dt}$$

where $x_1(t)$ is the serum concentration of cytokine
and its rate of change by $x_2(t)$

Common denominator: Language & Abstraction!

LLMs dramatically lowered the barriers for interpreting language





Did the life of Bernie Madoff embody Nietzschean values?



Bernie Madoff was a convicted American fraudster who ran a Ponzi scheme that is considered to be one of the largest financial frauds in history. While Nietzsche's philosophy includes many concepts, it is unlikely that Madoff's life embodies Nietzschean values in any meaningful way.



One of Nietzsche's key ideas is the concept of the Übermensch, or the "Superman." The Übermensch is an idealized human being who transcends traditional values and lives a life of creativity, self-realization, and personal growth. Madoff, on the other hand, lived a life of deception, dishonesty, and manipulation. He betrayed the trust of his clients, friends, and family members and caused them significant financial harm.

Furthermore, Nietzsche's philosophy emphasizes the importance of personal responsibility and self-determination. Madoff's actions, on the other hand, were driven by a desire for personal gain, without regard for the consequences for others.

Overall, it would be inaccurate to say that Madoff's life embodies Nietzschean values, as his actions were antithetical to many of the core ideas of Nietzsche's philosophy.

A lot happened here

Identifying and aligning elements of **intent** in the instruction.

Identifying **essential attributes** and **events** of the **target character**.

Identifying **essential attributes** of the **target ethical framework**.

Relating these attributes (e.g. contrasting).

Committing to a conclusion.

Sticking to what is relevant for the argument.

Organising into an **argumentation structure**.

Perfect fluency, meaning and thematic coherence.

A

Describe the dynamic behaviour of cytokines using differential equations.

A

Describe the dynamic behaviour of cytokines using differential equations.

Let's consider a simple model where a stimulus, S , induces the production of a cytokine, C . The rate of production and the rate of degradation can be modeled using ordinary differential equations.

1. **Production Rate:** The rate of cytokine production might be proportional to the stimulus, S . The proportionality constant is k_1 . Thus, the production rate is $k_1 \times S$.
2. **Degradation Rate:** Cytokines may degrade over time, and the degradation rate might be proportional to the amount of cytokine present. The proportionality constant is k_2 . Thus, the degradation rate is $k_2 \times C$.

Using the above two rates, the differential equation for the cytokine dynamics can be written as:

$$\frac{dC}{dt} = k_1 \times S - k_2 \times C$$

Where:

- $\frac{dC}{dt}$ is the rate of change of the cytokine concentration over time.
- k_1 is the rate constant for cytokine production.
- k_2 is the rate constant for cytokine degradation.
- S is the stimulus.

A

Can you add to the model:

T_s : antigen+ tumour

T_r : antigen-tumour

C : CAR T cells

B : bystander cells

1. Dynamics of T_s and T_r (antigen+ and antigen- tumors respectively)

- The growth rate of both tumors might be logistic to take into account carrying capacity:

$$\frac{dT_s}{dt} = r_s \times T_s \times \left(1 - \frac{T_s + T_r}{K}\right) - k_s \times C \times T_s$$

$$\frac{dT_r}{dt} = r_r \times T_r \times \left(1 - \frac{T_s + T_r}{K}\right)$$

Where:

- r_s and r_r are the growth rates for T_s and T_r , respectively.
- K is the carrying capacity of the tumor environment.
- k_s is the rate at which CAR T cells kill antigen+ tumor cells.

1. Dynamics of CAR T cells (C)

$$\frac{dC}{dt} = p_c \times T_s - d_c \times C$$

Where:

- p_c is the proliferation rate of CAR T cells in the presence of antigen+ tumor cells.
- d_c is the natural death rate of CAR T cells.

1. Dynamics of bystander cells (B)

$$\frac{dB}{dt} = r_b - k_b \times C \times B$$

Where:

- r_b is the growth rate of bystander cells.
- k_b is the rate at which CAR T cells affect bystander cells.

A

Can you add the following constraints to the model:

T_s : co-grow with T_r ; non-linear kill by CAR T cells; non-linear kill term by bystander cells

• T_r : co-grow with T_s ; non-linear kill term by bystander cells

• C : initial injection; linear death; Michaelis-Menten co-grow and competition with B ; bilinear exhaustion from antigen+ stim ~CTs

• B : constant recruitment; linear death; M-M co-grow and competition with B ; bilinear exhaustion from antigen+ stim ~C(T_s+T_r)

1. Dynamics of T_s and T_r (antigen+ and antigen- tumors respectively)

For T_s :

$$\frac{dT_s}{dt} = r_s \times T_s \times \left(1 - \frac{T_s+T_r}{K}\right) - \alpha_s \times \frac{C \times T_s}{K_m+T_s} - \beta_s \times B \times T_s$$

For T_r :

$$\frac{dT_r}{dt} = r_r \times T_r \times \left(1 - \frac{T_s+T_r}{K}\right) - \beta_r \times B \times T_r$$

Where:

- α_s is the non-linear killing rate of T_s by CAR T cells.
- β_s and β_r are the non-linear killing rates of T_s and T_r by bystander cells.
- K_m is the Michaelis-Menten constant.

1. Dynamics of CAR T cells (C)

$$\frac{dC}{dt} = p_c \times \frac{T_s}{K_m+T_s} - d_c \times C - \gamma_c \times C \times (T_s + T_r) - \delta \times B \times C$$

Where:

- γ_c is the bilinear exhaustion rate of CAR T cells due to antigen stimulation.
- δ is the competition rate between CAR T cells and bystander cells.

1. Dynamics of bystander cells (B)

$$\frac{dB}{dt} = r_b - d_b \times B + p_b \times \frac{B}{K_m+B} - \gamma_b \times B \times (T_s + T_r)$$

Where:

- r_b is the constant recruitment rate of bystander cells.
- d_b is the linear death rate of bystander cells.
- p_b is the Michaelis-Menten co-growth rate.
- γ_b is the bilinear exhaustion rate of bystander cells due to antigen stimulation.

A

Can you solve the dynamical system above and plot the target quantities over time?

```
import numpy as np
from scipy.integrate import odeint
import matplotlib.pyplot as plt

def system(y, t, params):
    Ts, Tr, C, B = y
    rs, rr, K, alpha_s, beta_s, beta_r, Km, pc, dc, gamma_c, delta, rb, db,

    dTs_dt = rs * Ts * (1 - (Ts + Tr) / K) - alpha_s * C * Ts / (Km + Ts) -
    dTr_dt = rr * Tr * (1 - (Ts + Tr) / K) - beta_r * B * Tr
    dC_dt = pc * Ts / (Km + Ts) - dc * C - gamma_c * C * (Ts + Tr) - delta
    dB_dt = rb - db * B + pb * B / (Km + B) - gamma_b * B * (Ts + Tr)

    return [dTs_dt, dTr_dt, dC_dt, dB_dt]

# Parameters (these values are just placeholders; use your actual data or e
params = [1, 1, 1000, 1, 1, 1, 1, 1, 0.1, 1, 1, 1, 0.1, 1, 1]

# Initial conditions (again, placeholders)
Ts0 = 100
Tr0 = 100
C0 = 100
B0 = 100
y0 = [Ts0, Tr0, C0, B0]

# Time grid
t = np.linspace(0, 10, 100)

# Solve using odeint
solution = odeint(system, y0, t, args=(params,))

# Plot
plt.figure()
plt.plot(t, solution[:, 0], label='Ts')
plt.plot(t, solution[:, 1], label='Tr')
plt.plot(t, solution[:, 2], label='C')
plt.plot(t, solution[:, 3], label='B')
plt.xlabel('Time')
plt.ylabel('Quantity')
plt.legend()
plt.show()
```

A close-up, profile view of a man wearing a brown tweed hat and a matching coat. He is smoking a dark wooden pipe with a curved stem. The background is a textured, greyish-brown wall. The text "Abductive Reasoning" is overlaid in white, sans-serif font across the center of the image.

Abductive Reasoning

Abductive inference

- First introduced by Peirce (1903).
- Inference to the best explanation.
- “Abduction is the mechanism via which we generate hypotheses about what we observe.”
- Dialogues closely with assumed background knowledge.

Veen, Creative leaps in theory: **the might of abduction** (2021)

What Sherlock does well.

Evidence-based inference

Cytokine release syndrome (CRS):

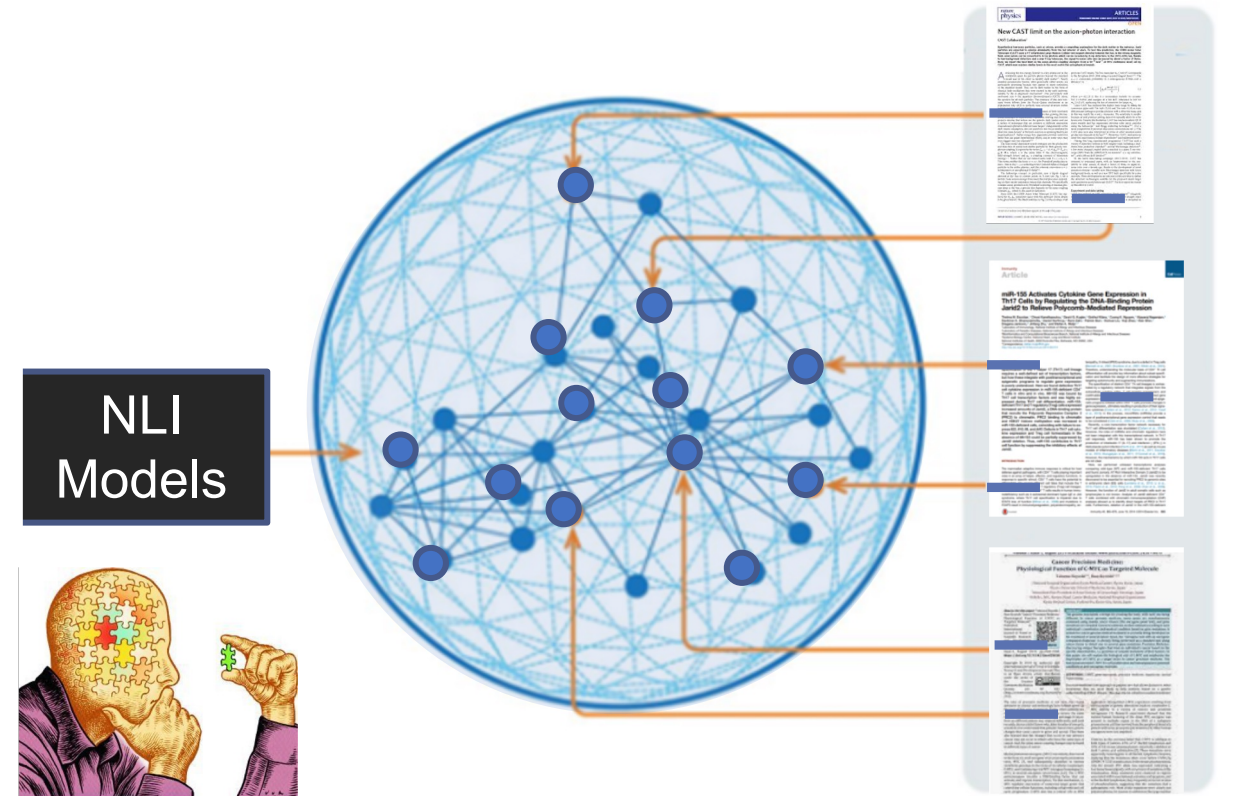
Significant adverse event of T cell-engaging therapies.

Need: Predictive models for CRS

Problem: Lack of patient-level datasets.

Can one explore relevant evidence in the literature?

Bogatu et al. (JBI, 2023)



Hypotheses
Questions

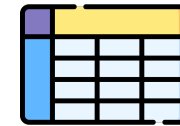
Natural Language
Inference (NLI)

Accumulated
Knowledge

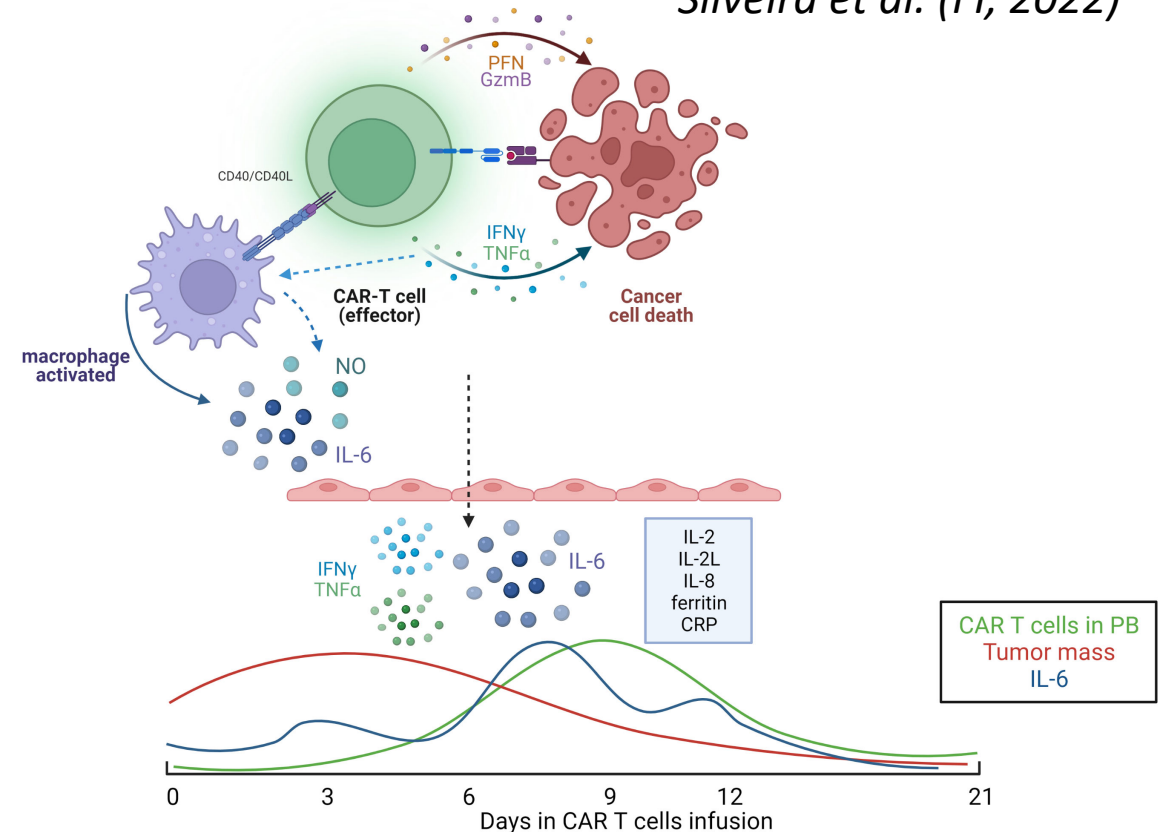
Detecting toxicity events for CAR-T cell therapies

Cytokine release syndrome

Problem: small cohorts



Silveira et al. (FI, 2022)



Bogatu et al. (JBI, 2023)

Detecting toxicity events for CAR-T cell therapies

Cytokine release syndrome

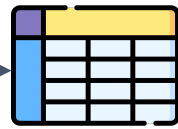
Integrating evidence from the literature

Problem: small cohorts

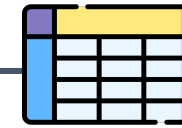


Meta-review analysis

Large Language Models

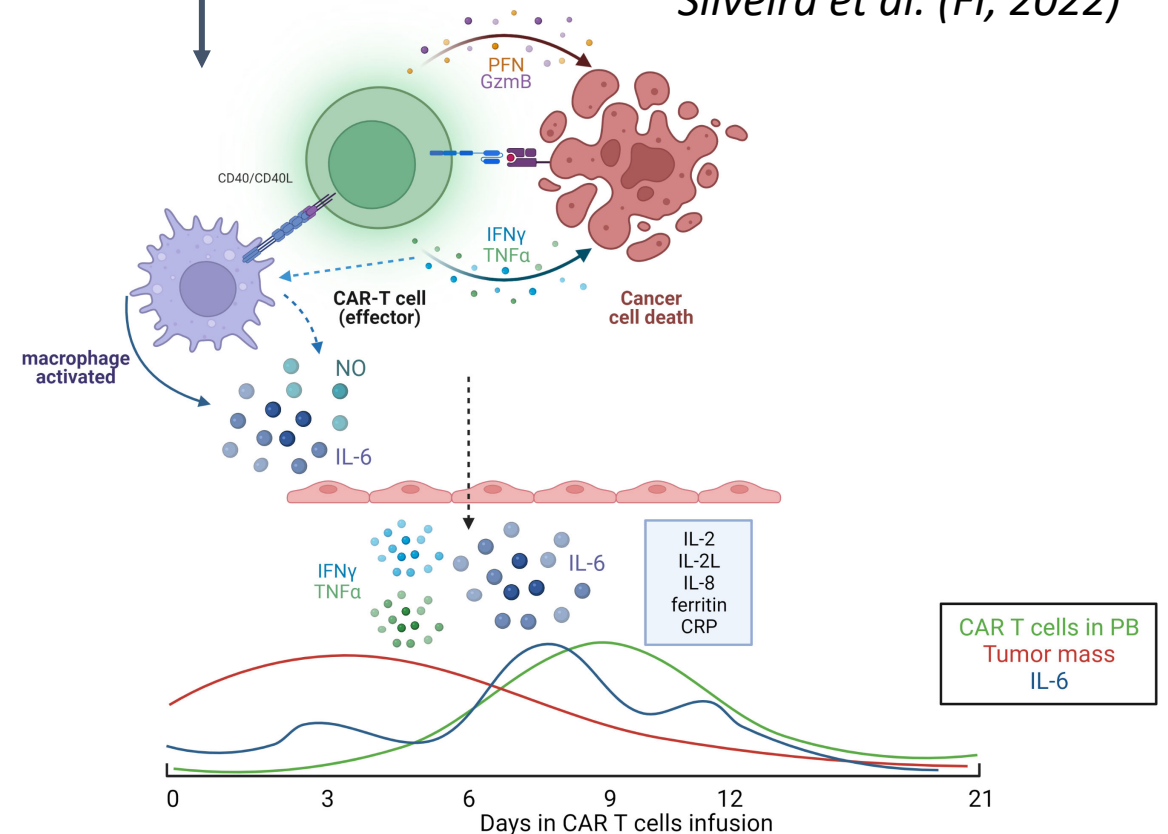


Meta-review informed
XAI Predictive model



Silveira et al. (FI, 2022)

Papers, reports



Bogatu et al. (JBI, 2023)

Detecting toxicity events for CAR-T cell therapies

Cytokine release syndrome

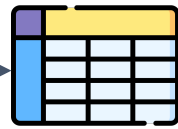
Integrating evidence from the literature

Problem: small cohorts

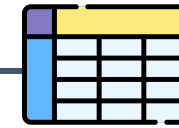


Meta-review analysis

Large Language Models

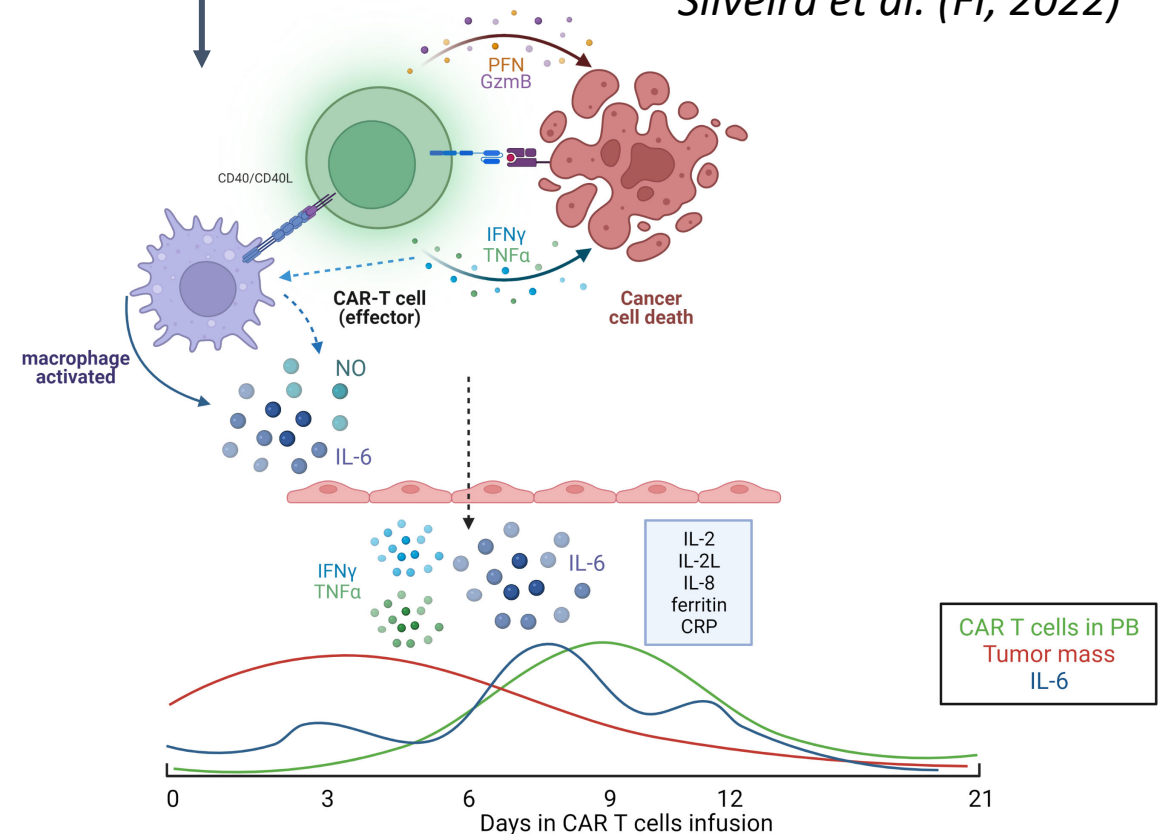


Meta-review informed
XAI Predictive model



Silveira et al. (FI, 2022)

Papers, reports



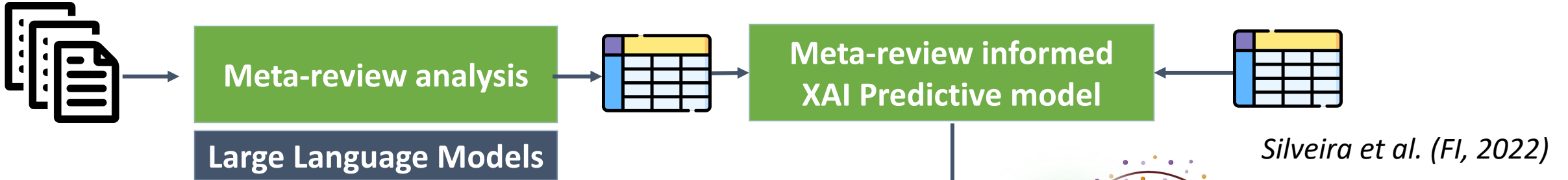
Bogatu et al. (JBI, 2023)

Detecting toxicity events for CAR-T cell therapies

Cytokine release syndrome

Integrating evidence from the literature

Problem: small cohorts



Papers, reports

19hs

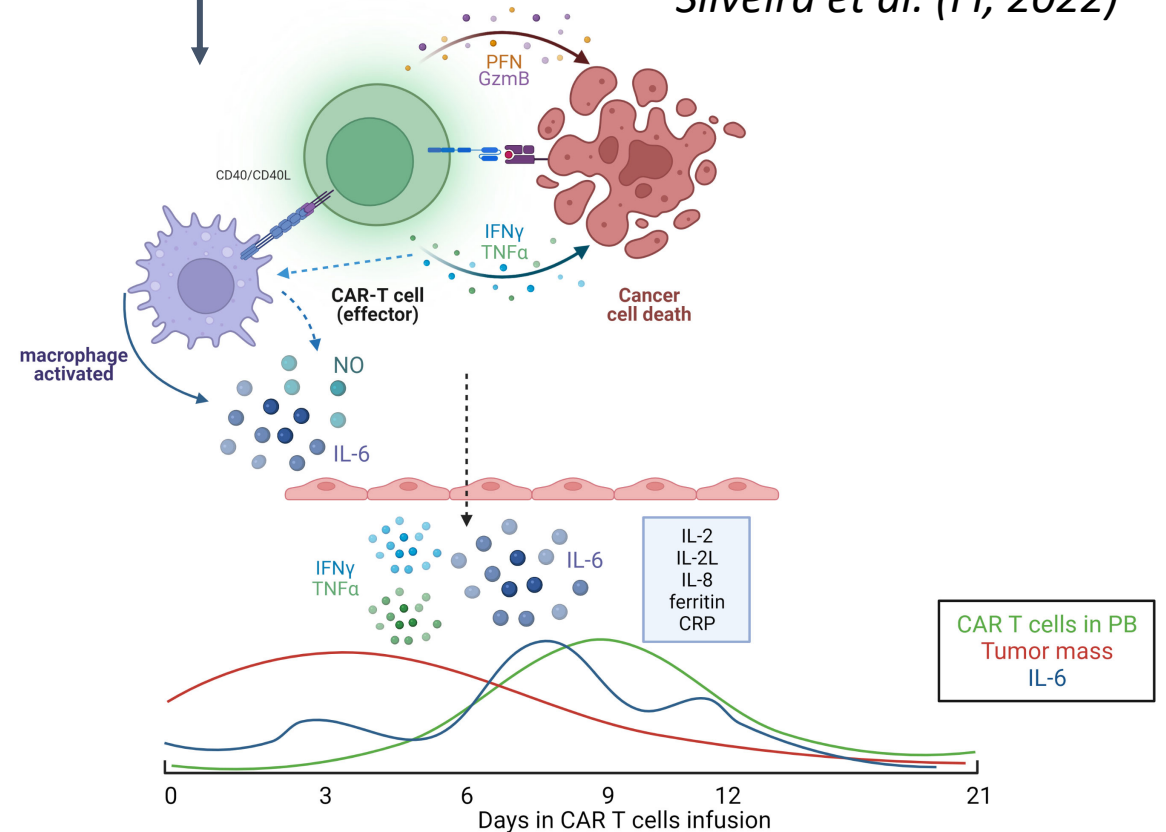
38hs 7 mins



~ 460 papers

17 highly aligned papers

Parameter extraction



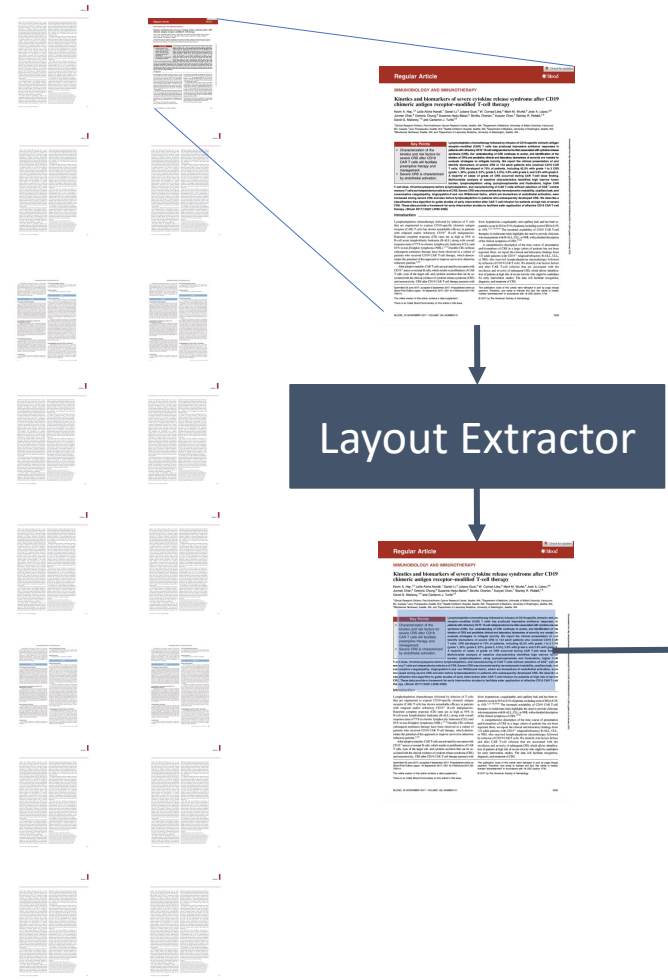
Study	IL2	IL4	IL6	IL8	IL10	IL15	IL2R α	TNF- α	IFN- γ	GM-CSF
1 Jacobson et al. [37]	R	R	R	R	R	R	R	R	R	R
2 Hong et al. [38]	R	MV	R	MV	R	MV	MV	R	R	MV
3 Yan et al. [39]	MV	MV	R	MV	MV	MV	MV	MV	MV	MV
4 Topp et al. [40]	R	R	R	R	R	R	R	R	R	R
5 Shah et al. [41]	MV	MV	R	R	R	R	R	R	R	R
6 Liu et al. [29]	R	R	R	MV	R	MV	MV	R	R	MV
7 Sang et al. [113]	MV	MV	R	MV	MV	MV	MV	MV	R	MV
8 Yan et al. [42]	MV	MV	R	MV	MV	MV	MV	MV	MV	MV
9 Zhao et al. [43]	MV	MV	R	MV	MV	MV	MV	MV	MV	MV
10 Neelapu et al. [44]	R	MV	R	R	R	R	R	MV	R	R
11 Hay et al. [24]	MV	MV	R	R	R	R	MV	MV	R	MV
12 Turtle et al. [45]	MV	MV	R	MV	R	MV	MV	R	R	MV
13 Hu et al. [15]	MV	MV	R	MV	R	MV	MV	MV	R	MV
14 Teachey et al. [118]	R	R	R	R	R	MV	MV	R	R	R
15 Porter et al. [16]	R	MV	R	MV	MV	MV	MV	R	MV	R
16 Davila et al. [5]	MV	MV	R	MV	R	MV	MV	MV	R	R
17 Kalos et al. [46]	R	R	R	R	R	R	R	R	R	MV

Bogatu et al. (JBI, 2023)

Meta-review

~ 460 papers

17 highly aligned papers
Parameter extraction



Study	IL2	IL4	IL6	IL8	IL10	IL15	IL2R α	TNF- α	IFN- γ	GM-CSF
1 Jacobson et al. [37]	R	R	R	R	R	R	R	R	R	R
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5 Shah et al. [41]	MV	MV	R	R	R	R	R	R	R	R
6 Liu et al. [29]	R	R	R	MV	R	MV	MV	R	R	MV
7 Sang et al. [13]	MV	MV	R	MV	MV	MV	MV	MV	R	MV
8 Yan et al. [42]	MV	MV	R	MV	MV	MV	MV	MV	MV	MV
9 Zhao et al. [43]	MV	MV	R	MV	MV	MV	MV	MV	MV	MV
10 Neelapu et al. [44]	R	MV	R	R	R	R	R	MV	R	R
11 Hay et al. [24]	MV	MV	R	R	R	R	MV	MV	R	MV
12 Turtle et al. [45]	MV	MV	R	MV	R	MV	MV	R	R	MV
13 Hu et al. [15]	MV	MV	R	MV	R	MV	MV	MV	R	MV
14 Teachey et al. [18]	R	R	R	R	R	MV	MV	R	R	R
15 Porter et al. [16]	R	MV	R	MV	MV	MV	R	MV	R	MV
16 Davila et al. [5]	MV	MV	R	MV	R	MV	MV	MV	R	R
17 Kalos et al. [46]	R	R	R	R	R	R	R	R	R	MV

context window

chain of prompts

LLM

GPT 3.5

Table builder

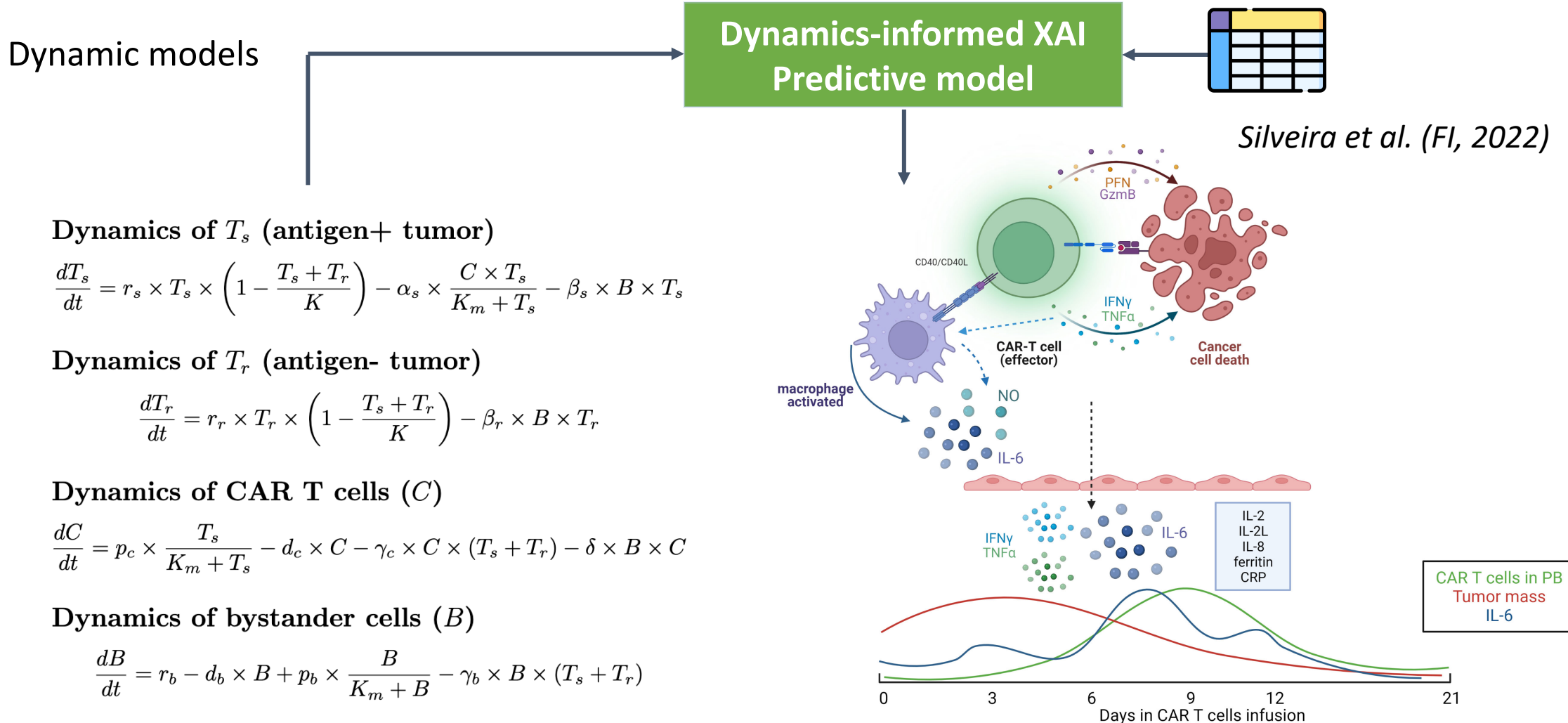
Not possible one year ago!

Detecting toxicity events for CAR-T cell therapies

Cytokine release syndrome

Integrating available mechanistic knowledge

Problem: small cohorts



Describing interactions between immune cells and cytokines

$$\frac{dS}{dt} = S_{in} - k_s S(t) - \beta V(t) S(t)$$

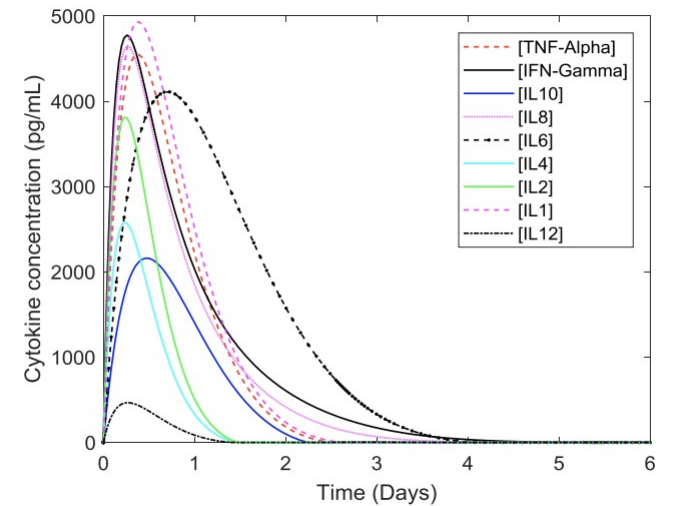
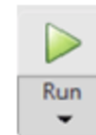
$$\frac{dI}{dt} = \beta V(t) S(t) - k_I I(t) - \gamma x(t) I(t)$$

$$\frac{dV}{dt} = v_{in} I(t) - k_V V(t)$$

$$\frac{dx}{dt} = x_{in} - k_1 x(t) + \gamma_1 x(t) I(t) + b_1 \frac{x(t)}{c_1 + x(t)} (x(t) - m) (y_1 - y(t)) (y(t) - y_2)$$

$$\frac{dy}{dt} = y_{in} - k_2 y(t) + b_2 \frac{a_1 y(t) x(t)}{a_2 c_2 + x(t)}$$

Parameter	Description	Value	Units
$S(0)$	Initial size of population of susceptible cells	1	vol.
$I(0)$	Initial size of population of infected cells	0	vol.
$V(0)$	Initial size of population of virus particles	0	vol.
$x(0)$	Initial size of population of immune cells	0.07	vol.
$y(0)$	Initial size of population of cytokines	0.18	vol.
S_{in}	Production rate of susceptible cells, $S(0) \times k_s$	0.01	vol./time
k_s	Normal decay rate of susceptible cells	0.01	1/time
k_I	Normal decay rate of infected cells	0.01	1/time
γ	Rate of elimination of infected cells by immune cells	0.5	1/vol*time
v_{in}	Rate of viral replication in infected cells	0.1	1/time
k_V	Natural virus decay rate	0.1	1/time
β	Rate at which virus infects susceptible cells	0.1	1/vol./time
x_{in}	Normal production of immune cells, $x(0) \times k_1$	7e-4	vol./time
k_1	Normal decay rate of immune cells	0.01	1/time
γ_1	Conversion of immune cell kill of infected cells into immune cell proliferation	0.05	1/vol*time
m	Threshold of activation of additional immune cell proliferation (second touch)	0.1	vol.
y_{in}	Cytokine production rate, $y(0) \times k_2$	0.018	vol./time
y_1	Cytokine-mediated threshold of immune cell expansion	1	vol.
y_2	Cytokine-mediated threshold of immune cell regulation	3	vol.
b_1	Rate of additional immune cell expansion as mitigated by cytokines	1	1/(time*vol. ³)
b_2	Rate of cytokine stimulation by immune cells	1	1/time
k_2	Normal cytokine decay rate	0.1	1/time
c_1	Population size that results in half-maximal growth of $x(t)$ in response to cytokine stimulation	1	vol.
c_2	Population size that results in half-maximal increase in production of cytokines in response to stimulation by immune cells	1	vol.



Very abstract intent!

[Equations, numerical values](#)

[Code](#)

Kareva et al., bioarxiv: 2022.02.15.48058 (2022)
Hopkins et al., IFAC (2018)



Evidence Retrieval



Patient-Trial Matching: Trial Finder

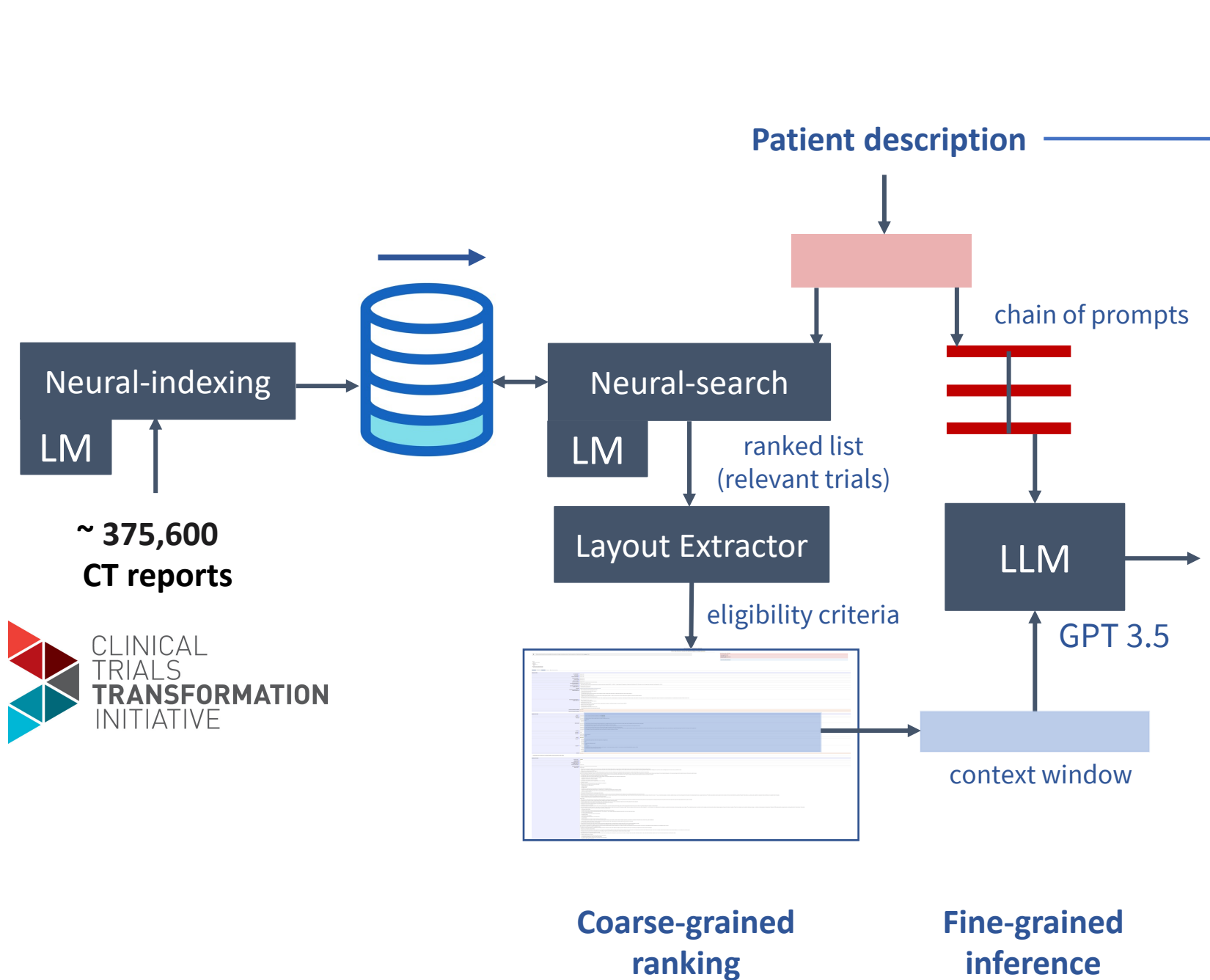
Statement
Patients living in the San Francisco area with ErbB2+ breast cancer, a body weight > 60 kg, and a history of treatment with Cyclophosphamide in the last year, are eligible for this clinical trial.

Clinical Trial Report Eligibility Criteria
Inclusion Criteria:
<ul style="list-style-type: none">• HER2-positive T1 histologically confirmed invasive carcinoma of the breast.
<ul style="list-style-type: none">• Body weight > 110 lbs
<ul style="list-style-type: none">• Age \geq 60 years
<ul style="list-style-type: none">• Patients with a history of chemotherapy treatment within the last 24 months.
<ul style="list-style-type: none">• Patients must be California residents
Exclusion Criteria:
<ul style="list-style-type: none">• Pregnant women

~ 375,600
CT reports



Jullien et al. (Semeval 2022)



Statement


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*Demo from Bogatu, Jullien
Jullien et al. (Semeval 2021)*



Patient-Trial Matching: Trial Finder

 digital ECMT cancer trial matching tool (data refreshed 04 July 2023)

Filter studies on cancer type

Include matches on solid tumour?

Rank matching studies based on genetic alterations

(Use Entrez symbol, e.g. ERBB2 instead of HER2)

Filter matching studies on study drug mechanisms

Hide matches on cancer type alone?

Show sites still in setup?

Map view of sites | **Study details** | Shortlist (0 studies) | About | Legal

[Download table](#) | [Shortlist selected studies](#)

Search:

Brief title	Matching alteration(s)	Matching cancer type(s)	Eligibility	Drug rationale	Est. completion date
Sotorasib Activity in Subjects With Advanced Solid Tumors With KRAS p.G12C Mutation (CodeBreak 101)	KRAS mutation	Advanced Solid Tumors	Stratified on KRAS mutation	Study intervention (Sotorasib) targets KRAS	12 Jul 2026
Phase 3 Study of MRTX849 With Cetuximab vs Chemotherapy in Patients With Advanced Colorectal Cancer With KRAS G12C Mutation (KRYSTAL-10)	KRAS mutation	Advanced Colorectal Cancer; Metastatic Colorectal Cancer	Enrolling subjects with KRAS mutation	Study intervention (MRTX849) targets KRAS	30 Apr 2024
Phase I Trial of VS-6766 Alone and in Combination With Everolimus	KRAS mutation	Solid Tumours	Stratified on KRAS mutation	Study drug (VS-6766) targets downstream gene(s) (RAF1)	28 Feb 2023
A Study to Evaluate the Safety, Pharmacokinetics, and Activity of GDC-6036 Alone or in Combination in Participants With Advanced or Metastatic Solid Tumors With a KRAS G12C Mutation	KRAS mutation	Advanced Solid Tumors; Colorectal Cancer	Enrolling subjects with KRAS mutation	Study drug (Inavolisib) targets downstream gene(s) (PIK3CA)	30 Nov 2024

Showing 1 to 118 of 118 entries



Generating explanations



Abductive Natural Language Inference (ANLI)

Inference to the best explanation
(facts, evidence)

Claim: Specialized cells protect the human body from disease-causing microbes by producing chemicals that destroy the microbes.

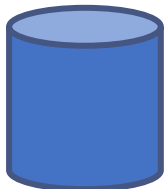
True | False

Why? (Explanation)

Multi-hop
Multi-premise

Specialized cells are a source of chemicals that destroy disease-causing microbes.

disease-causing microbes have a negative impact on the body.



~10.000 facts

Abductive Natural Language Inference (ANLI)

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~10.000 facts

Encoding scientific statements

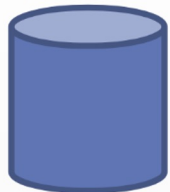
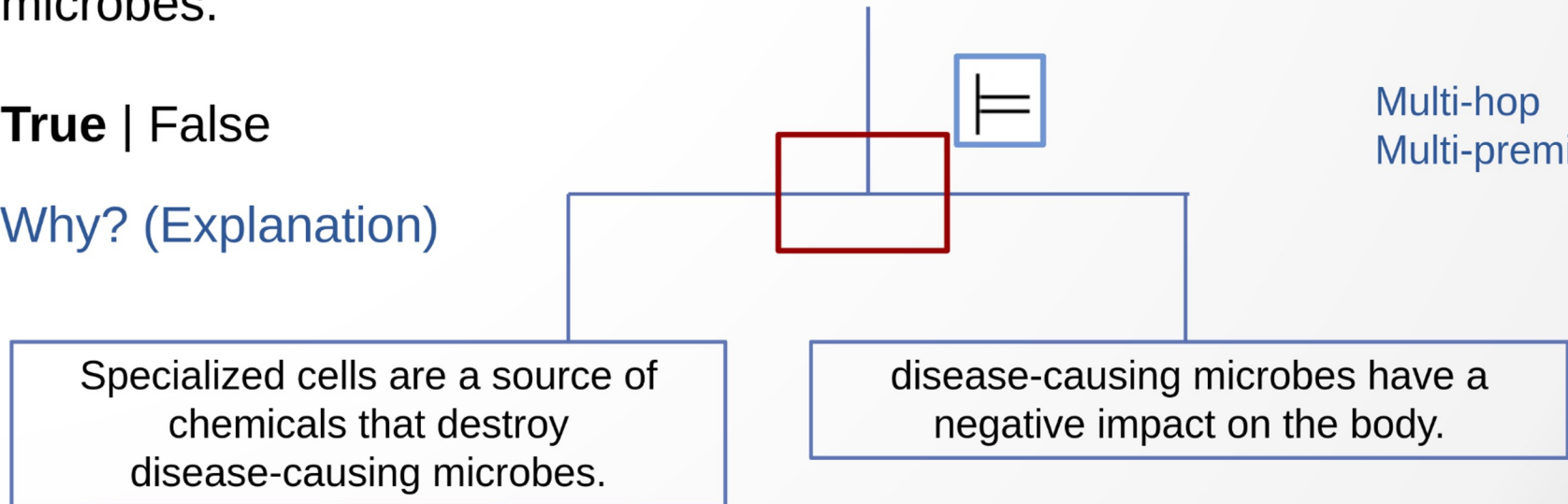
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True | False

Why? (Explanation)



~10.000 facts

Encoding inference relations

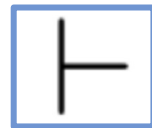
Scientific inference

- Step-wise explicit (verbalised) inference.
- Formal, verifiable argument & explanation.
- Preserving the positive aspects of LLMs.
- Improving control.

$$\Gamma \models \Phi$$

Γ semantically entails Φ

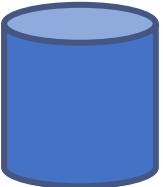
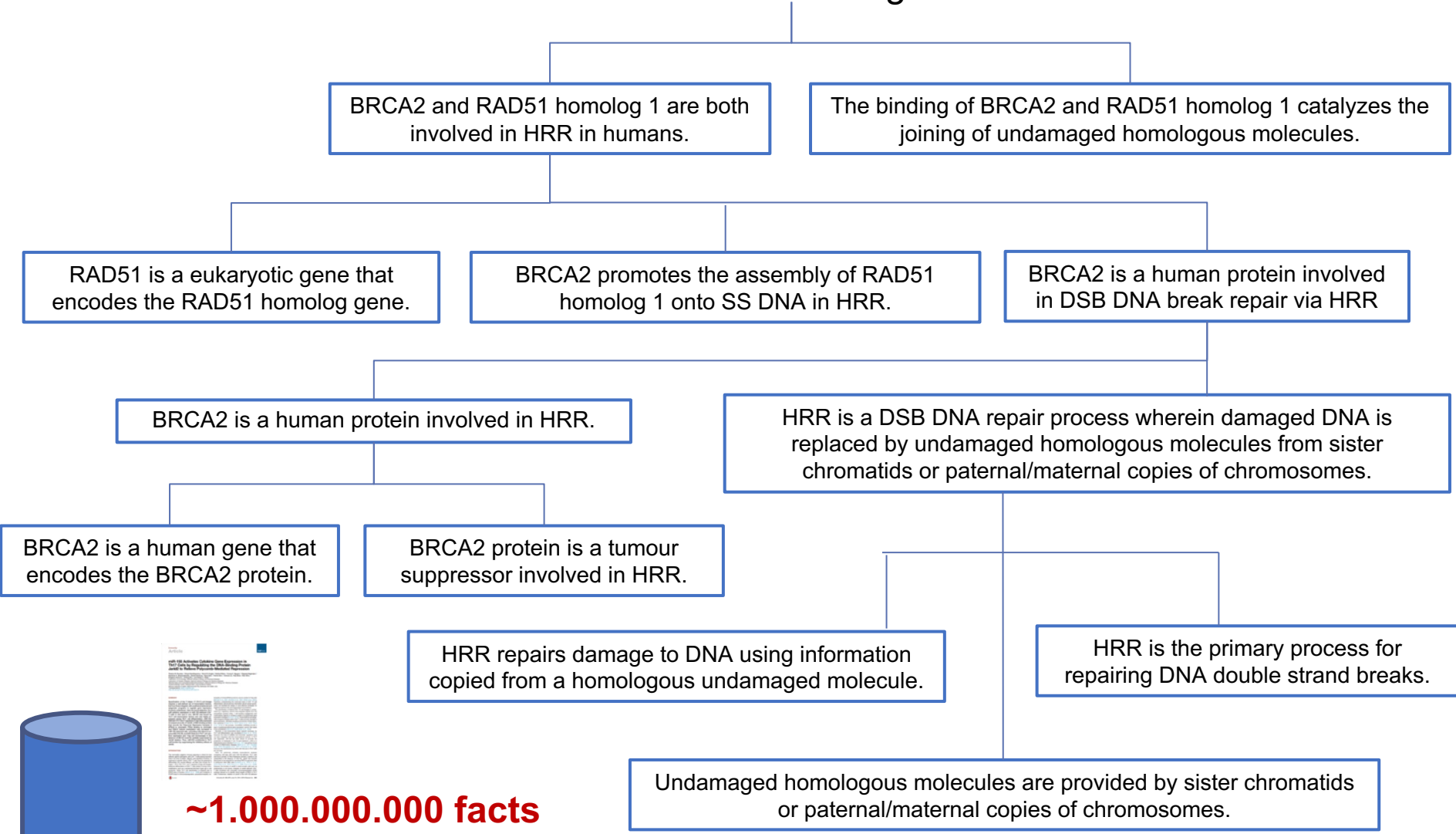
$$\frac{\Gamma \vdash \Phi}{\Gamma \text{ proves } \Phi}$$



- interpretability
- verifiability
- control (inference guarantees)

Expert-level scientific inference & explanation

Claim: BRCA2 promotes the joining of undamaged homologous repair molecules via RAD51 homolog 1 in humans.

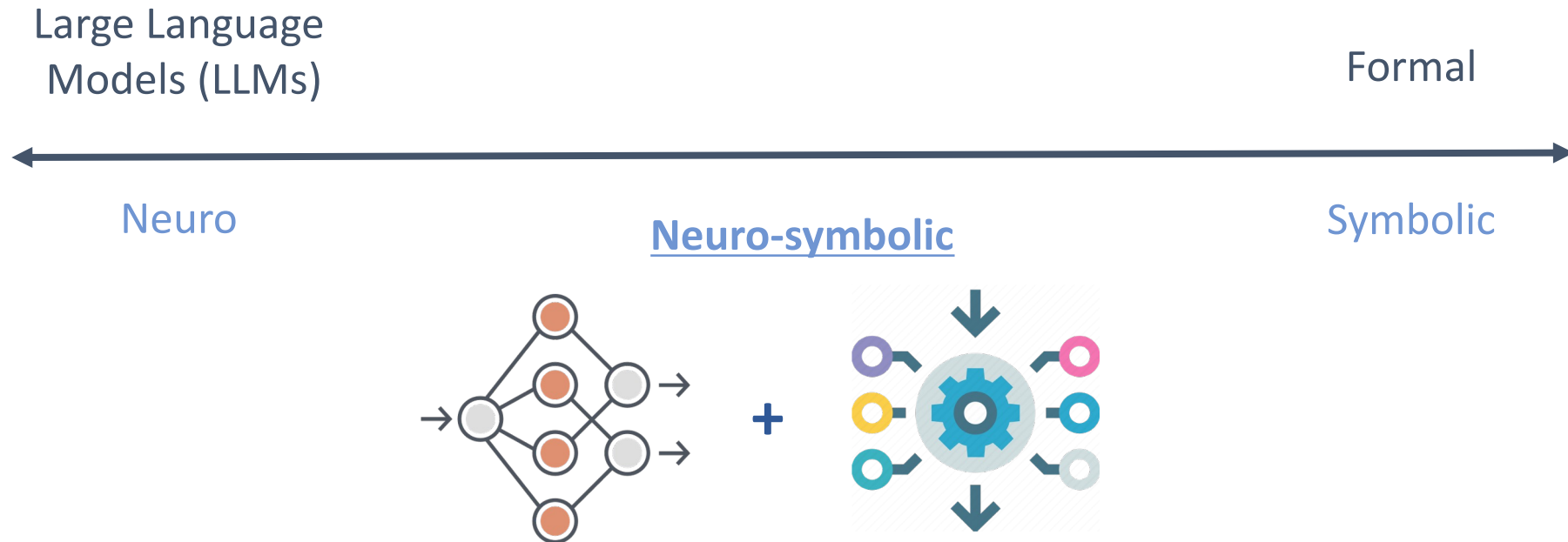


~1.000.000.000 facts

Undamaged homologous molecules are provided by sister chromatids or paternal/maternal copies of chromosomes.

Scientific inference

- Step-wise explicit (verbalised) inference.
- Formal, verifiable argument & explanation.
- Preserving the positive aspects of LLMs.
- Improving control.



Architectures for Explanation generation

claim



(Loss of BRCA2) **may** cause
(increased genomic instability).

Why?

Architectures for Explanation generation

claim

(Loss of BRCA2) may cause
(increased genomic instability).

Why?

Loss of BRCA2 causes the cell to
default to NHEJ repair processes.

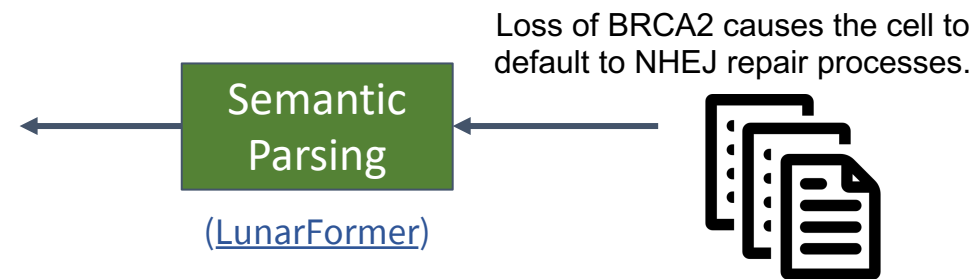


Architectures for Explanation generation

claim

(Loss of BRCA2) **may** cause
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Why?



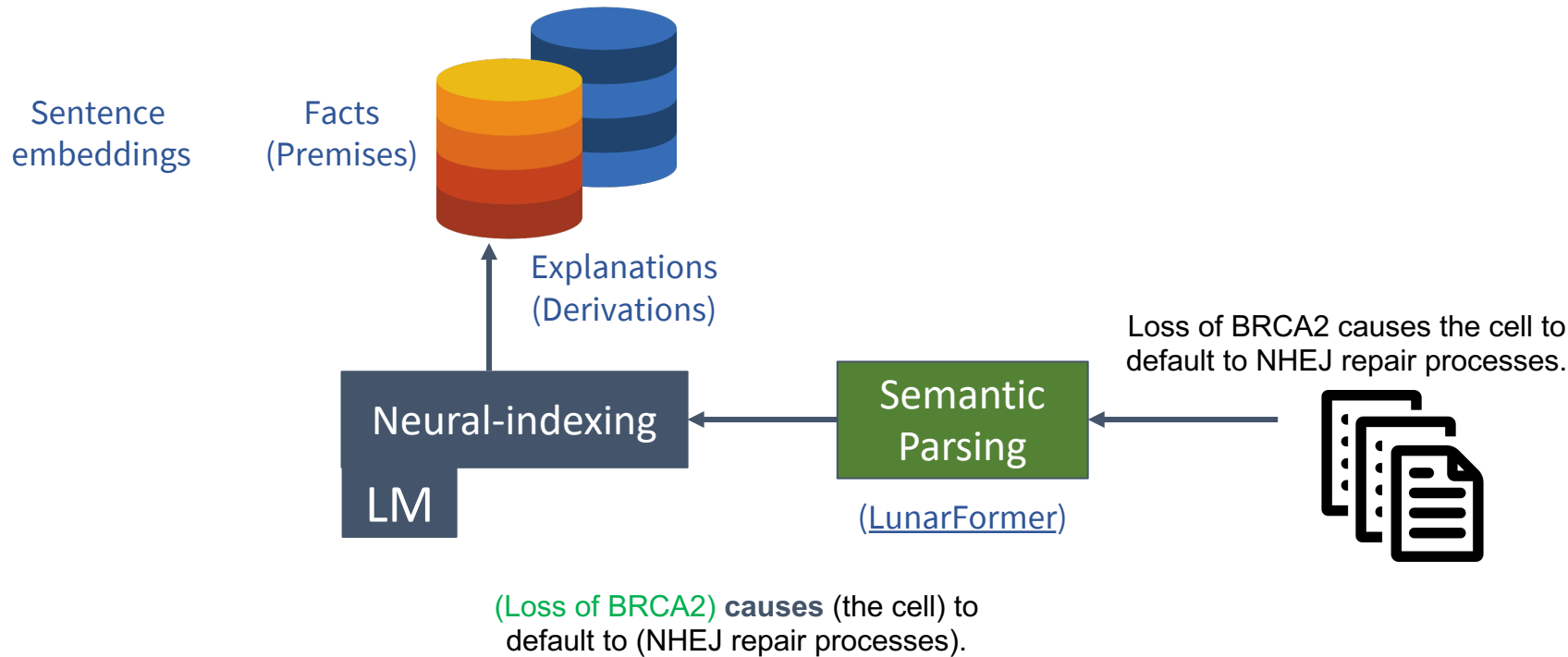
(Loss of BRCA2) **causes** (the cell) to
default to (NHEJ repair processes).

Architectures for Explanation generation

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Why?



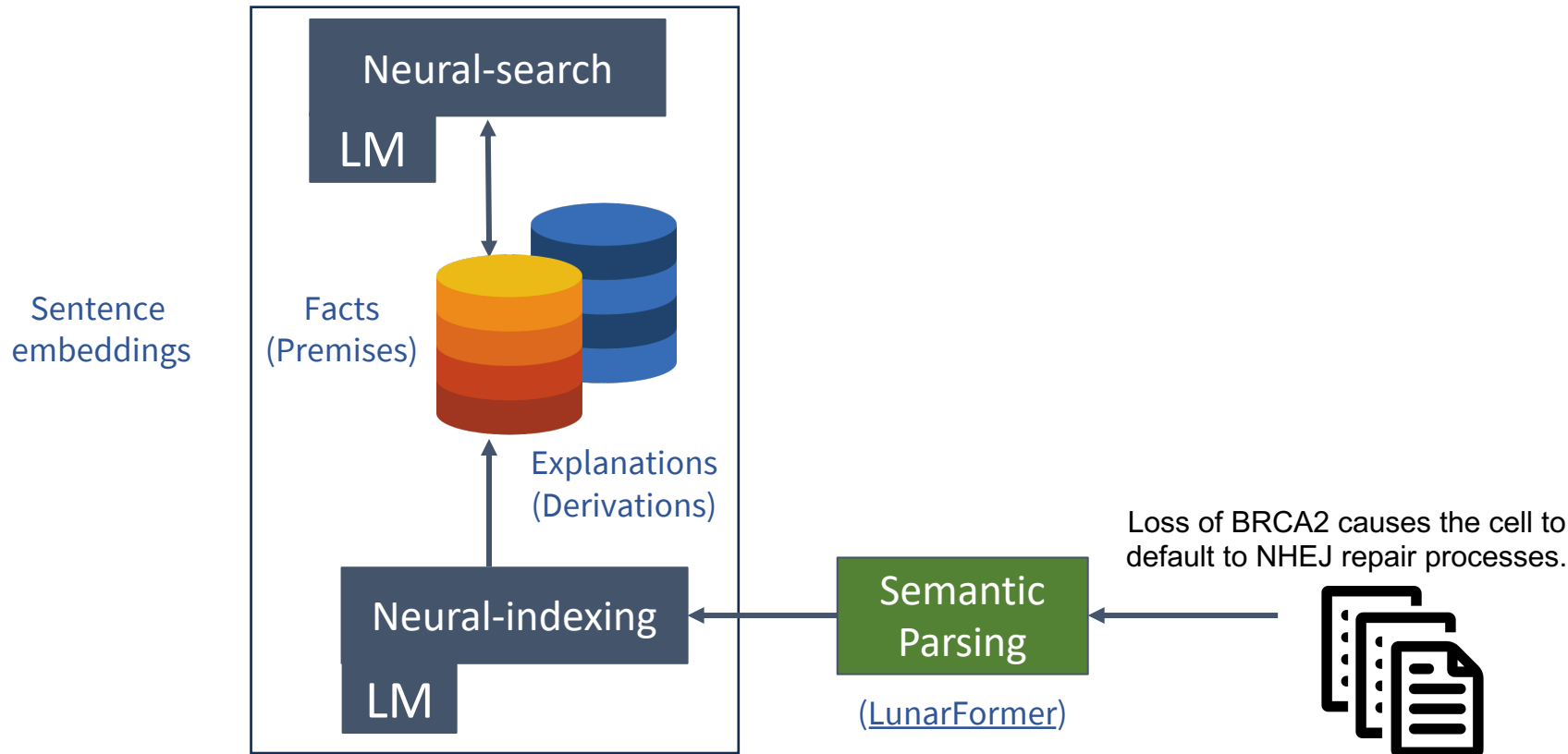
Architectures for Explanation generation

claim

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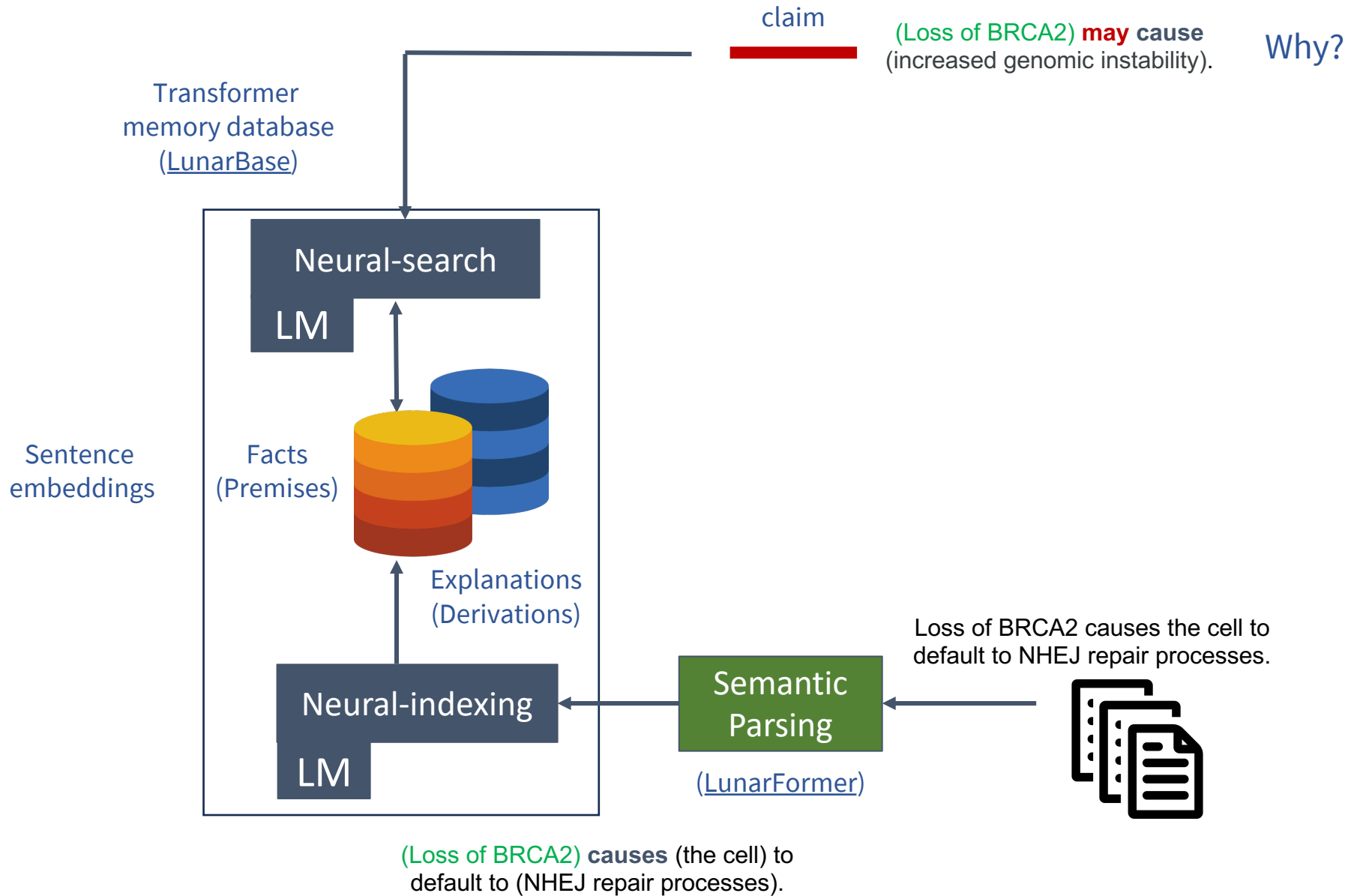
Why?

Transformer
memory database
(LunarBase)

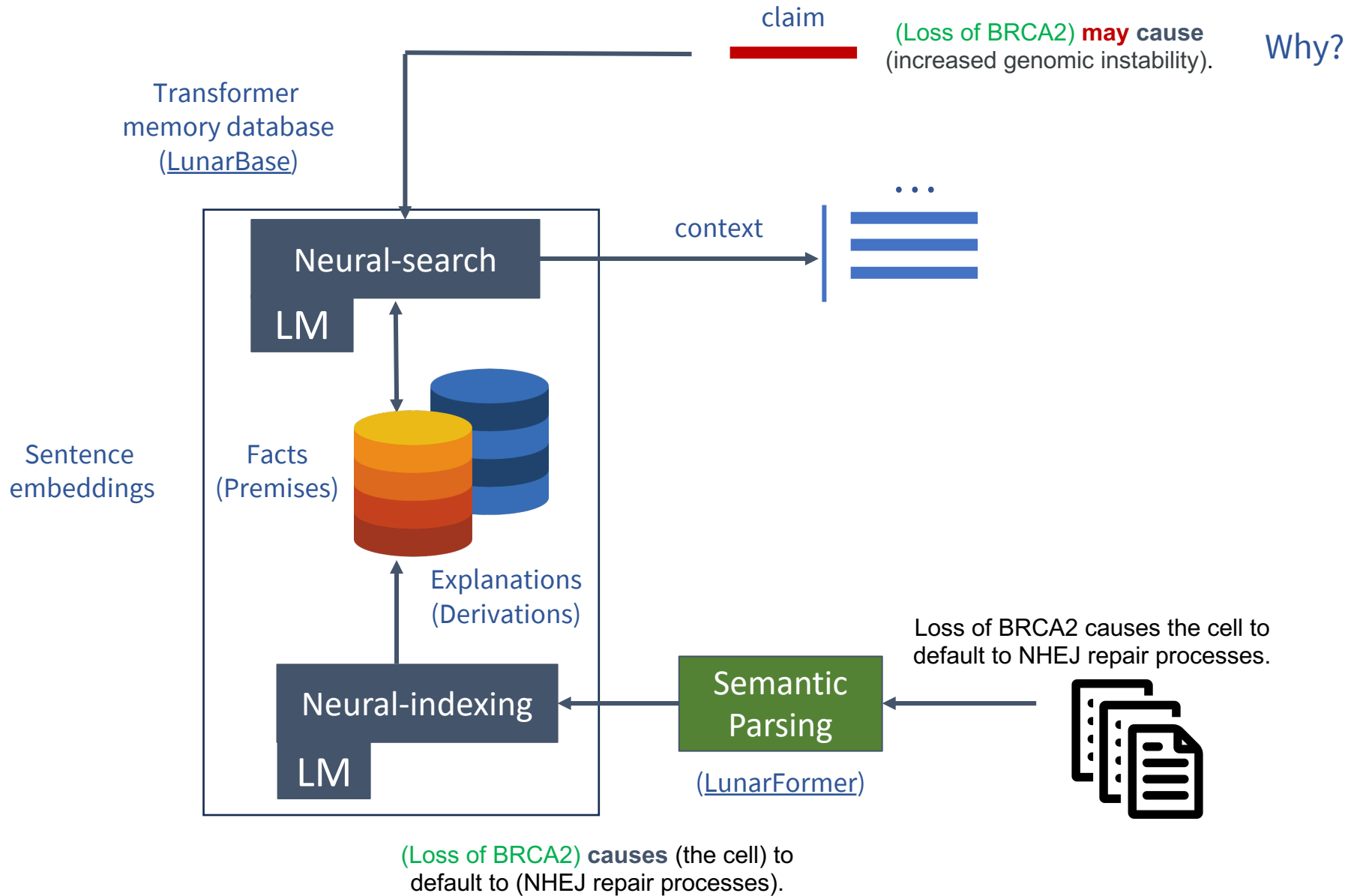


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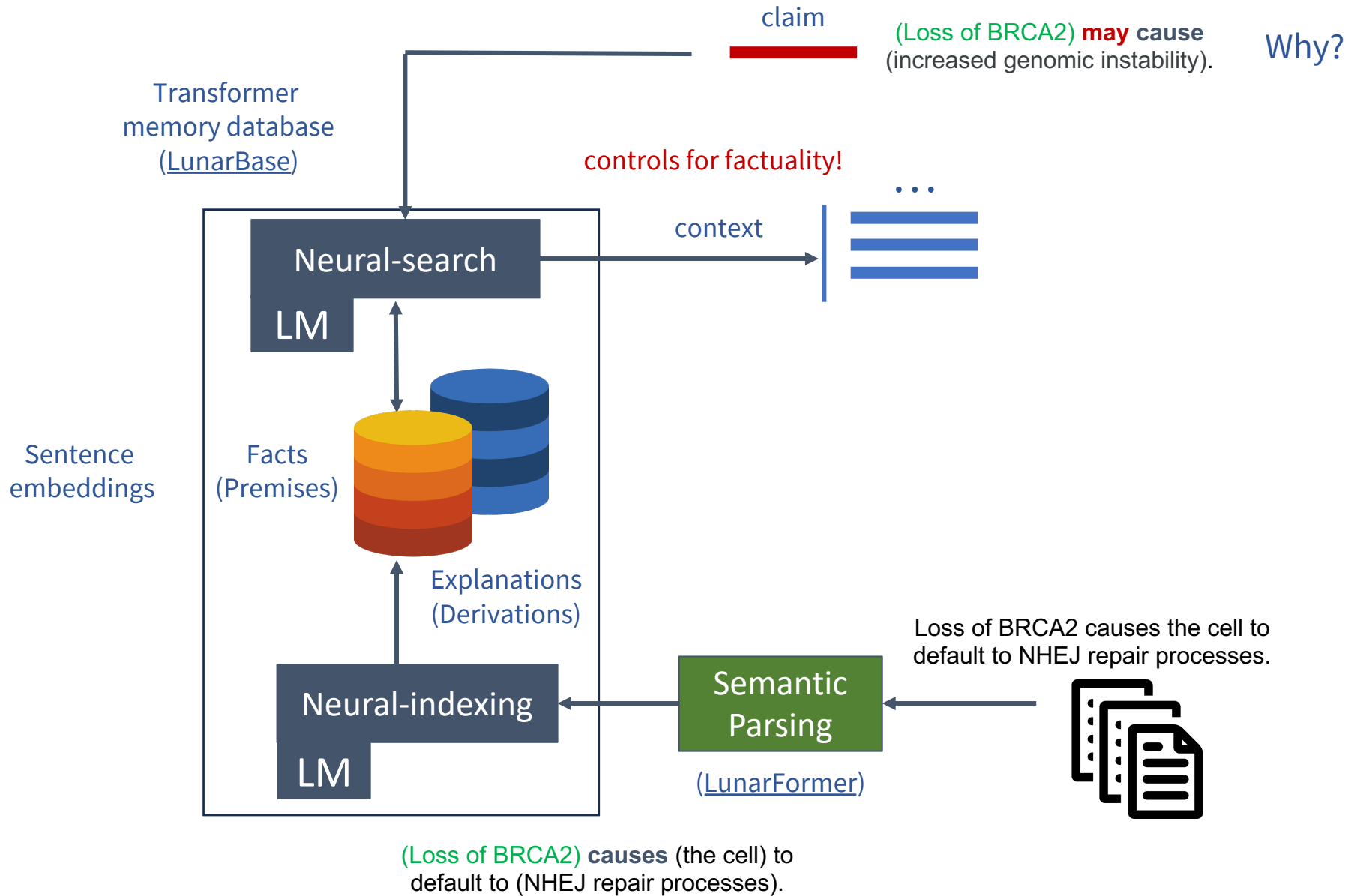
Architectures for Explanation generation



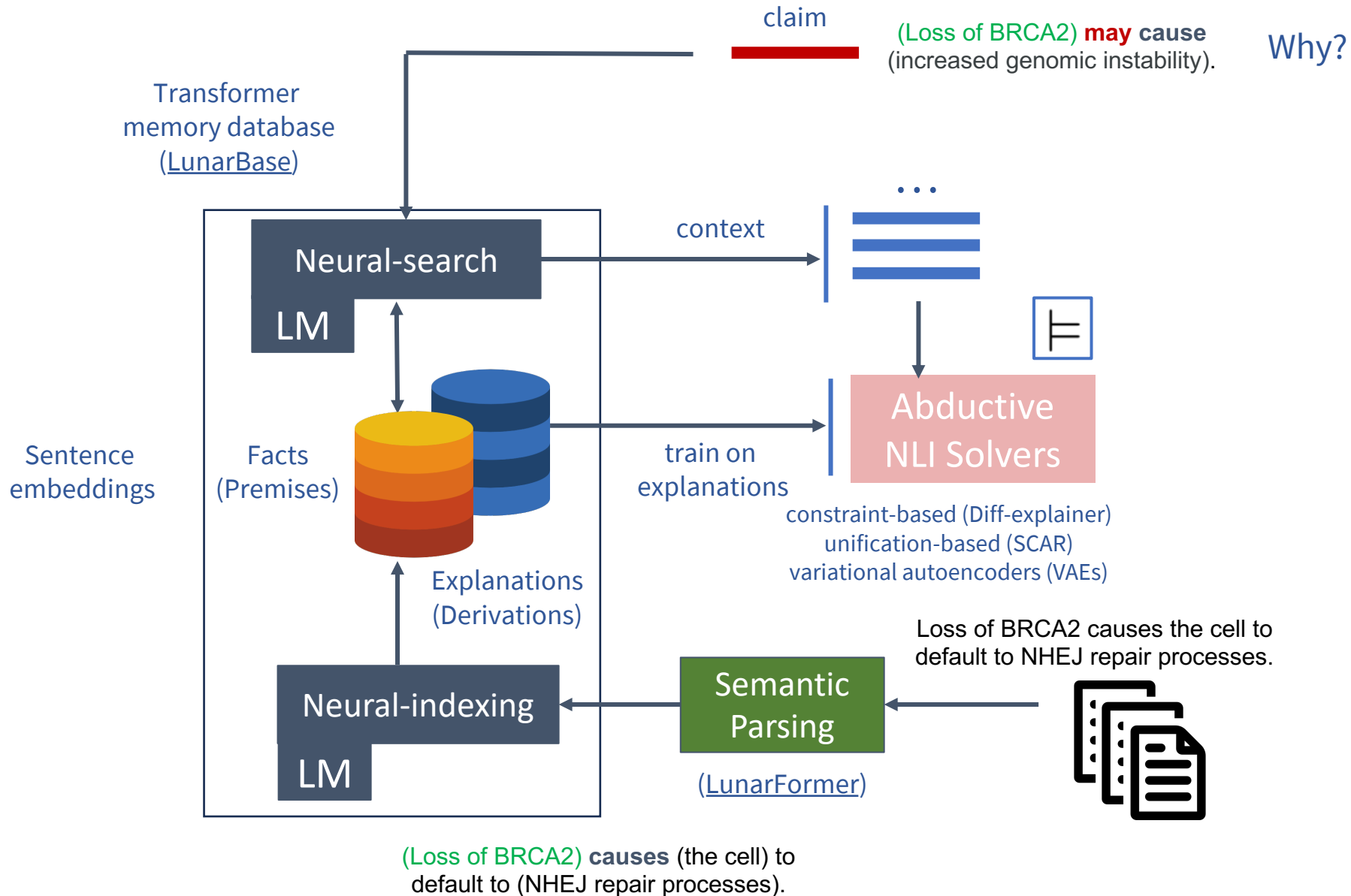
Architectures for Explanation generation



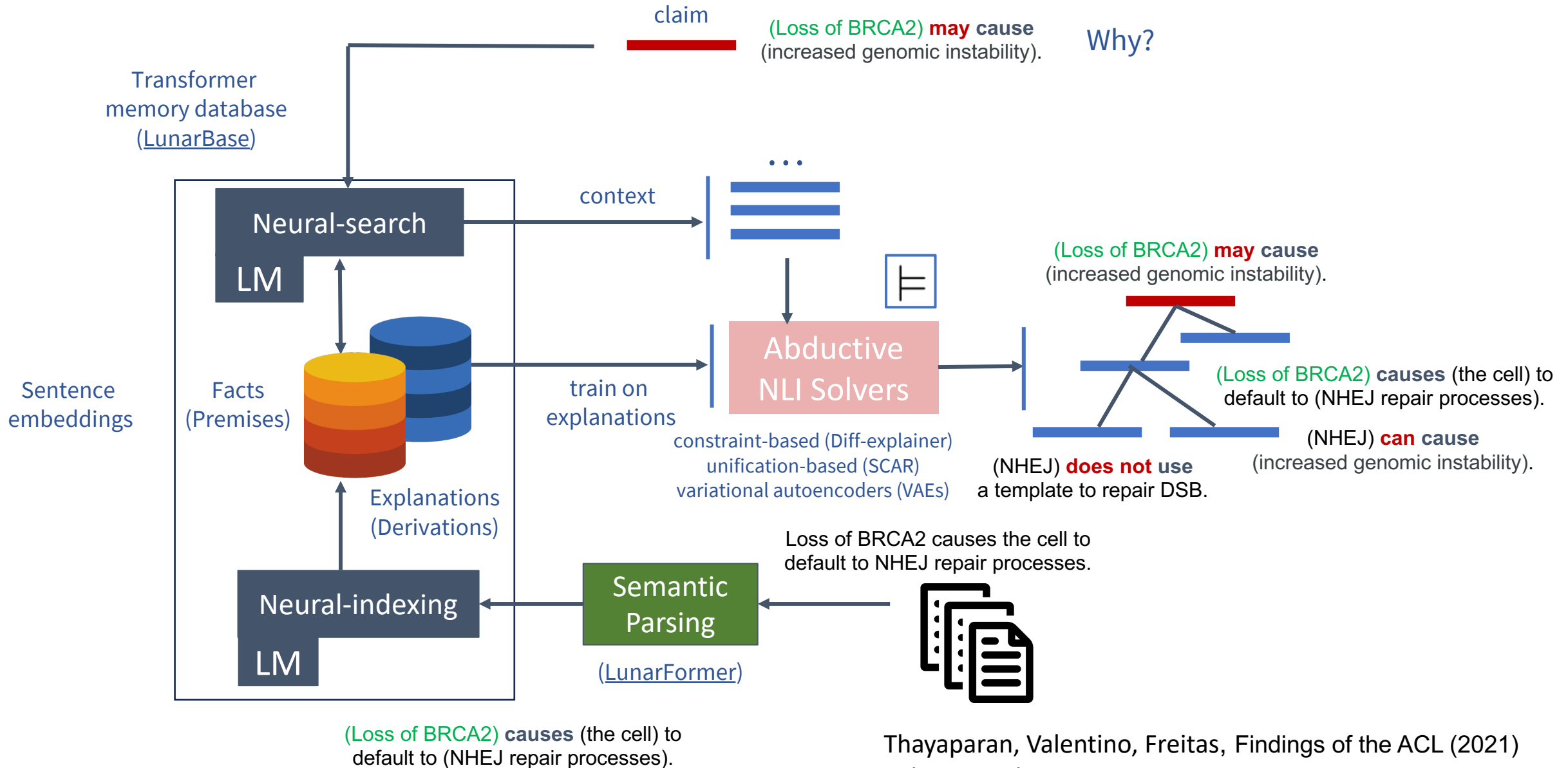
Architectures for Explanation generation



Architectures for Explanation generation



Architectures for Explanation generation

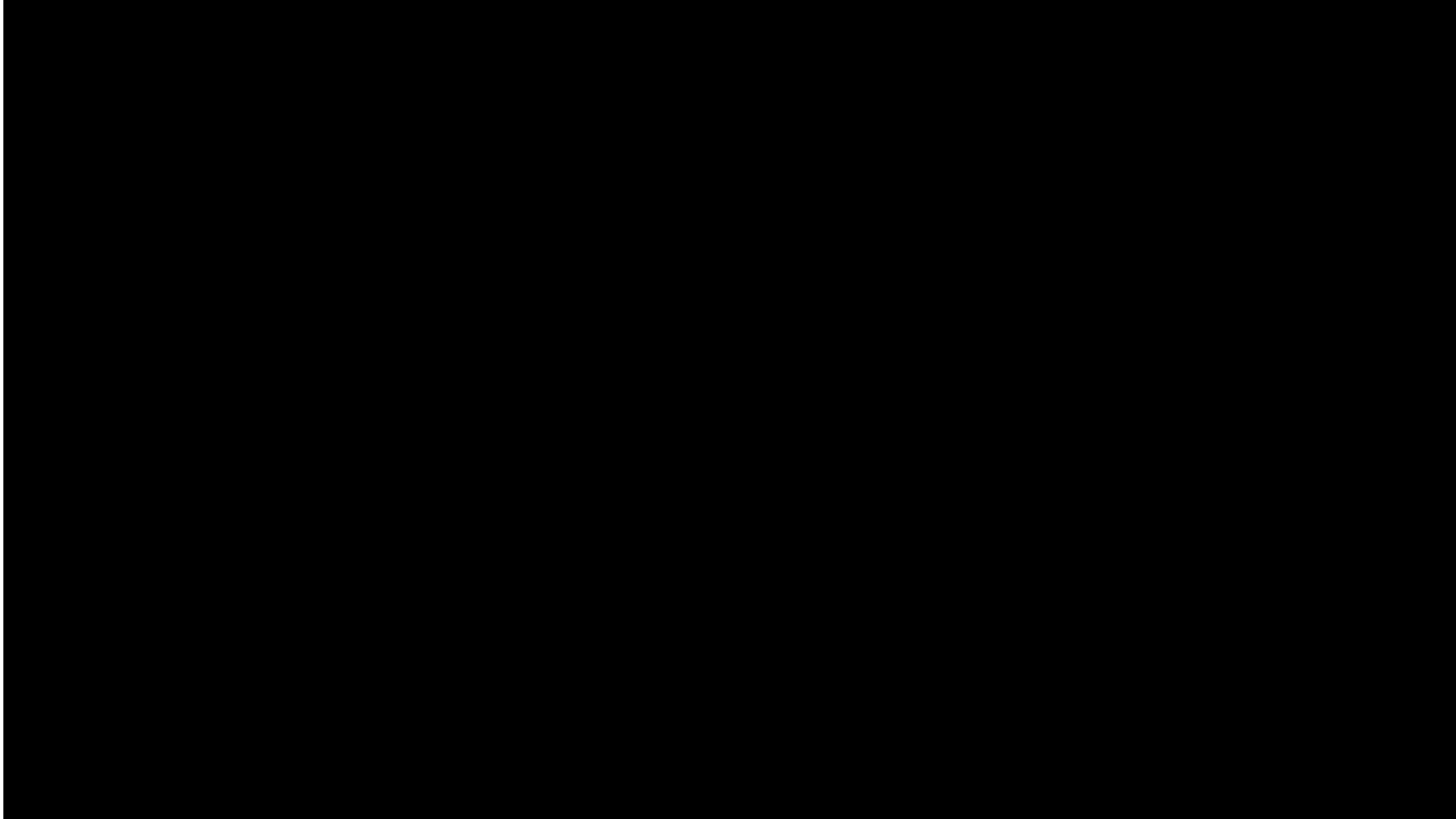


On Reasoning Infrastructures



Lunar





Take-away

Emerging foundations for industrialised scientific inference

Universal framework for integrating and organising heterogeneous evidence

Large Language Models

Are a **(monumental!)** game-changing foundation.

Transformers are an efficient substrate for modelling language and reasoning.

Fluidity/lower impedance between representation modalities:

... -> Text -> Structure -> Equation -> Code -> ...

Alone they are not fit for purpose for scientific reasoning.

Controlling reasoning

Scientific reasoning requires complex pipelines.

Robust methods already exist to extend LLMs in the direction of rigorous reasoning.

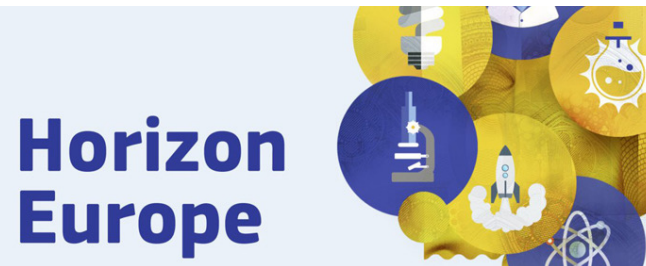
(multiple models, chains/trees-of-thought, symbolic augmentation, retrieval augmentation – text, tables and graphs, toolformers, differentiable symbolic solvers)

Need for a coordination infrastructure.

***Very* exciting times to do AI for Science!**

Thank you for your attention!

Generously supported by:



contact: andre.freitas@manchester.ac.uk

