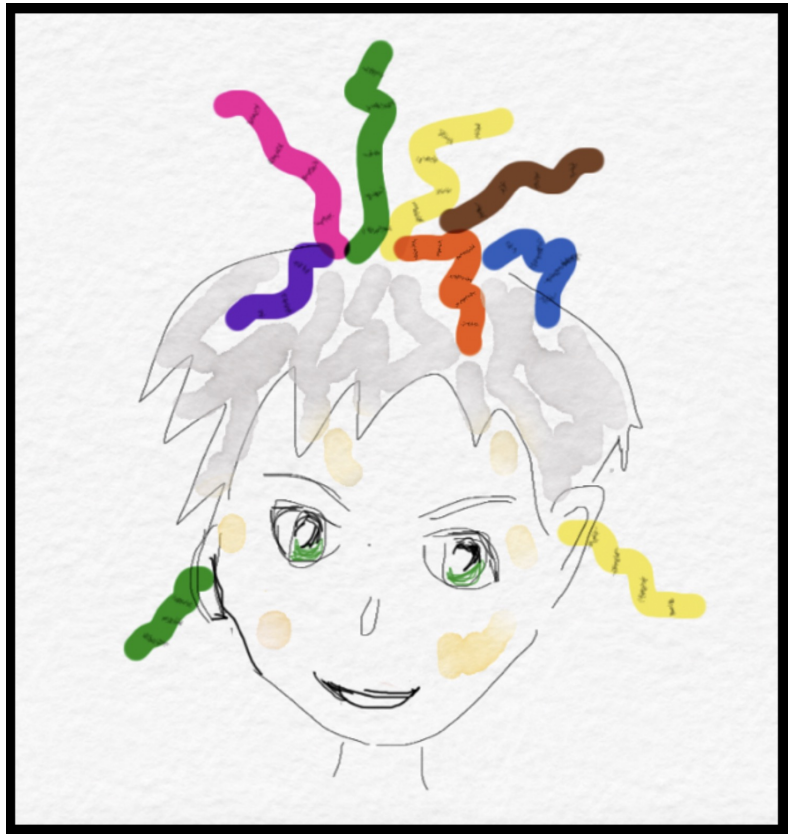
Minhocas na cabeça



Worms in the head

What I am going to talk about

1. **Obsessive Compulsive Disorder (OCD)**

2. **Black hole and books**

3. **Adoption (by the young) and resurrection**

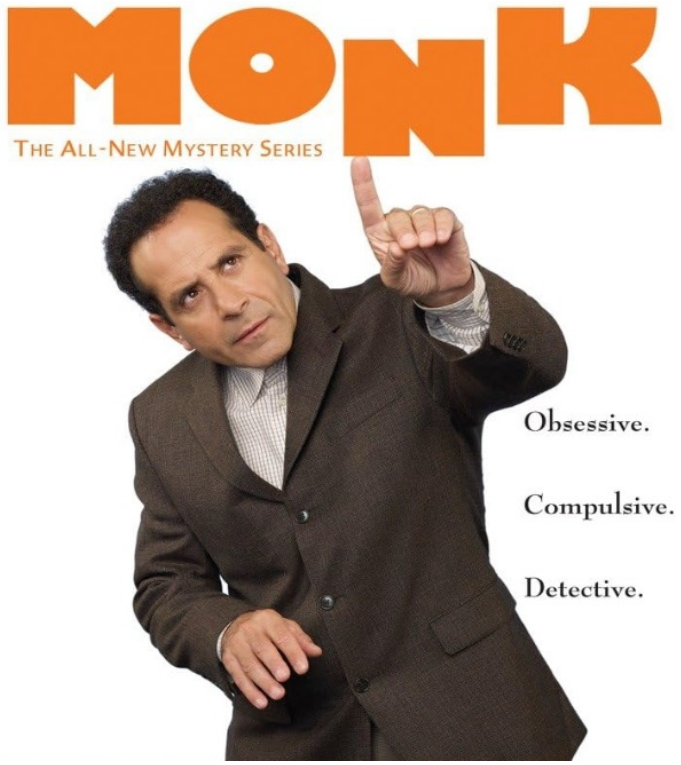
4. **“Abbey” (“Abbaye”) and biology**

5. **Caminhando e cantando, e seguindo a canção (Walking and singing, and following the song)**

6. **Jobim (and the young)**

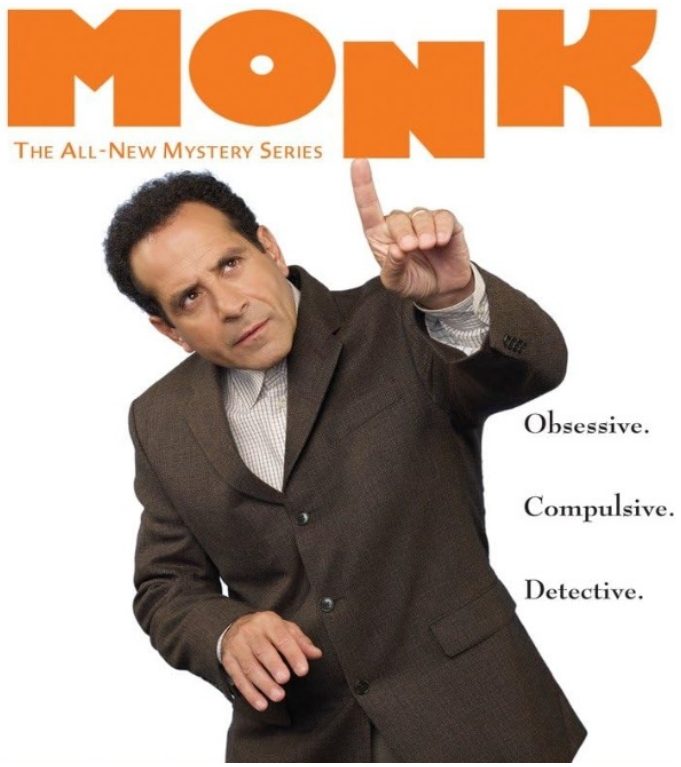
7. **To have in oneself all the dreams of the world (F. Pessoa) – Other obsessions**

Obsessive compulsive disorder (OCD)



American series a little bit old (2002-2009) but still broadcasted until recently in France

Obsessive compulsive disorder (OCD)



OCD more personal

I will actually talk about science, in the fields of math and algorithms more particularly

This is the only science I will talk about, well almost

Cophylogeny reconciliation

Input:
Two undated phylogenetic trees *H* and *P*
A mapping *f* of the leaves of *P* onto the leaves of *H*
Output:
An optimal extension of *f* to the internal vertices of *P* onto the vertices of *H* given that *f* induces a partition of the vertices of *P* in three sets, each corresponding to an "event" with its own associated cost

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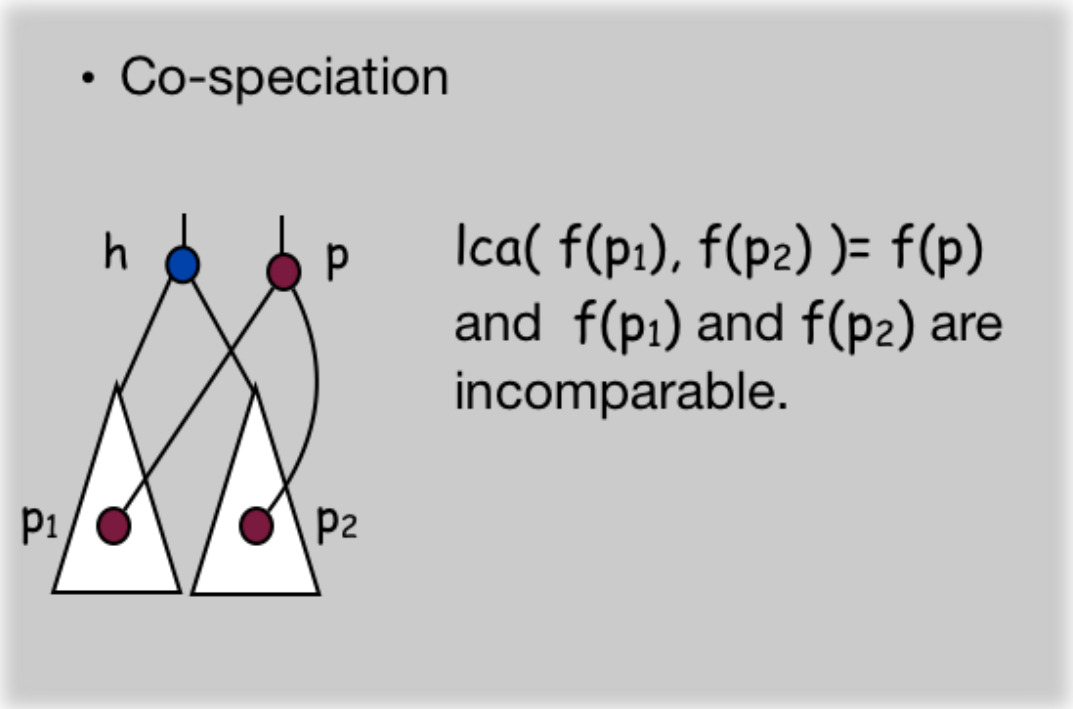

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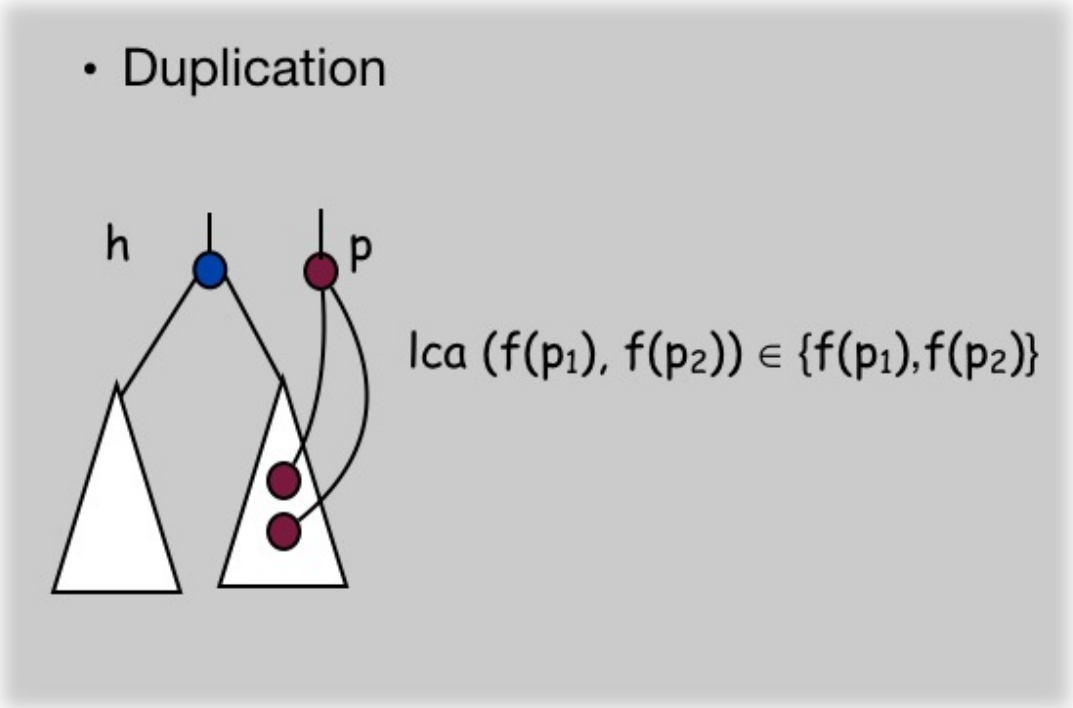

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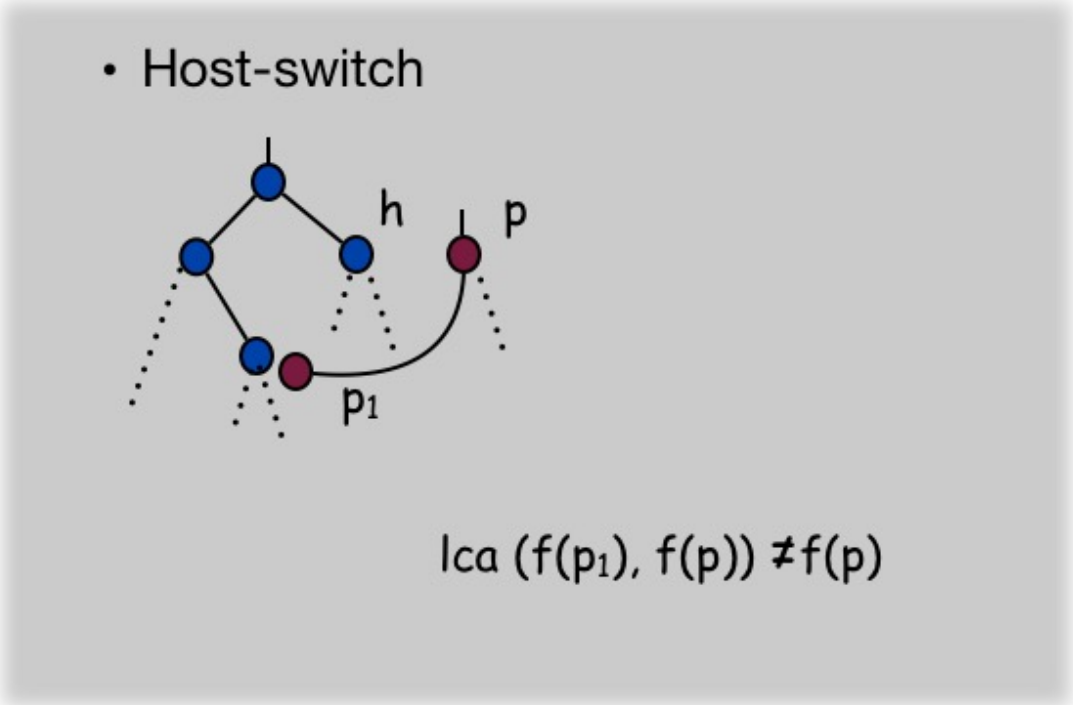

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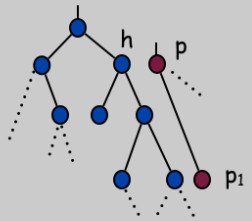
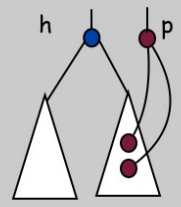
plus a cost for a fourth type of event – corresponding to a loss – induced by *f*

- Loss



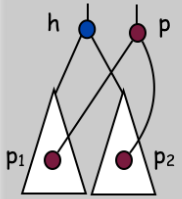
the edge (p, p_1) contributes with 1 loss.

- Duplication



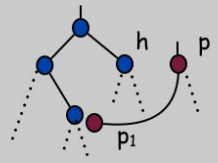
lca ($f(p_1)$, $f(p_2)$) ∈ {$f(p_1)$,$f(p_2)$}

- Co-speciation



lca($f(p_1)$, $f(p_2)$)= $f(p)$
and $f(p_1)$ and $f(p_2)$ are incomparable.

- Host-switch



lca ($f(p_1)$, $f(p)$) ≠ $f(p)$

Problem

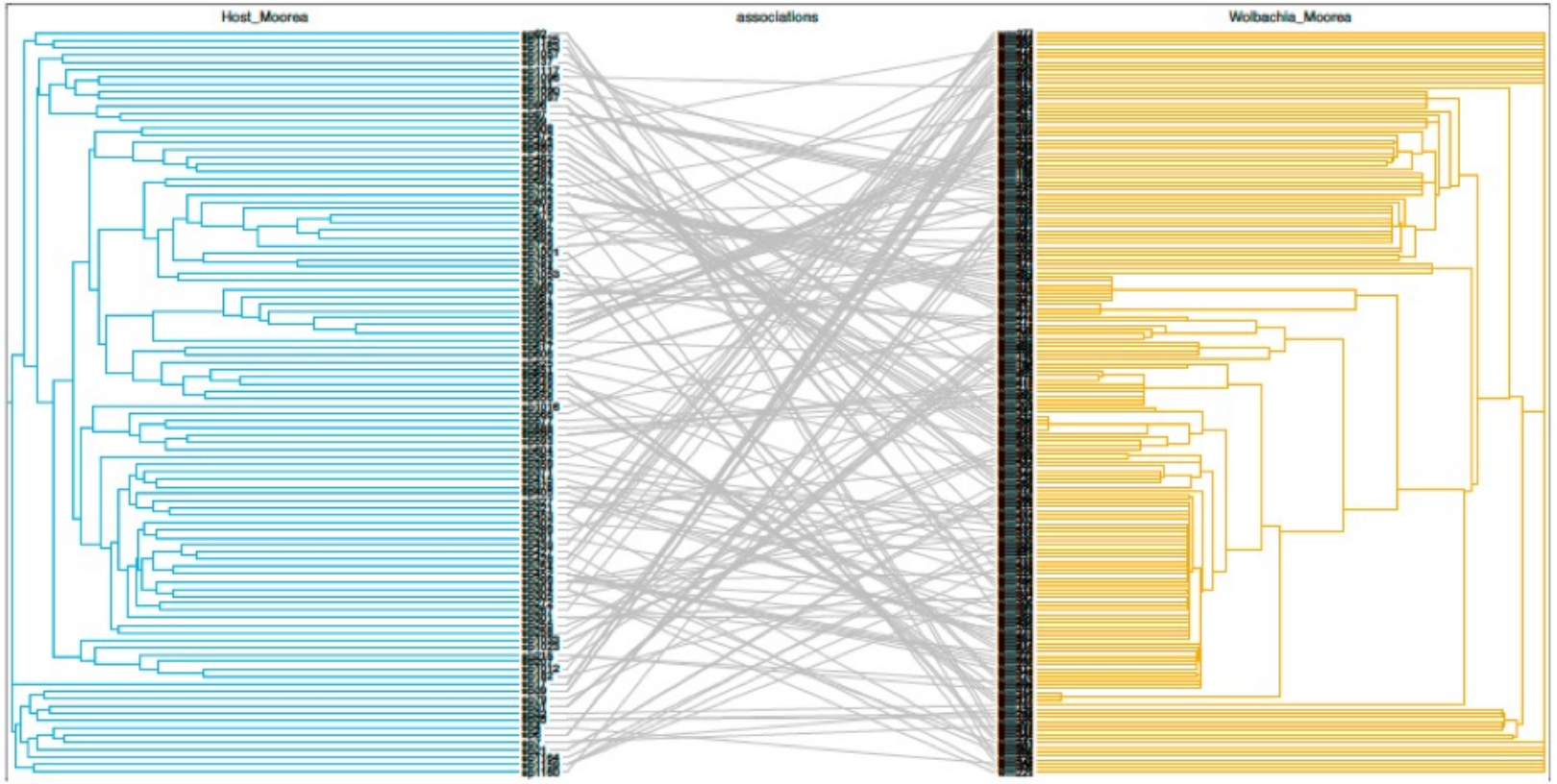
Illustrated by an example

Two undated phylogenetic trees with 773 leaves each

Number of optimal solutions above 10^{42} depending on the cost assigned to each of the four events

Tree *H*: Arthropods

Tree *P*: *Wolbachia*



Which solution to choose?

Who cares, just pick one!

Which solution to choose?

Who cares, just pick one!

Noooooooo! This is not possible!

There may be big differences among the solutions, even in terms of just the number of each event
Of course this depends on the cost assigned to each event, and on the trees
However, these differences are observed even for quite small trees (approximately 10 leaves each)

Which solution to choose?

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Of course this depends on the cost assigned to each event, and on the trees
However, these differences are observed even for quite small trees (approximately 10 leaves each)

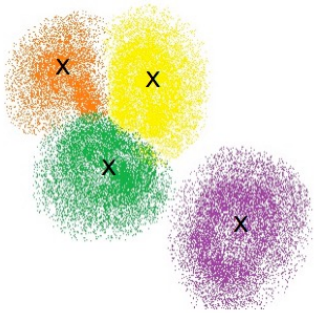
So what does the person suffering from the obsessive compulsive disorder (OCD) recommend?

Enumerate all the solutions!
BUT in a smart, and at the same time well-controlled way!!!!

Possible approaches

First natural approach:

Agglomerative clustering that produces consensus or centroid solutions



Problem:

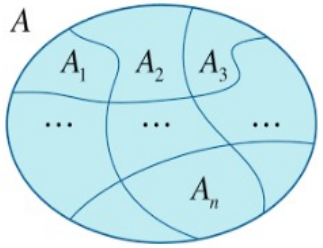
Requires some kind of distance or diversity measure between solutions

Might be less easy to interpret (in terms of biology/evolution)

Second approach:

Establish an a priori equivalence relation among solutions that makes sense (in terms of biology/evolution)

Enumerate the classes of equivalence only, meaning their characteristics and one representative per class

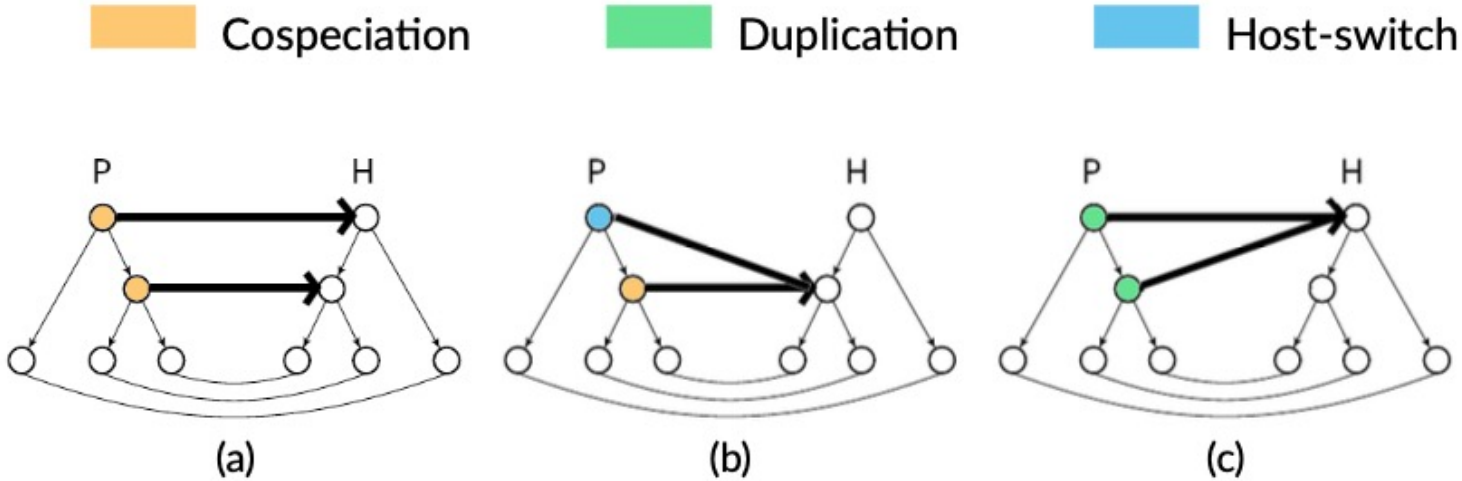


Equivalence relation/classes

First, one important observation:

Each internal vertex of the tree *P* is associated to one, and only one of 3 events

The tree P is thus fully coloured



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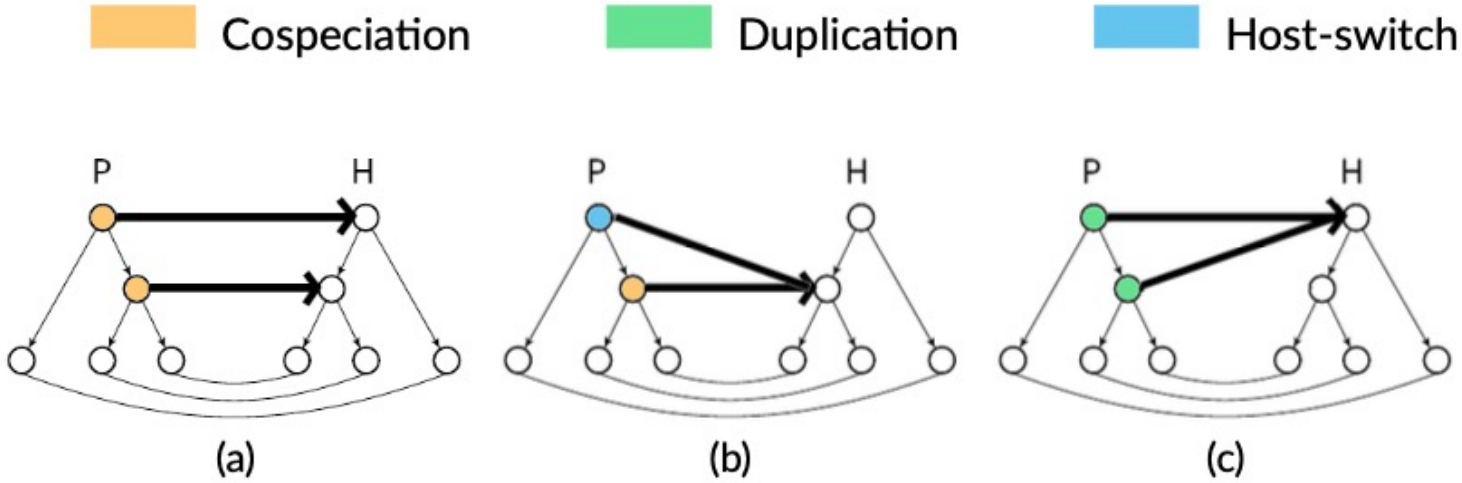

Possible equivalence relations based on such colouring of the vertices of *P*

V-equivalence: 2 solutions are equivalent if the number of each colour is the same (same event vectors)

E-equivalence: 2 solutions are equivalent if the vertices of *P* are coloured the same way (but we do not care where they are mapped)

EL-equivalence: Same as E-equivalence plus the host-switch arcs are the same

DC-equivalence: Same as E-equivalence plus the co-speciation and duplication arcs are the same

Enumeration of equivalence classes / representatives per class

Does it make a difference in terms of complexity?

Enumerating the classes / one representative per class can be done in polynomial-time delay (namely, in $O(n^2m)$ time where n is the number of vertices in H and m the number of vertices in P)

Does it make a difference in terms of the number of solutions?

V*: does not count losses

199 leaves each tree

773 leaves each tree

Dataset	Cost vector	#Optimal reconciliations	#V-(V*-)equiv. classes	#E-equiv. classes	#EL-equiv. classes	#CD-equiv. classes
COG4965	(−1, 1, 1, 1)	44800	5	13	23456	13
	(0, 1, 1, 1)	17408	2	4	17408	4
	(0, 1, 2, 1)	640	2	3	576	3
	(0, 2, 3, 1)	6528	3	5	448	5
	(0, 1, 1, 0)	907176	324 (10)	12	17	11958
WOLB	(−1, 1, 1, 1)	10^{47}	10	4080	*	24192
	(0, 1, 1, 1)	10^{48}	11	40960	*	76800
	(0, 1, 2, 1)	10^{47}	10	4080	*	24192
	(0, 2, 3, 1)	10^{42}	7	96	10^{36}	1152
	(0, 1, 1, 0)	10^{136}	* (74)	10^{27}	*	*

An important comment

Approach generalisable to other problems, not only in computational biology

Two examples:

- Frequency assignment (arising for instance in telecommunication networks)
- Alignment of a sequence (for instance gene sequence) on a tree (for example phylogenetic tree)

Open questions of this more general context

- Is the approach generalisable to other examples?
- Is it easy in such cases to establish relevant equivalence relations, and if yes, which ones?

And many more open questions, in fact many, many, many questions…

An important comment

Approach generalisable to other problems, not only in computational biology
Two examples:
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- Alignment of a sequence (for instance gene sequence) on a tree (for example phylogenetic tree)

Open questions of this more general context
- Is the approach generalisable to other examples?
- Is it easy in such cases to establish relevant equivalence relations, and if yes, which ones?

And many more open questions, in fact many, many, many questions…

And more generally, importance (as far as I am concerned in any case) of:
- Clear formalisation of the initial problem, whatever it may be
  - (clear definition of the model – not easy! – and of the objects sought)
- Exact algorithms
- Enumeration of all solutions when there is more than one (most often the case, if not always)

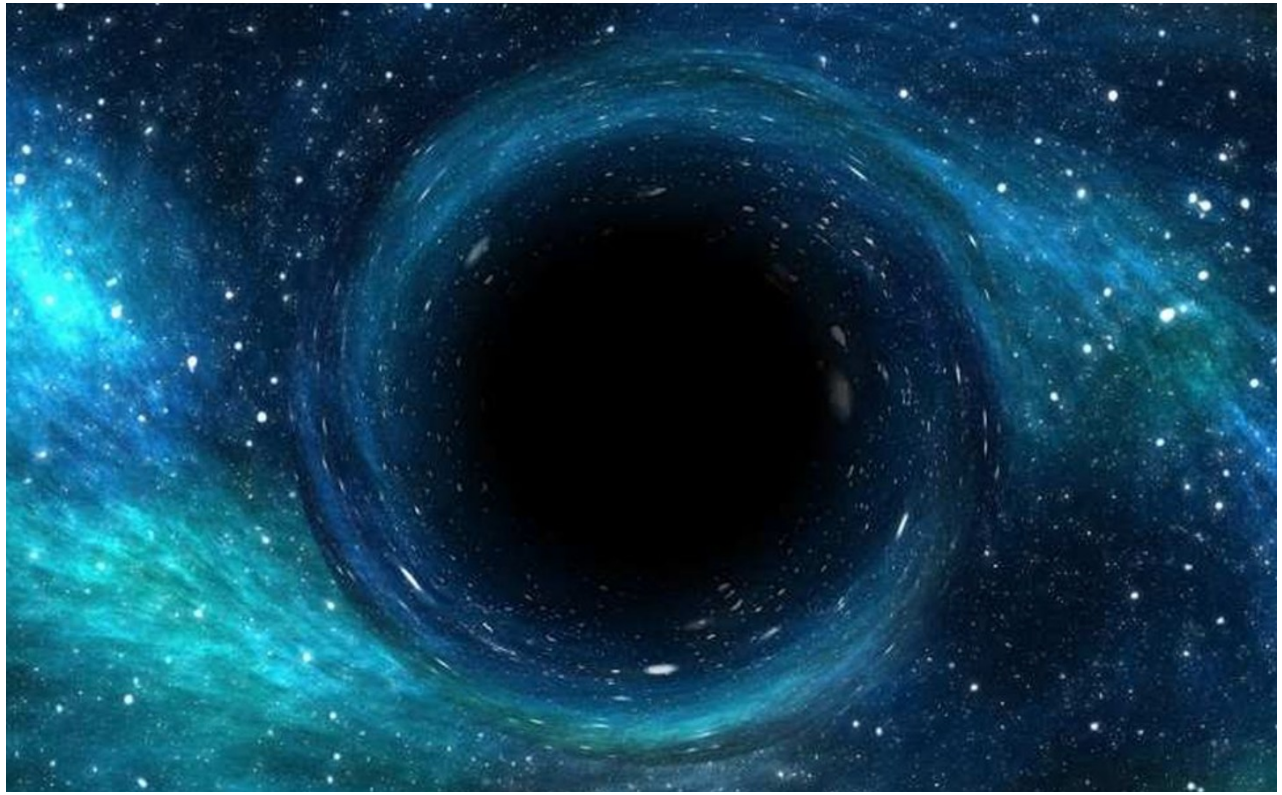
However, this is still far from being achievable (*e.g.* parameters such as cost/probability of each event)

Black hole and books

OCD not the only psychological problem
And psychological problem(s) often lead(s) to physical problems, sometimes very serious
Consequence:

Year of the "baccalauréat" ("Lycée français" in Brazil) studying alone except for the math classes, then the following year failed attempt to return to normal, and after that total isolation for 12 years

Black hole
1974-1988



Black hole and books

But there are things that continued to happen despite everything throughout all these years

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Books

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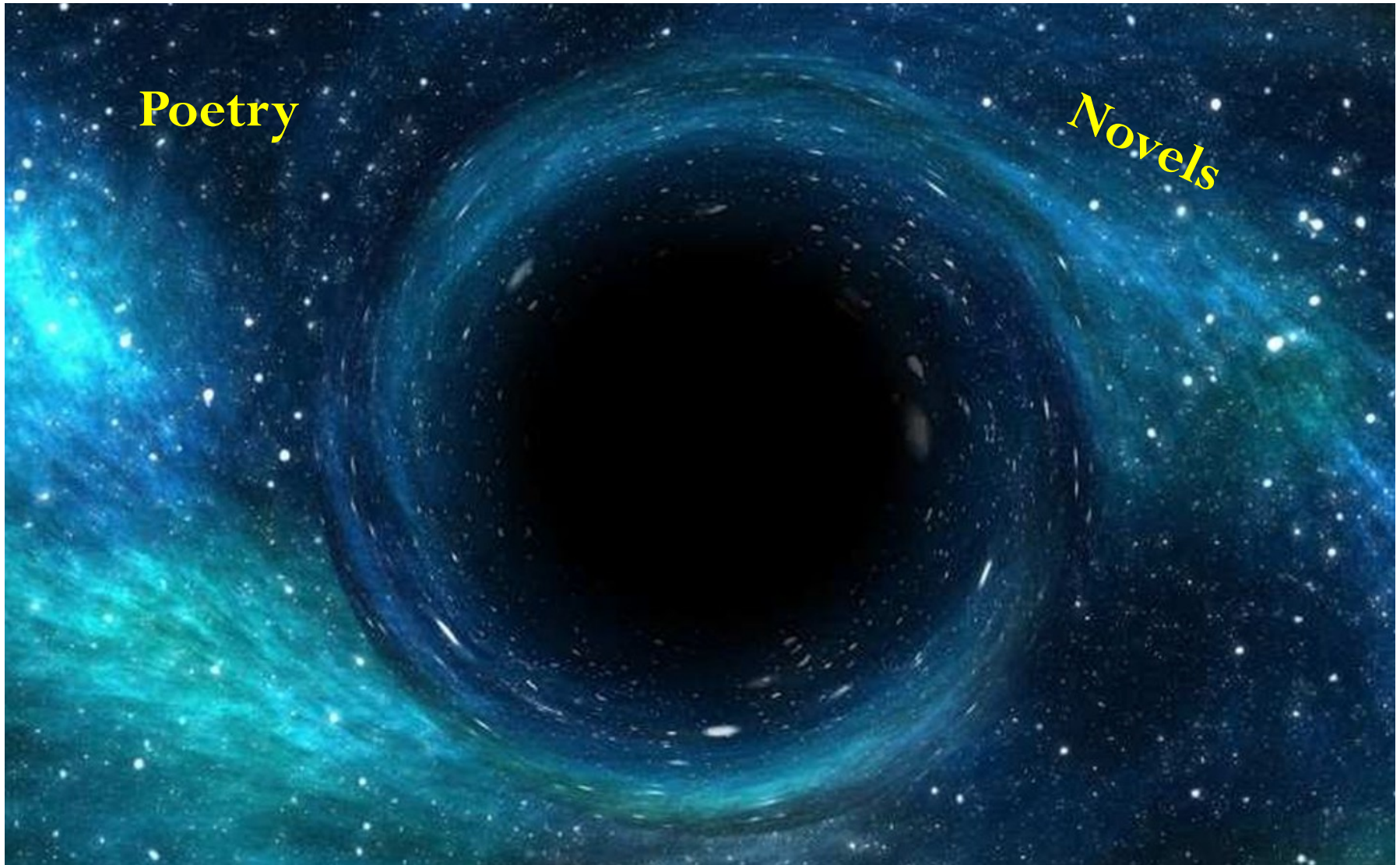

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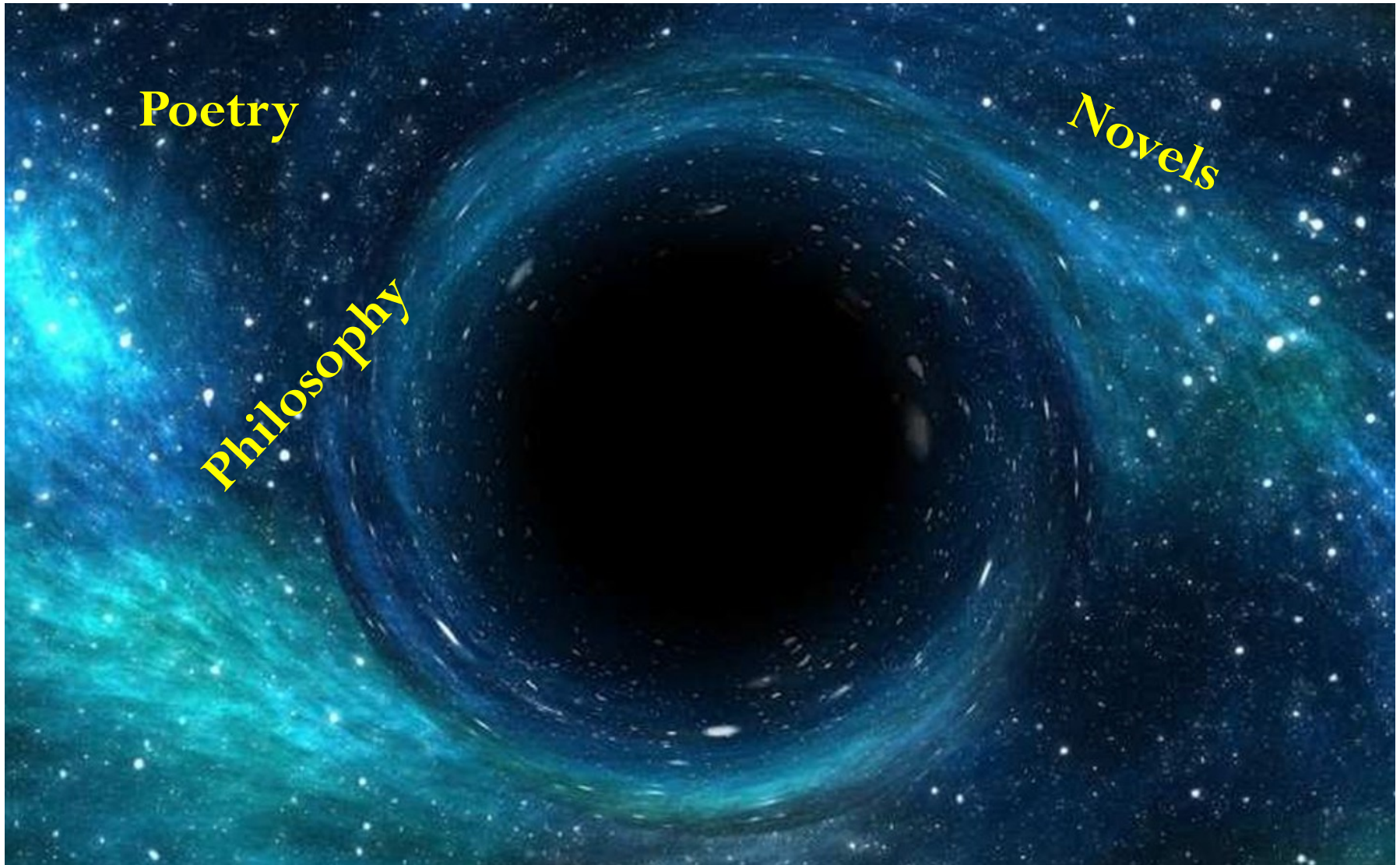

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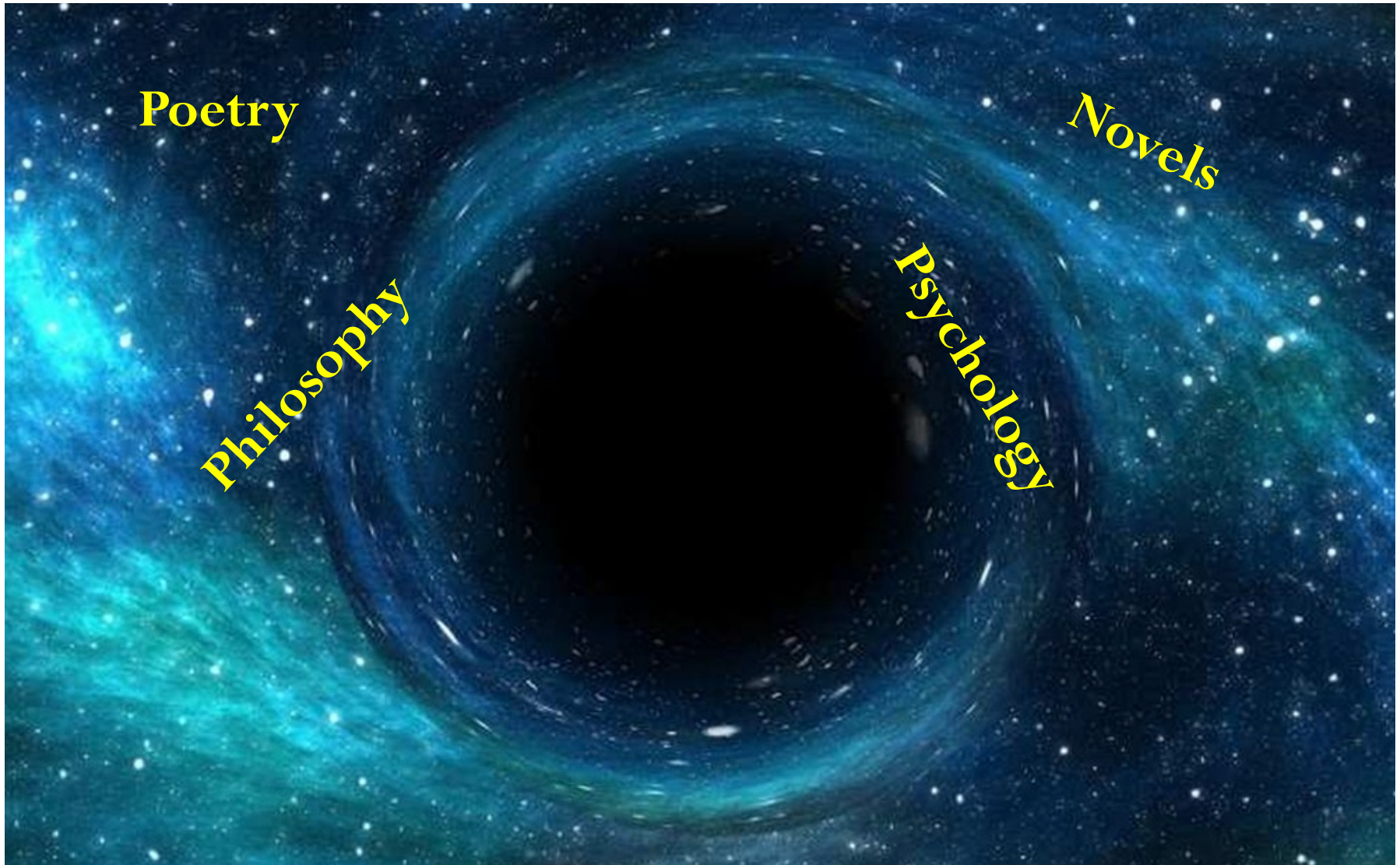

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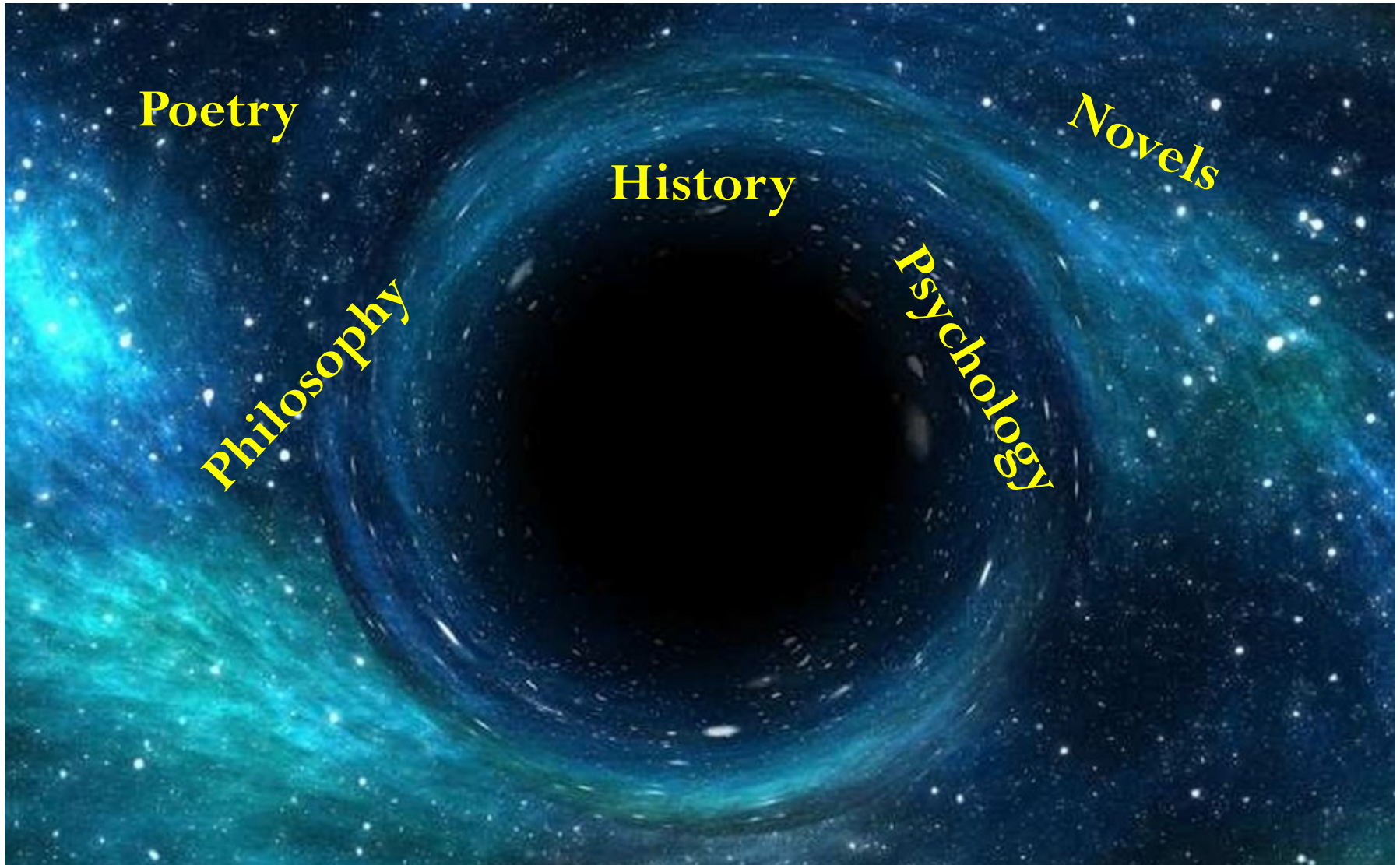

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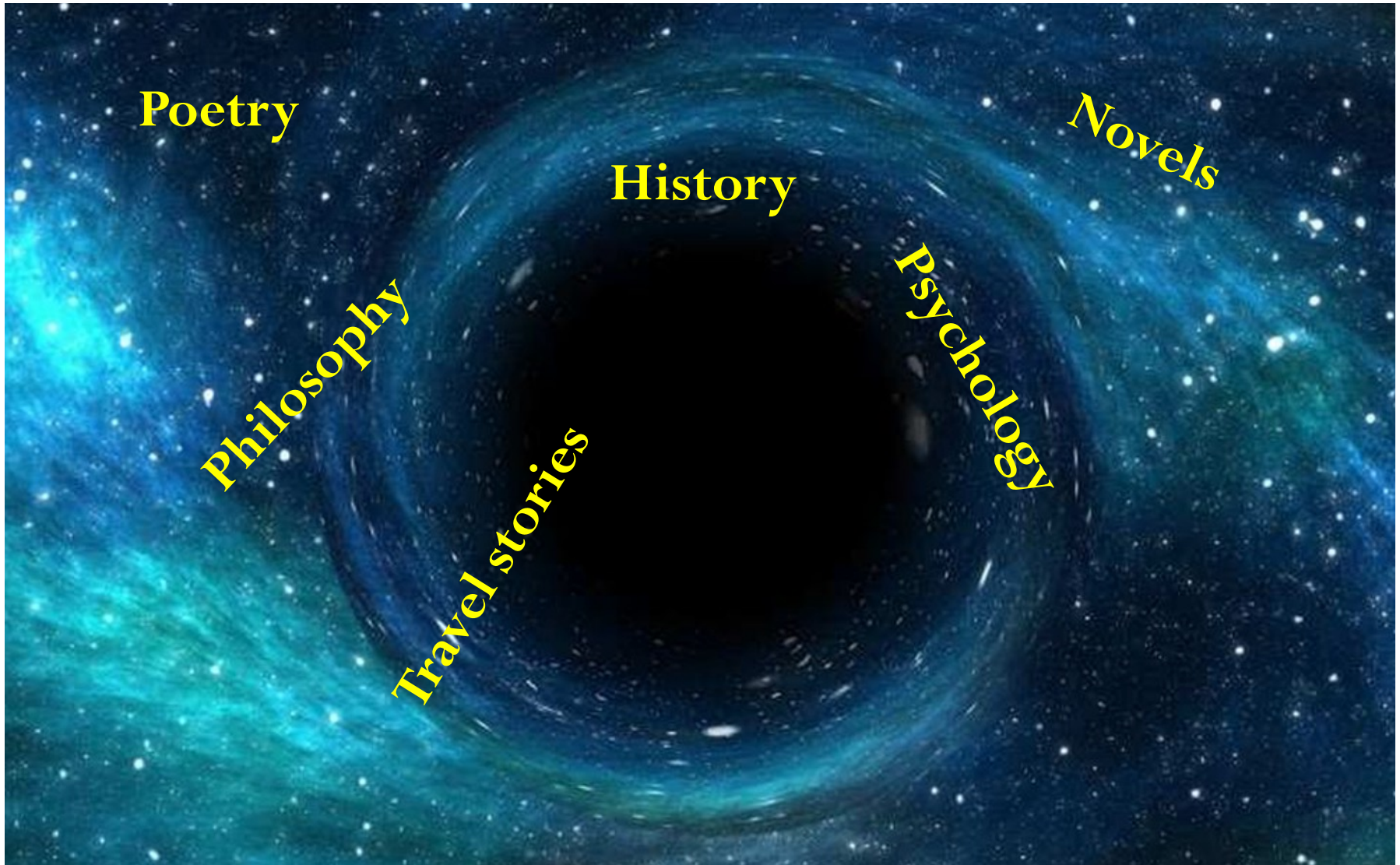

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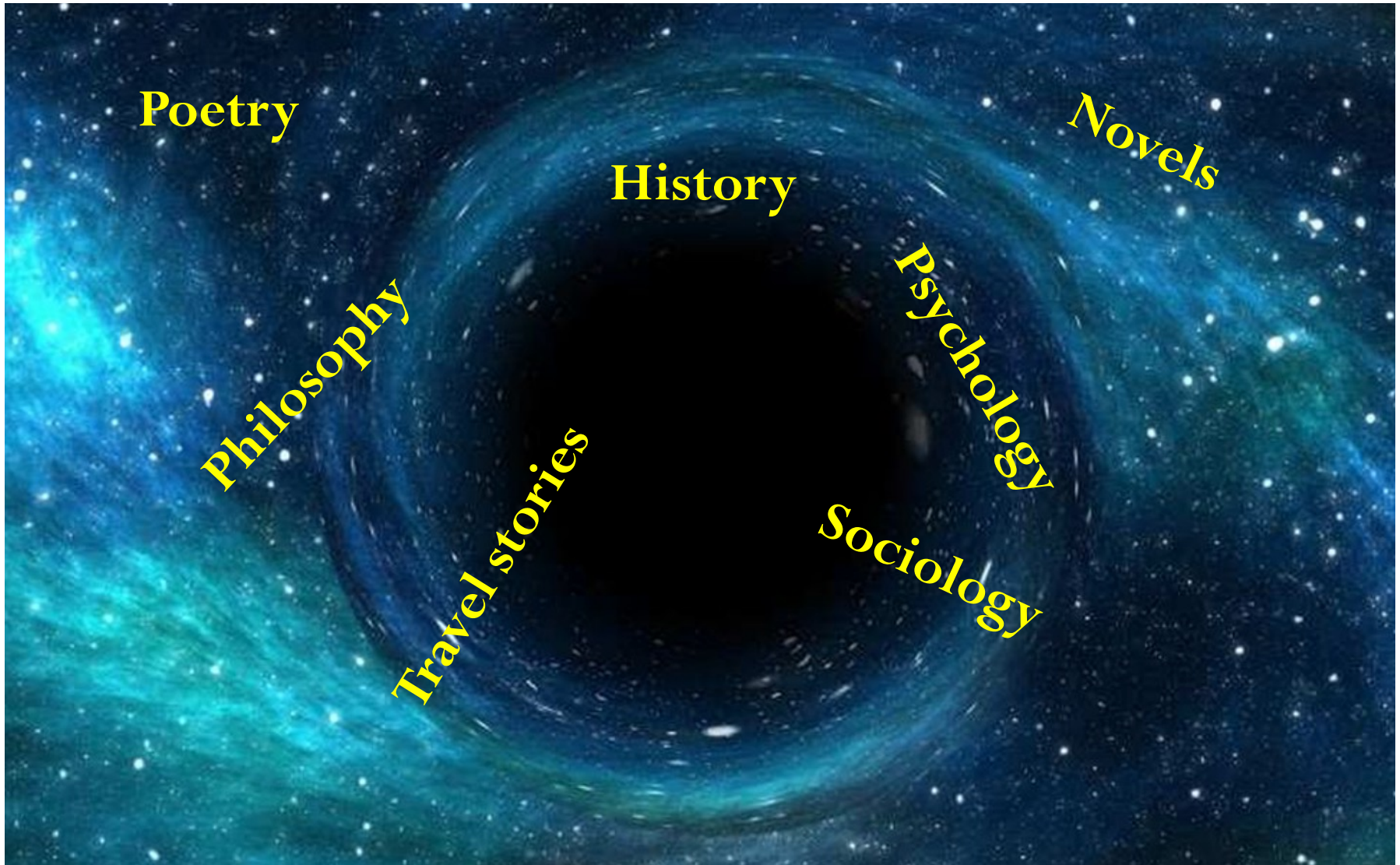

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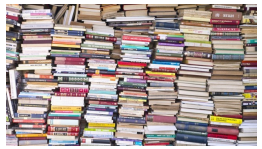

Poetry
Novels
Philosophy
Psychology
History
Travel stories
Sociology
Math!
Science in general
Etc, etc, etc…

France
Brazil
Japan
Scandinavian countries
Europe
America - South, Central, North
Africa
Asia
Oceania
Etc, etc, etc…

Black hole and books

Why?! Does it serve any purpose other than passing the time!?!?

Black hole and books

Why?! Does it serve any purpose other than passing the time!?!?

It actually helps to pass the time

But also

Already learn to better express one's thoughts and ideas

Then

Discover different, extremely varied universes and ways of living and of thinking

Appreciate that there are actually millions of ways to perceive and understand the world (and do science)

Gradually value all that comes with completely opening one's mind

Learn to "voler très haut, libre comme un poisson dans l'eau"

"fly very high, free like a fish in water"

↓

Je veux vivre

Arno, Belgian singer, 1949-2022

Adoption (by the young) et resurrection

And then the black hole disappears!

Start of the university studies, Univ. of São Paulo, Brazil, for 4 years until the Bachelor's degree in computation
Four years during which the slightly older person (32) is completely adopted by the young students of 17-18 years old (some a bit older)

And the person resurrects

“Abbey” (“Abbaye”) and biology

Then, departure to France, Paris, for a Master (DEA in fact) at…

L’ “Abbey”!?!?!?!

“Abbey” (“Abbaye”) and biology

Then, departure to France, Paris, for a Master (DEA in fact) at…

L’ “Abbey”!?!?!?!

No! ABI ! Atelier de BioInformatique,
a bunch of merry, slightly crazy fellows, scientists also, rather experts in biology (biophysics)

Master defence in 1993, just 30 years before you
And then…

Caminhando e cantando, e seguindo a canção

Walking and singing, and following the song

Not yet completely easy

- No thesis grant (age limit to have one at the time)
- Age limit also to apply for certain research positions in academia
- Considered a little too old even for those who did not have such a limit
- And then after a PhD not only in math, not completely in biology, what is your profile?!?!

Caminhando e cantando
E seguindo a canção
Somos todos iguais
…
(Geraldo Vandré)

Walking and singing
And following the song
We are all equal
…

We walk, with those who hold our hand and with the others also
One day, it will be important to do the same for others

Jobim (and the young)

After a first position at the Pasteur Institute, Junior Researcher, in 1998
Departure for a new position, Junior Researcher, at Inria, and in Lyon this time, in 2001

But before this departure, in 2000, Jobim!

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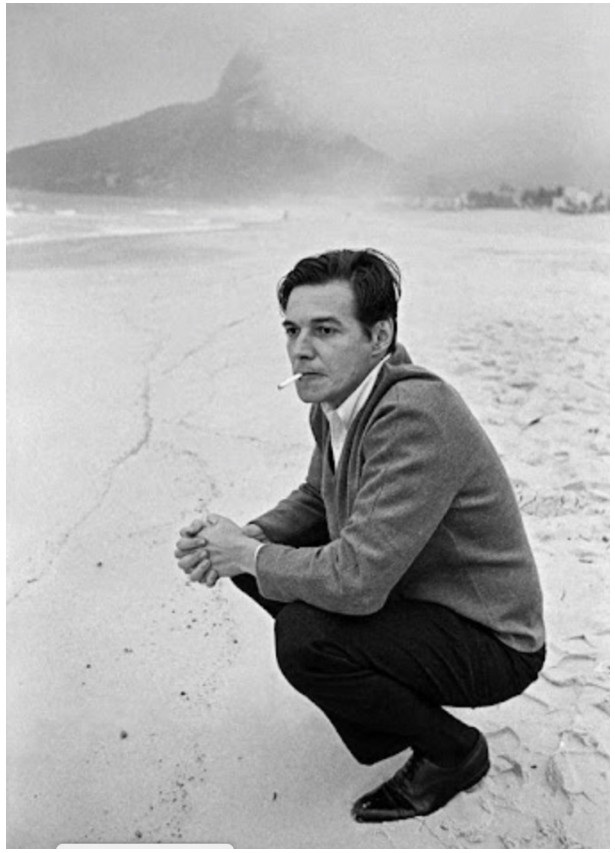

Uh, Jobim the composer, musician, singer
Author of Garota de Ipanema
And of Águas de Março
And of a thousand other wonderful songs!?!?!?!

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But before this departure, in 2000, Jobim!

No, Jobim = Journées Ouvertes en Biologie, Informatique et Mathématiques!!!!
First edition in Montpellier, May 3-5, 2000, where we expected a maximum of 100 participants and where there were about 330!

Jobim (and the young)

Jobim, which is then a conference, but which also represents an atmosphere…

Uh, of work

But not only!

First Jobim in 2000
Improvised concert of Djembe
Dominique Cellier with students from Rouen

And then we dance

even the old ones!

Jobim (and the young)

Above all, and wonderfully, Jobim, in which the young people not only participate very strongly
But also, which they very, very quickly take in hand, on the animation side but also on the science side!

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And then SFBI – Société Française de BioInformatique – an association under the 1901 law of guardianships and public institutes created in 2005 by a not (too) young person (Alain Guénoche) but which little by little the young (younger but also really young) also took in hand, as for Jobim

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Jobim and SFBI where, thanks to them, thanks to you, science reigns, but also cooperation and friendship

Besides, is it not true that
Science (non only) = Cooperation and friendship?

Which brings me to my final point of this presentation

To have in oneself the dreams of the world (F. Pessoa) – Other obsessions

Two stories (scientific! Yes, I come back, a little, to science) to fuel my speech here

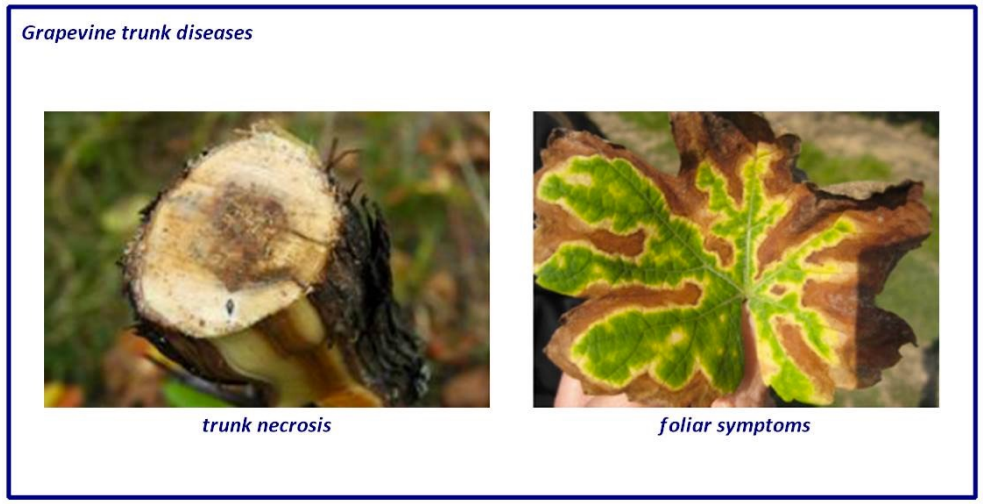
A first one related to a plant disease probably caused by fungi

This disease is the Esca one of the grapevine trunk
Little is known, apart from the fact that 3 fungi are possibly involved:

- ***Phaeomoniella chlamydospora***
- ***Phaeoacremonium aleophilum***
- ***Fomitiporia mediterranea***

Plus others (*Epicoccum*) that may act as antagonists!

Peaceful antagonists!

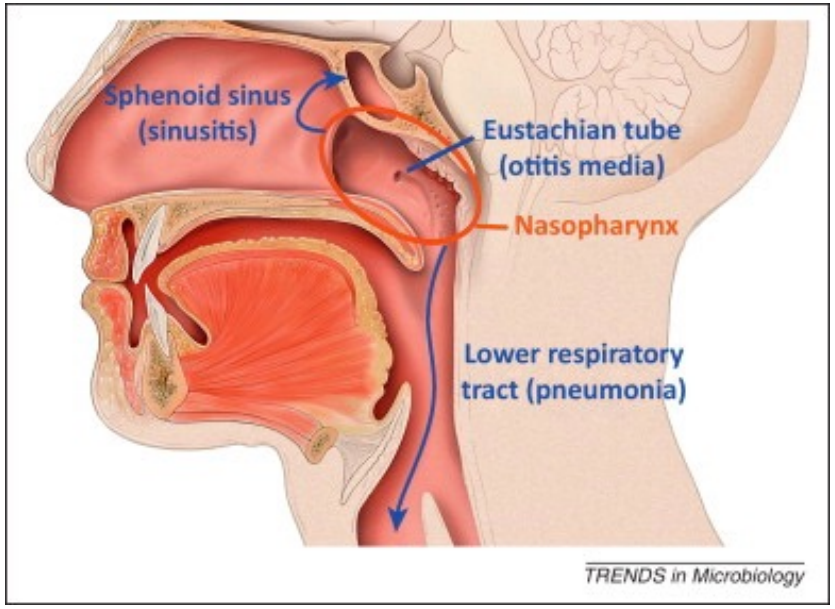


Ricardo Boavida Ferreira
Instituto Superior de Agronomia
Universidade de Lisboa, Portugal

To have in oneself the dreams of the world (F. Pessoa) – Other obsessions

A second story now, which was told to me by a scientist who at the time worked in Portugal and who has been in Denmark for some years now

A story that is this time related to *Streptococcus pneumoniae*, a bacterium that is commensal when it is in the nasopharynx but becomes pathogenic when it descends in the lungs (pneumonia), only when it is in the lungs



Ana Rute Neves

To have in oneself the dreams of the world (F. Pessoa) – Other obsessions

Usual treatment for plant diseases: Insecticides

Please note: earthworms threatened by the use of glyphosate

Usual treatment for pneumonia: Antibiotics

WHO

Antimicrobial resistance is not a new problem but one that is becoming more dangerous; urgent and consolidated efforts are needed to avoid regressing to the pre-antibiotic era.

For World Health Day 2011, WHO introduced a six-point policy package to combat the spread of antimicrobial resistance.

To have in oneself the dreams of the world (F. Pessoa) – Other obsessions

Obsession
Instead of looking for interventions that "eliminate" some of the partners (insecticides, antibiotics, etc.), should we not instead be looking for interventions that are non-aggressive, involving antagonists as (possibly) in the case of *Epicoccum*, or a change in the environment as (possibly) in the case of *Streptococcus pneumoniae*?

This is the idea, very general and, I admit, very vague, which has obsessed me since many years, and which had also been fueled by a certain number of the innumerable readings that I did during my long period in the black hole

Is this crazy?

Perhaps, most probably, no doubt

Certainly there is still a lot to be done to show

- **Whether this is possible even at a very small scale – for instance, Esca disease**
- **And if it is possible, how far / fast can we then extend this type of approach?**

Certainly, in order to do this, three things are crucial

- **Not look at only one aspect of biology – Tango of different areas within a discipline**
- **Not look only at biology but also, *e.g.*, ecology – Tango of different disciplines within life sciences**
- **And then also Tango with other disciplines outside the life sciences**

Which brings me back to Jobim (and SFBI) – and to the young

- **Science (not only) = Cooperation and friendship**

And brings me back also to my readings

- **Importance of opening one's mind completely**

To all

From Lyon

From Paris

From Brazil

From many other places also

Deep thank you

Thanks to you and to persons like you,
I have been able to live, and to dream
Despite the minhocas na cabeça…