CoVIDA: Reposicionamiento de medicamentos para el tratamiento de COVID-19 mediante Inteligencia Artificial

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Avances del Proyecto
(parte 2)

Enfoque 1
Pharmacologia de Sistemas

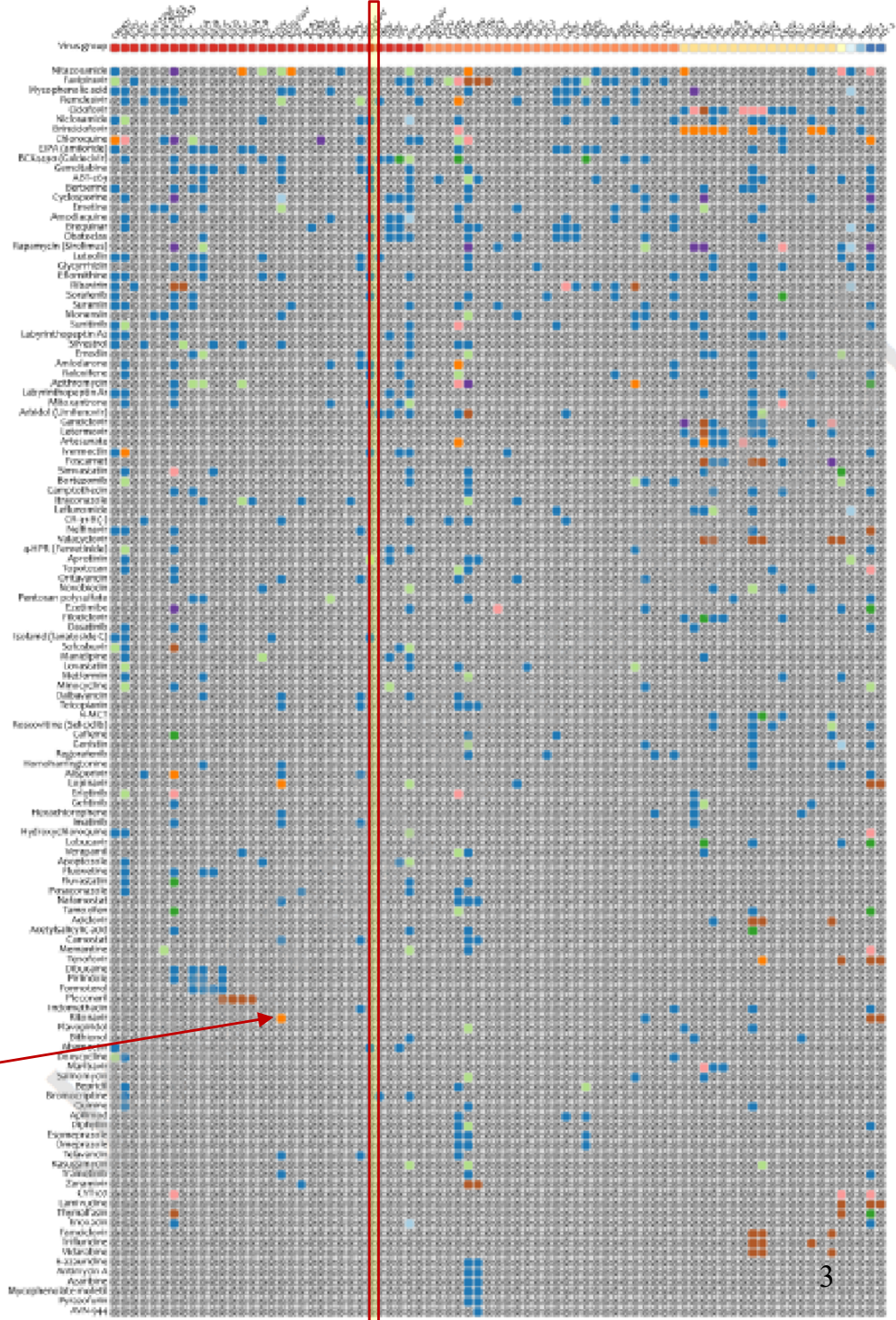# Datos de actividad antiviral

https://drugvirus.info/

Drug development

- cell culture
- organoids
- animal model
- Phase I
- Phase II
- Phase III
- Launched

80 viruses

126 Broad Spectrum Antivirals

Ritonavir
Phase III for MERS-CoV

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Que tenemos para SARS-CoV-2?

Drug	Primary indication	Evidence for SARS-CoV-2
Arbidol (Umifenovir)	Approved antiviral	Cell culture, Phase III
Cepharanthine	Approved anti-inflammatory and cancer (Japan)	Cell culture
Chloroquine	Approved antimalarial	Cell culture
Homoharringtonine	Approved anticancer	Cell culture
Hydroxychloroquine	Approved antimalarial	Cell culture, Phase III
Ivermectin	Approved antiprotozoal	Cell culture
Lopinavir	Approved antiviral	Cell culture
Mefloquine	Approved antimalarial	Cell culture
Remdesivir	Investigational antiviral	Cell culture
Ribavirin	Approved antiviral	Cell culture

Will any of these prove to be effective for COVID-19?

Will any of the other drugs prove to be effective for COVID-19?

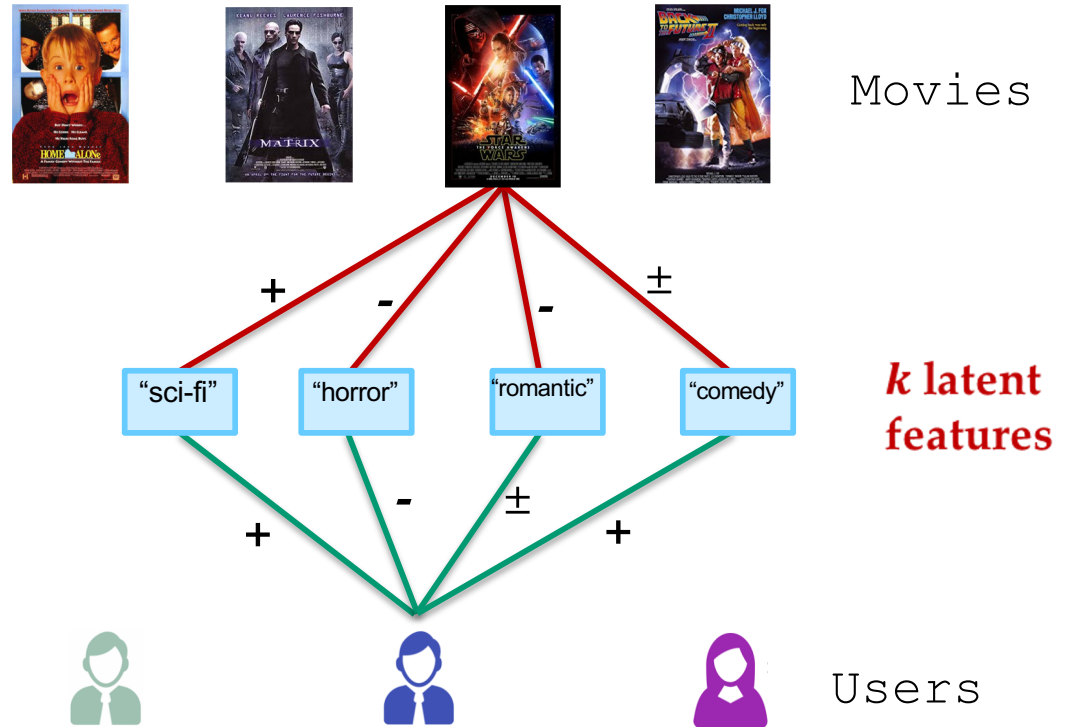*Which drug should we <u>recommend</u> for further experimentation?*

4

Como Netflix recomienda peliculas?

Movies (q)

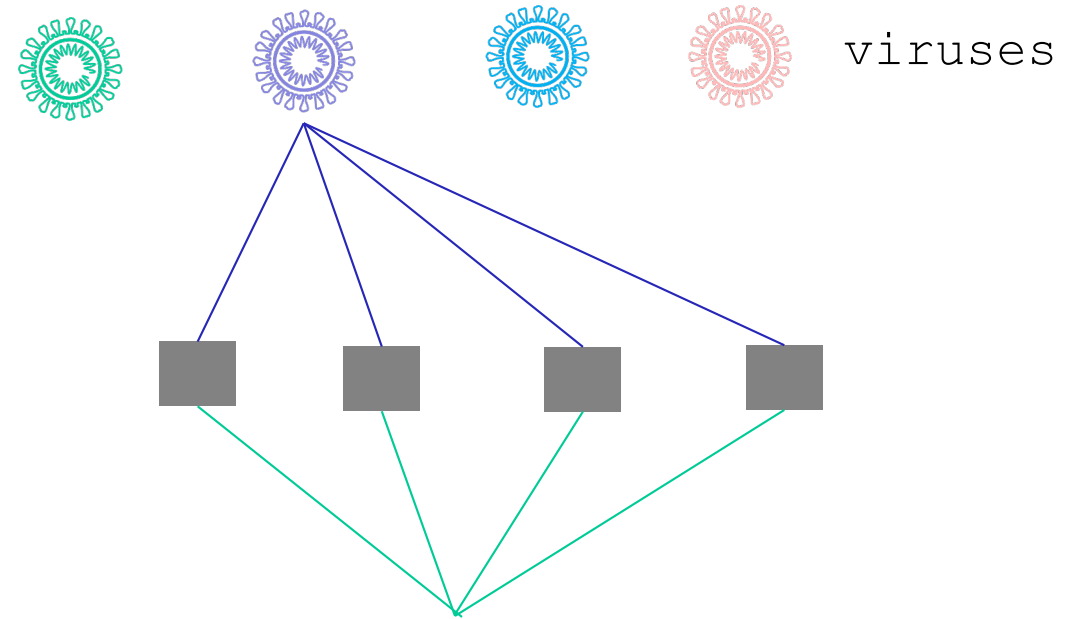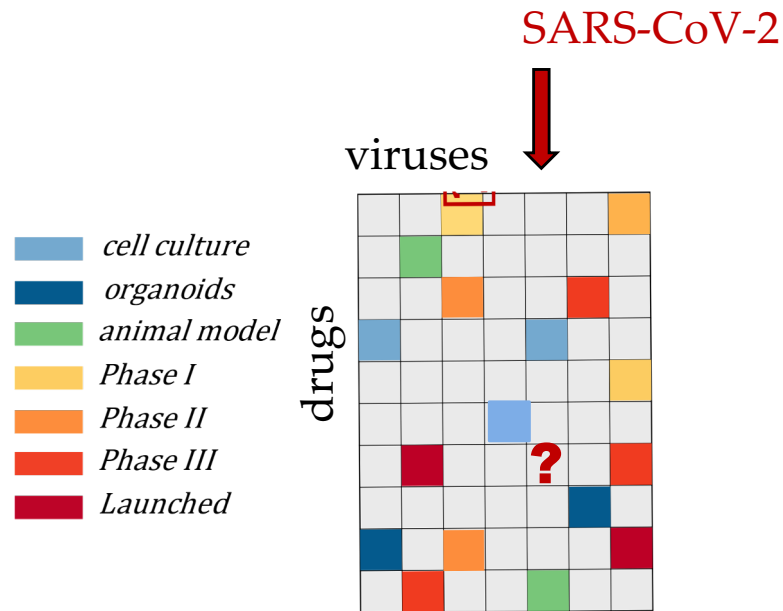|									
1	0	0	0	2	0	3	0	4	0
4	0	0	3	0	4	0	0	0	1
0	0	4	0	0	0	1	0	3	0
5	0	0	0	0	5	0	1	0	0
0	0	4	0	3	0	2	0	0	0

Users (p)

Y

Hemos utilizados estas ideas para predecir efectos secundarios de farmacos
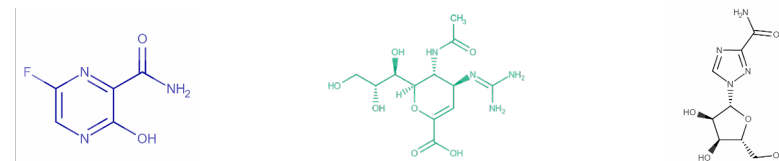
[Galeano, Paccanaro *Nature Communications*, 2020]

Movies

+   -   -   ±

"sci-fi"   "horror"   "romantic"   "comedy"

k latent features

+   -   ±   +

Users

Nuestra idea

SARS-CoV-2

viruses

cell culture
organoids
animal model
Phase I
Phase II
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Launched

drugs

?

viruses

Drugs

$$Y_{i,j} \approx \boldsymbol{p}_i^T \cdot \boldsymbol{q}_j$$

$$Y_{n \times m} \approx P_{n \times k} \cdot Q_{k \times m}$$
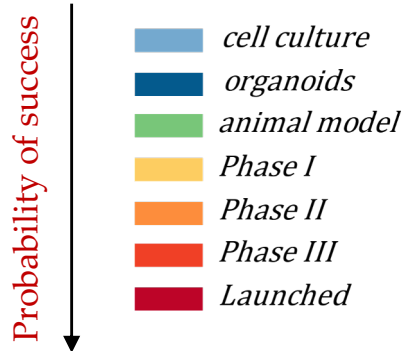
$$\min_{P,Q} Q(P,Q) = \| Y - PQ \|_F^2 + \zeta(P,Q)$$

Sistemas de Recomendacion convencionales no funcionan

Modelando probabilidades de exito

Experimental stages

Probability of success

- cell culture
- organoids
- animal model
- Phase I
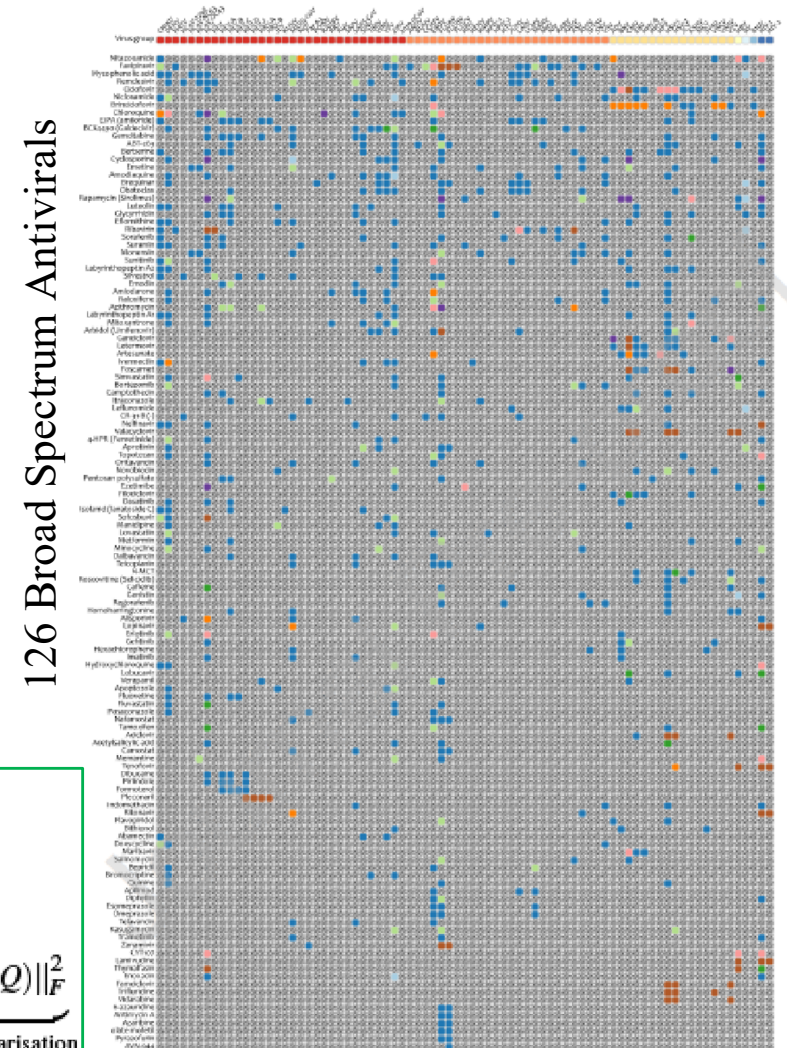- Phase II
- Phase III
- Launched

- Queremos predecir si el farmaco sera aprobado para una enfermedad viral

- Tenemos que relacionar el estado R&D con la probabilidad de exito

confidence Non-negative Matrix Factorization (cNMF)

$$\min_{P,Q\geq 0} \mathscr{L}(P,Q) = \underbrace{\frac{1}{2}\left\|M^A \circ (Y - PQ)\right\|_F^2}_{\text{approved, phase IV}} + \underbrace{\frac{1}{2}\sum_{s\in\{B,C,D,E\}}\alpha_s\left\|M^s \circ (Y - PQ)\right\|_F^2}_{\text{In-vitro, animal model, clinical trials}} + \underbrace{\frac{\alpha_z}{2}\left\|M^z \circ (PQ)\right\|_F^2}_{\text{zero-driven regularisation}}$$

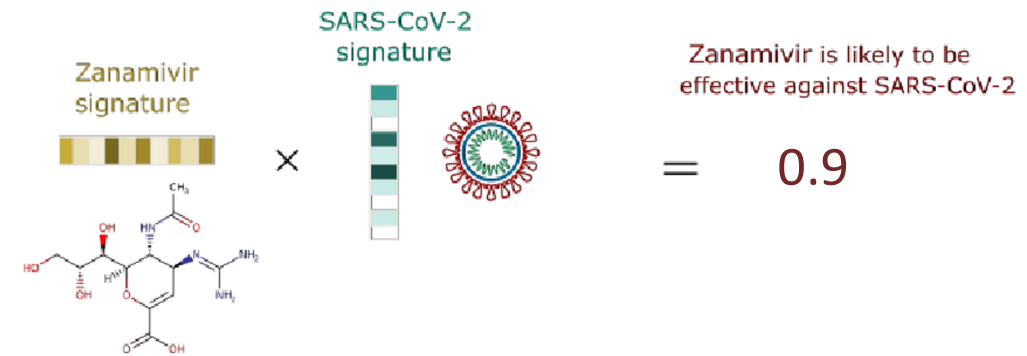subject to non-negative constraints $P, Q \geq 0$

80 viruses

126 Broad Spectrum Antivirals

Dataset: https://drugvirus.info/ 8

Enfoque 1

Developmental status
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- organoids
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$Y \approx P \times Q = \hat{Y}$

Zanamivir signature $\times$ SARS-CoV-2 signature $=$ 0.9

Zanamivir is likely to be effective against SARS-CoV-2

Resultados del enfoque 1