

# Power of the players and rules of the games played by cancer

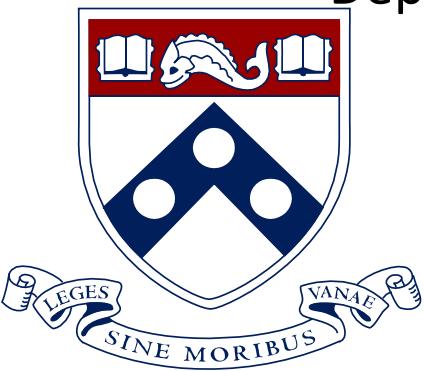
Artem Kaznatcheev

@kaznatcheev

Department of Biology, University of Pennsylvania

Department of Computer Science, University of Oxford

Hi,



JAMES S. McDONNELL FOUNDATION



# Tumour vs Doctor

# Tumour vs Doctor

- (1) the relative power of the two players and
- (2) the rules of the game that they are playing.

# Population-environment game

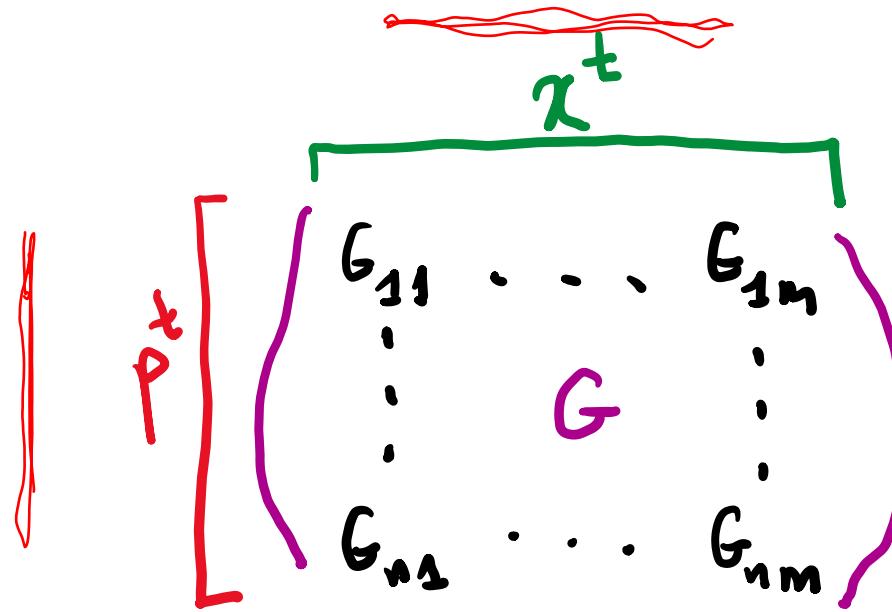


**Ryan Seamus McGee**  
[@RS\\_McGee](https://twitter.com/RS_McGee)  
University of Washington



# Population-environment game

$\rho^t G \chi^t$



Ryan Seamus McGee

@RS\_McGee

University of Washington

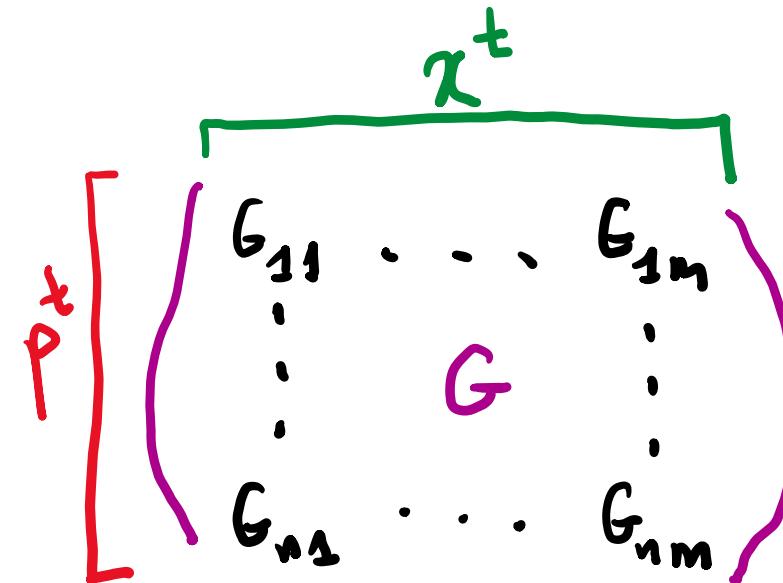


# Population-environment game

$p^t \in \chi^t$



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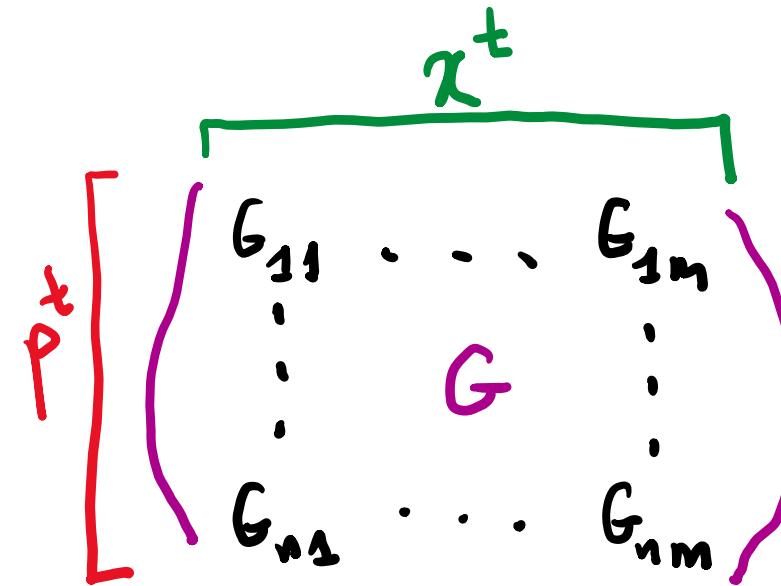
$$\left[ \chi^t := \chi^{t-1} \right] \rightarrow \text{Static fitness landscape}$$



# Population-environment game $\rho^t \mathcal{G} x^t$



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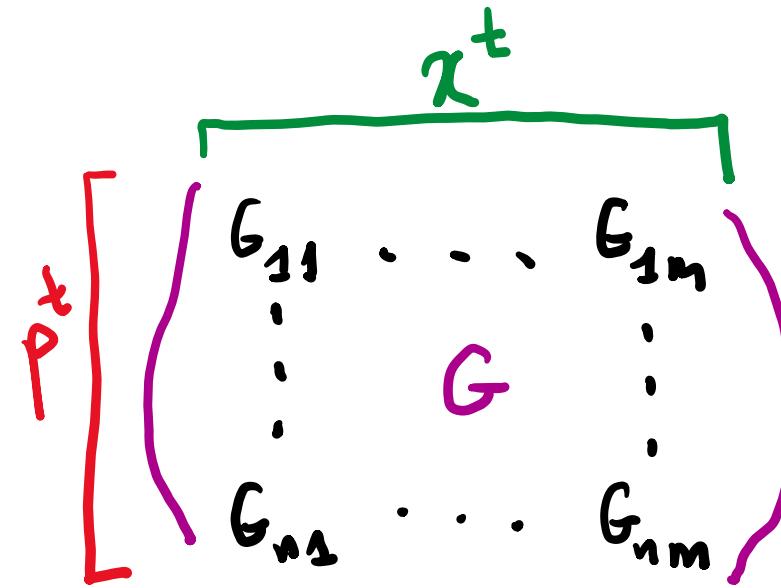


- $\left[ x^t := x^{t-1} \right] \rightarrow$  Static fitness landscape
- $\left[ x^t := \rho^t \right] \rightarrow$  Effective evolutionary game

# Population-environment game $\rho^t \mathcal{G} x^t$



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- $x^t := x^{t-1}$  → Static fitness landscape
- $x^t := \rho^t$  → Effective evolutionary game
- $x^t := \text{arbitrary}$  → Tumour-doctor game

# Responding to tumour's optimal play



(1) the relative power of the two players

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# Responding to tumour's optimal play



(1) the relative power of the two players

1. Make new drugs to change  $G$  so that any strategy is bad for the tumour

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# Responding to tumour's optimal play



## (1) the relative power of the two players

1. Make new drugs to change  $G$  so that any strategy is bad for the tumour
2. Improve how we pick  $x$  in hopes that by improving our strategy we can force a setting where the best tumour strategy is bad for the tumour

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# Responding to tumour's optimal play



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## (1) the relative power of the two players

1. Make new drugs to change  $G$  so that any strategy is bad for the tumour
2. Improve how we pick  $x$  in hopes that by improving our strategy we can force a setting where the best tumour strategy is bad for the tumour
3. Change our goal in the game: focus not on minimizing or controlling the tumour size but on minimizing or controlling the negative effect of the tumour on health.



# From modelling to measuring



Tool migration and adjusting narrative and method in response to the field's pressures:

**Chia-Hua Lin**

[@chiahua\\_lin\\_phd](https://twitter.com/chiahua_lin_phd)

University of Virginia



# From modelling to measuring



Tool migration and adjusting narrative and method in response to the field's pressures:

Oncology tends to demand more biological accuracy and precision at the potential expense of generality

**Chia-Hua Lin**

[@chiahua\\_lin\\_phd](https://twitter.com/chiahua_lin_phd)

University of Virginia



# From modelling to measuring



**Chia-Hua Lin**  
[@chiahua\\_lin\\_phd](https://twitter.com/chiahua_lin_phd)  
University of Virginia



“Modeling ... is the indirect theoretical investigation of a real-world phenomenon using a model. This happens in three stages:

In the first stage, a theorist constructs a model.

In the second, she analyzes, refines, and further articulates the properties and dynamics of the model.

Finally, in the third stage, she assesses the relationship between the model and the world if such an assessment is appropriate.

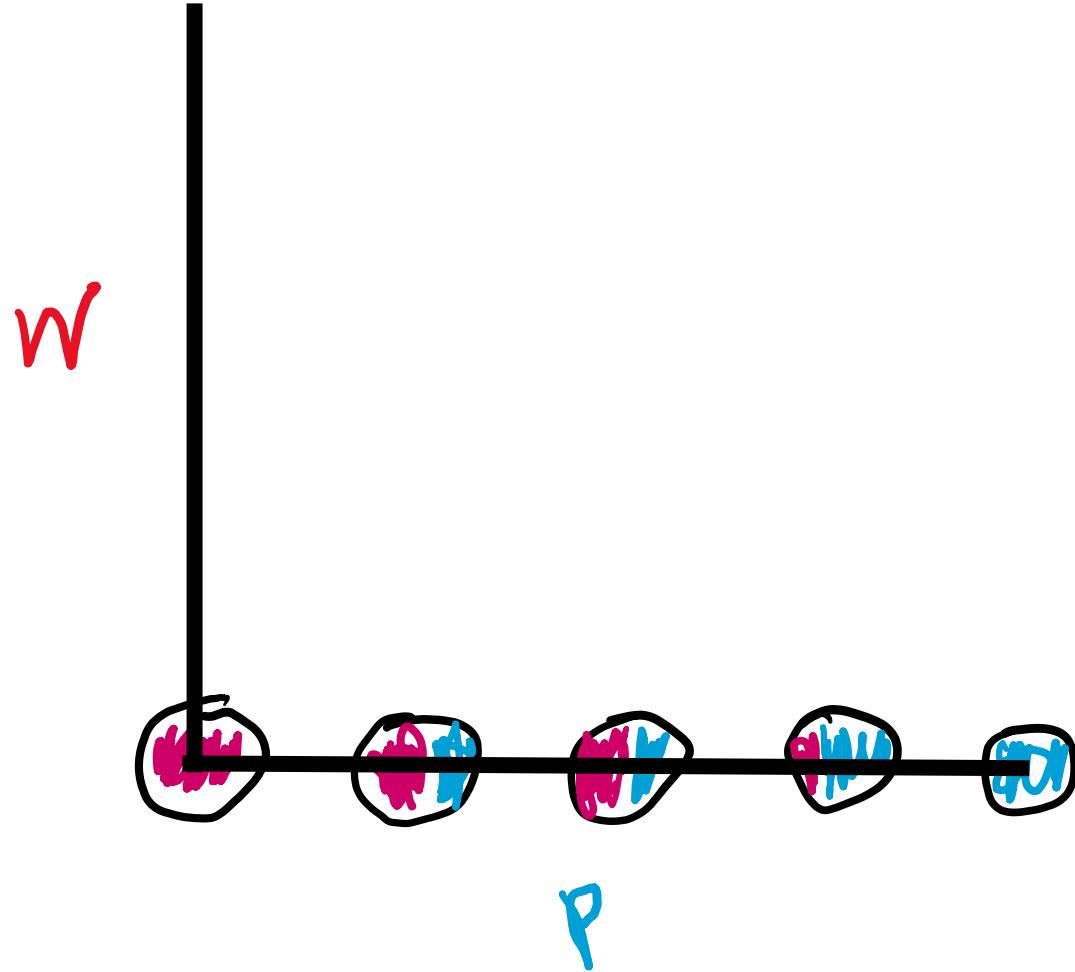
If the model is sufficiently similar to the world, then the analysis of the model is also, indirectly, an analysis of the properties of the real-world phenomenon. Hence modeling involves indirect representation and analysis of real-world phenomena via the mediation of models.”

- Weisberg, M. (2007). *Who is a Modeler?*

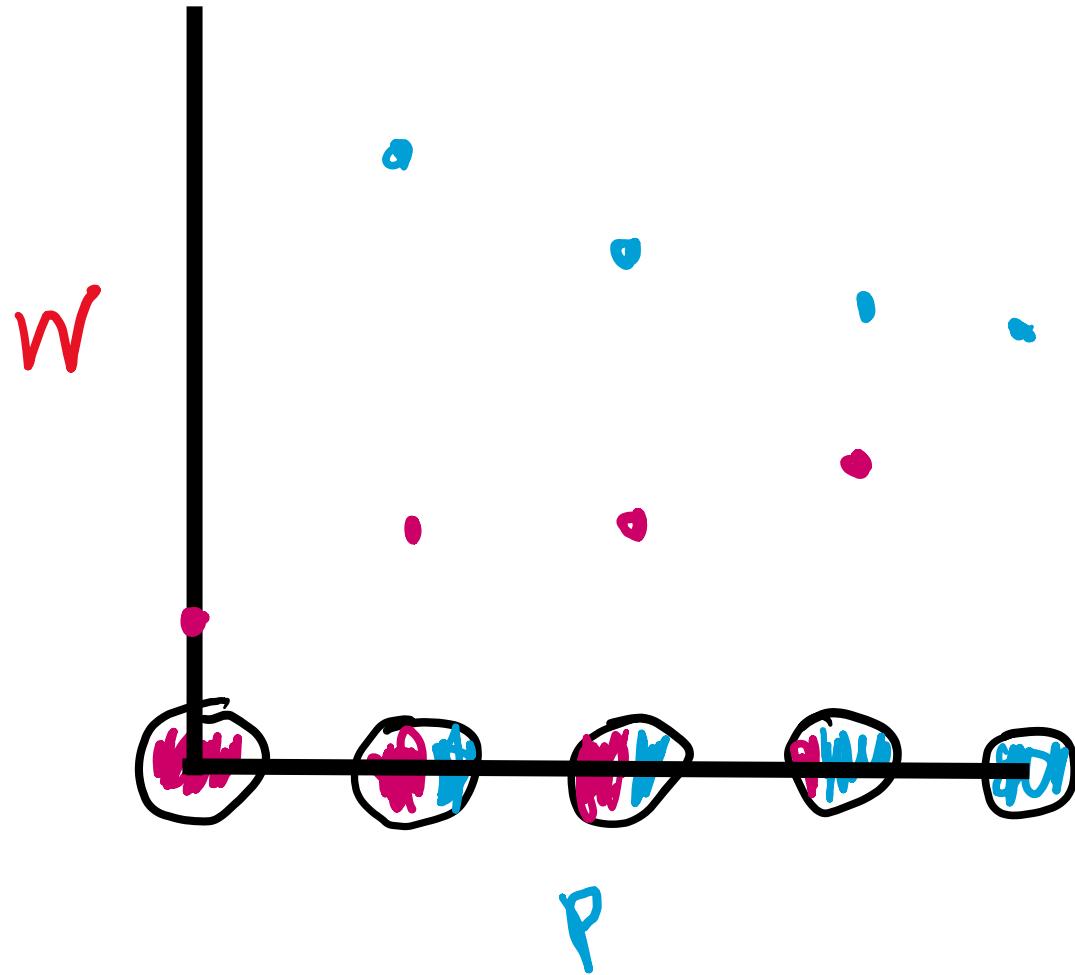
# Direct measurement with game assay



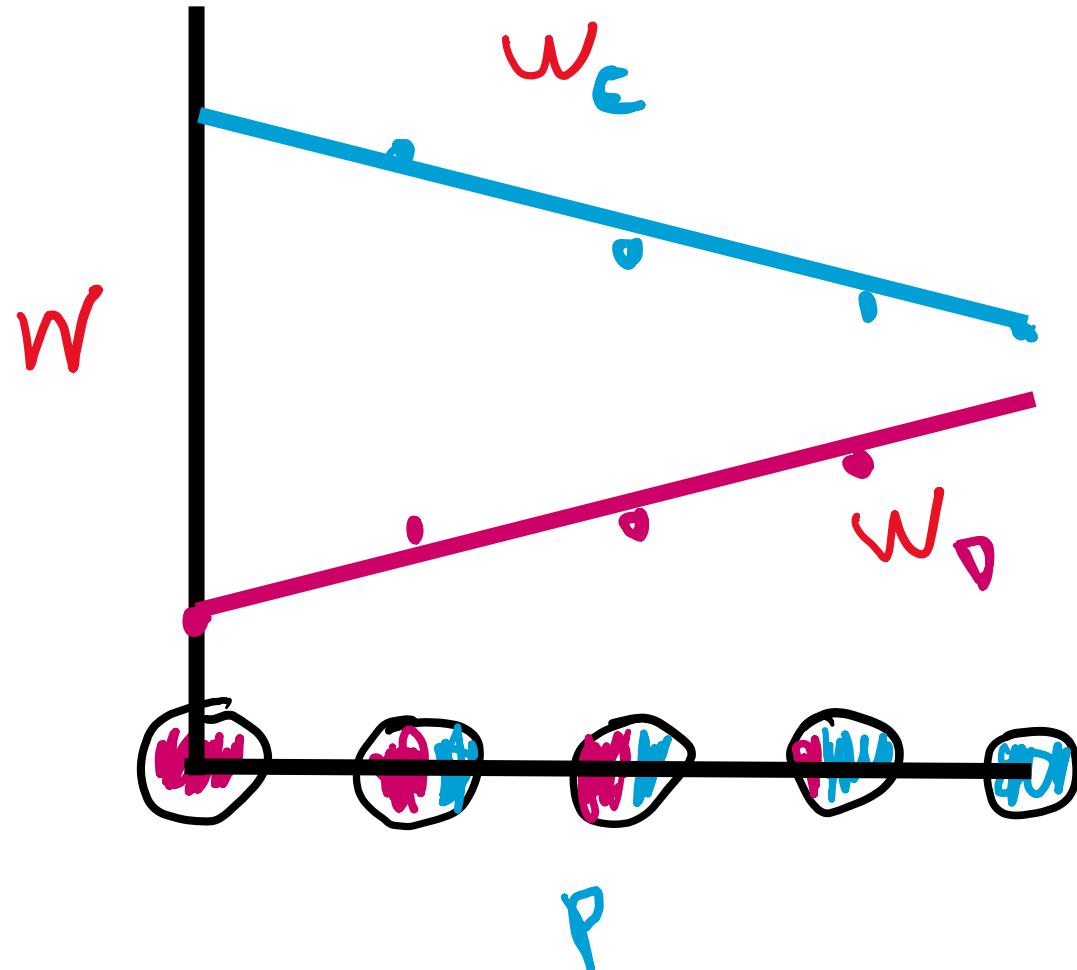
# Direct measurement with game assay



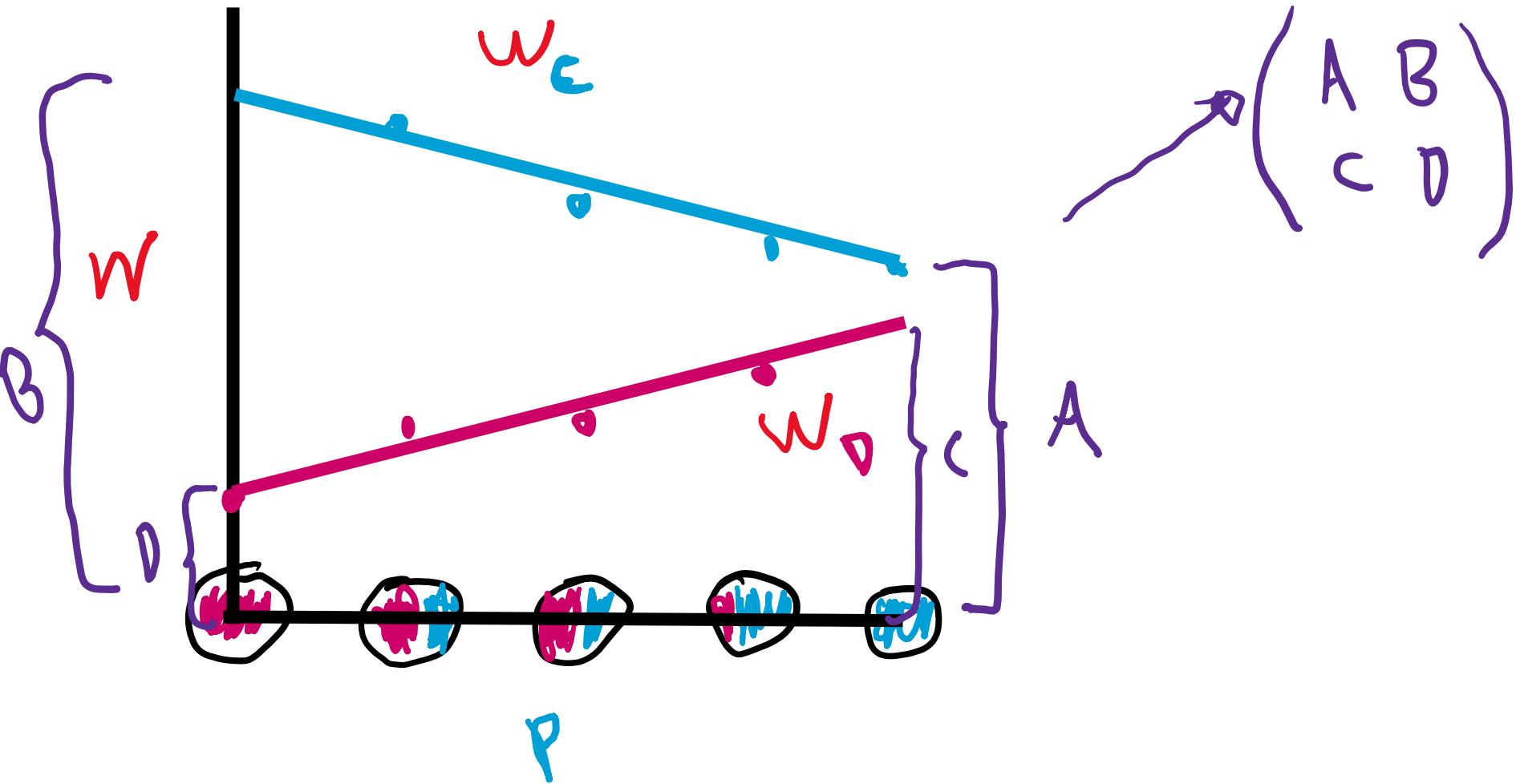
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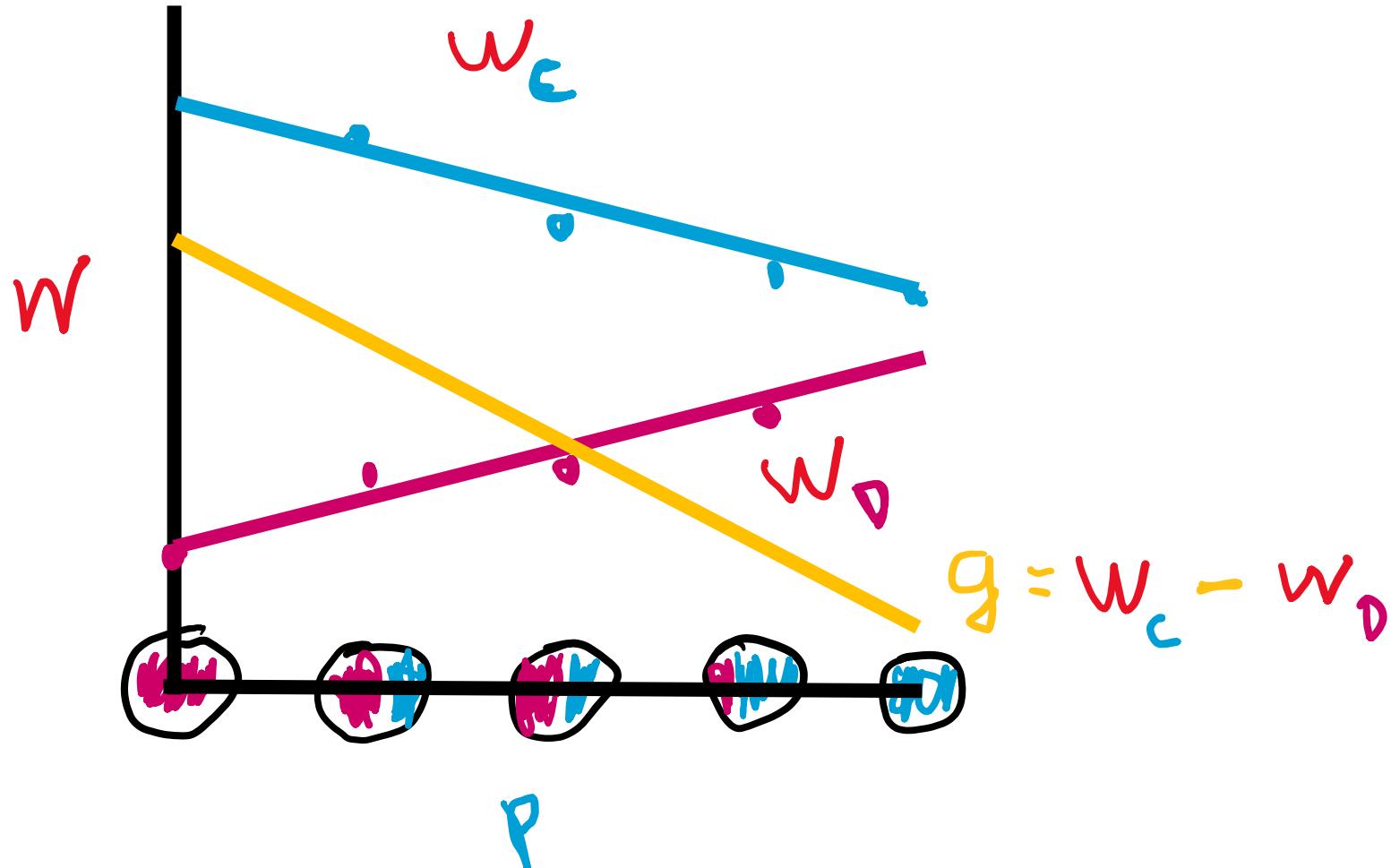
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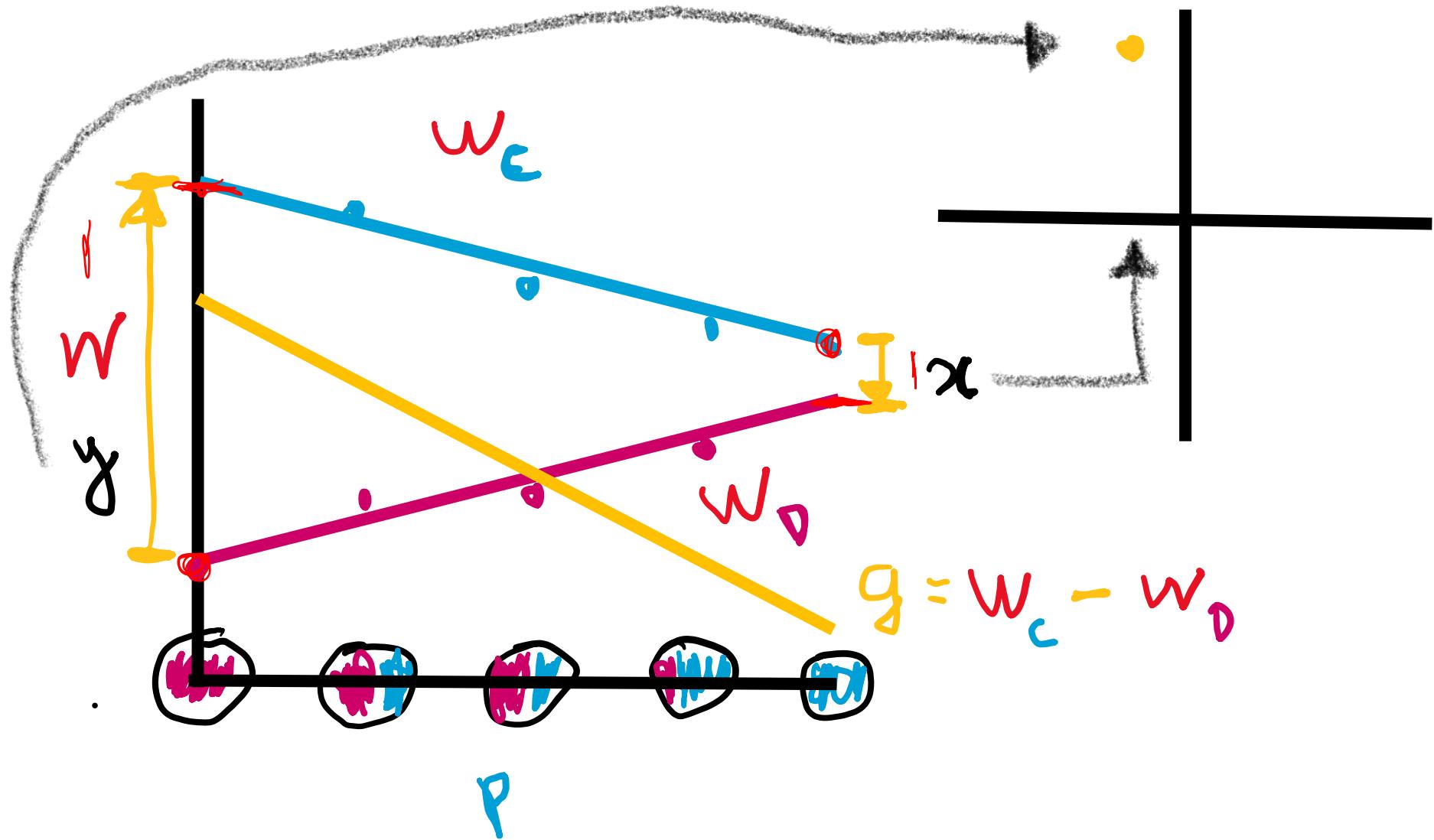
# Direct measurement with game assay



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# Direct measurement with game assay



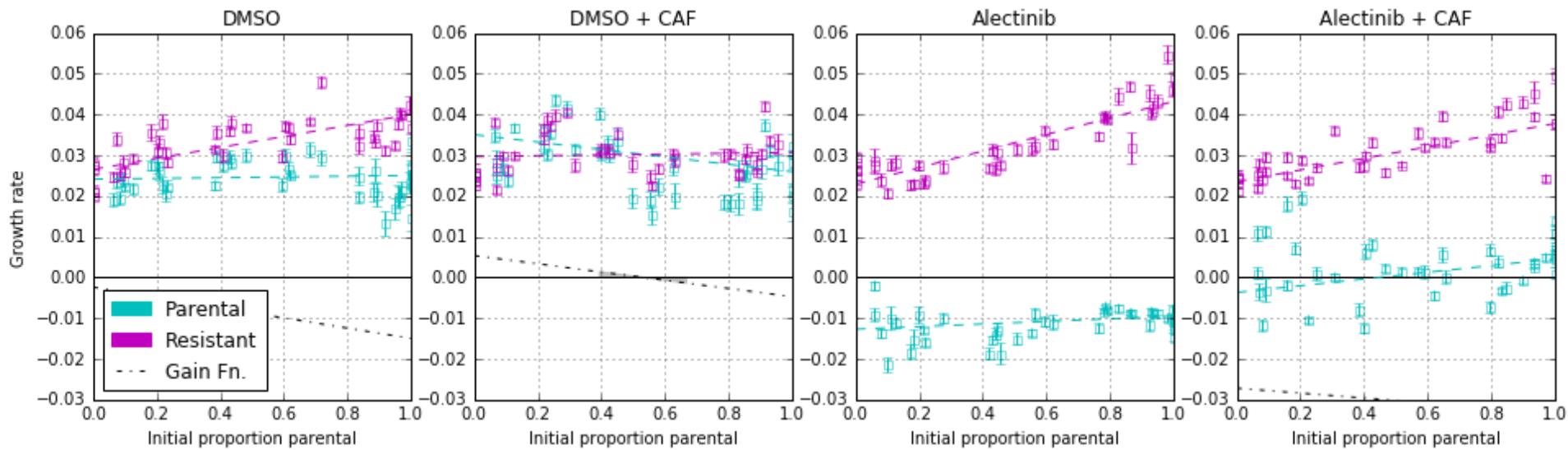
# Evolutionary games by NSCLC

A

B

C

D

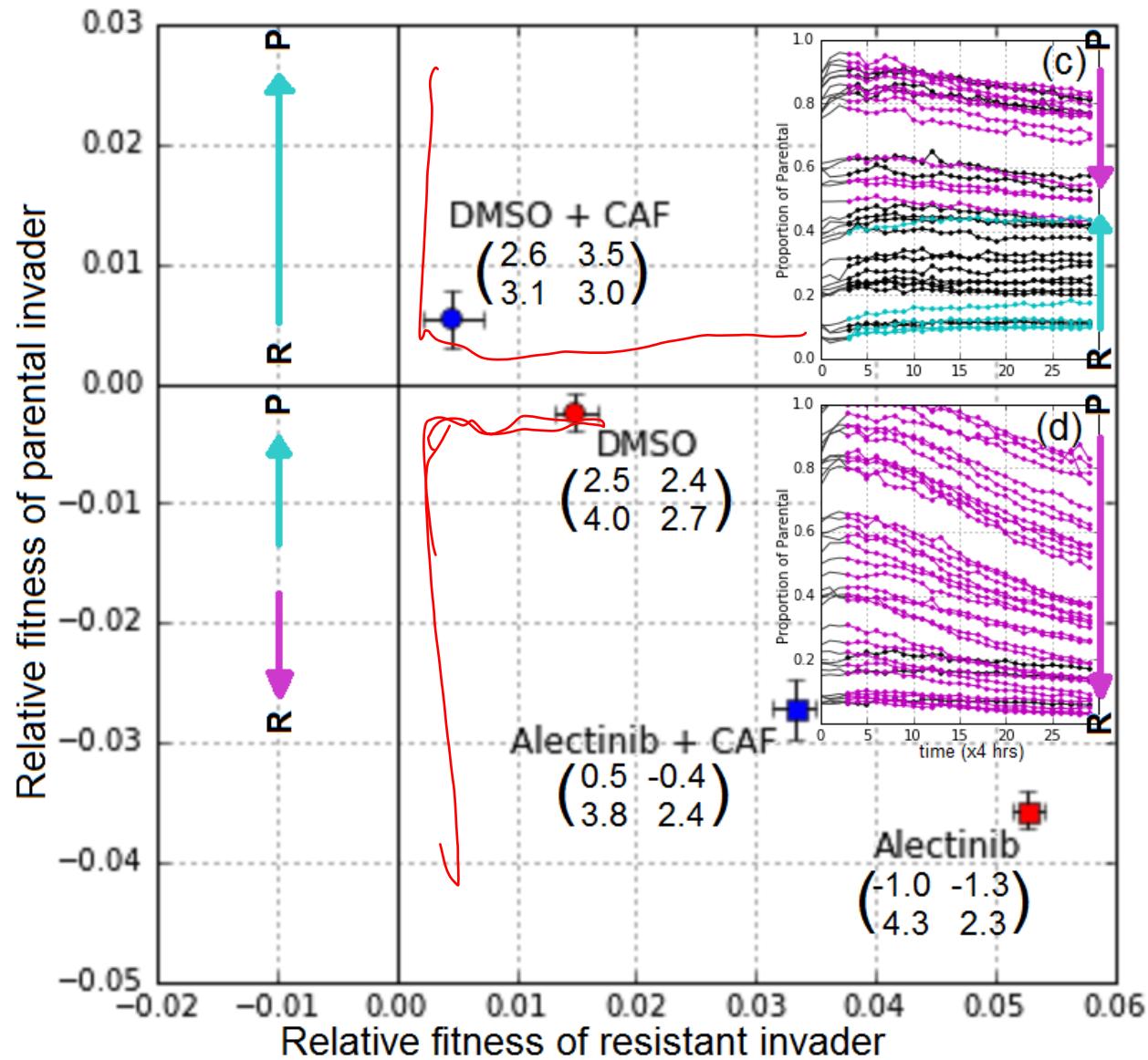


Kaznatcheev, A., Peacock, J., Basanta, D., Marusyk, A., & Scott, J. G. (2019).

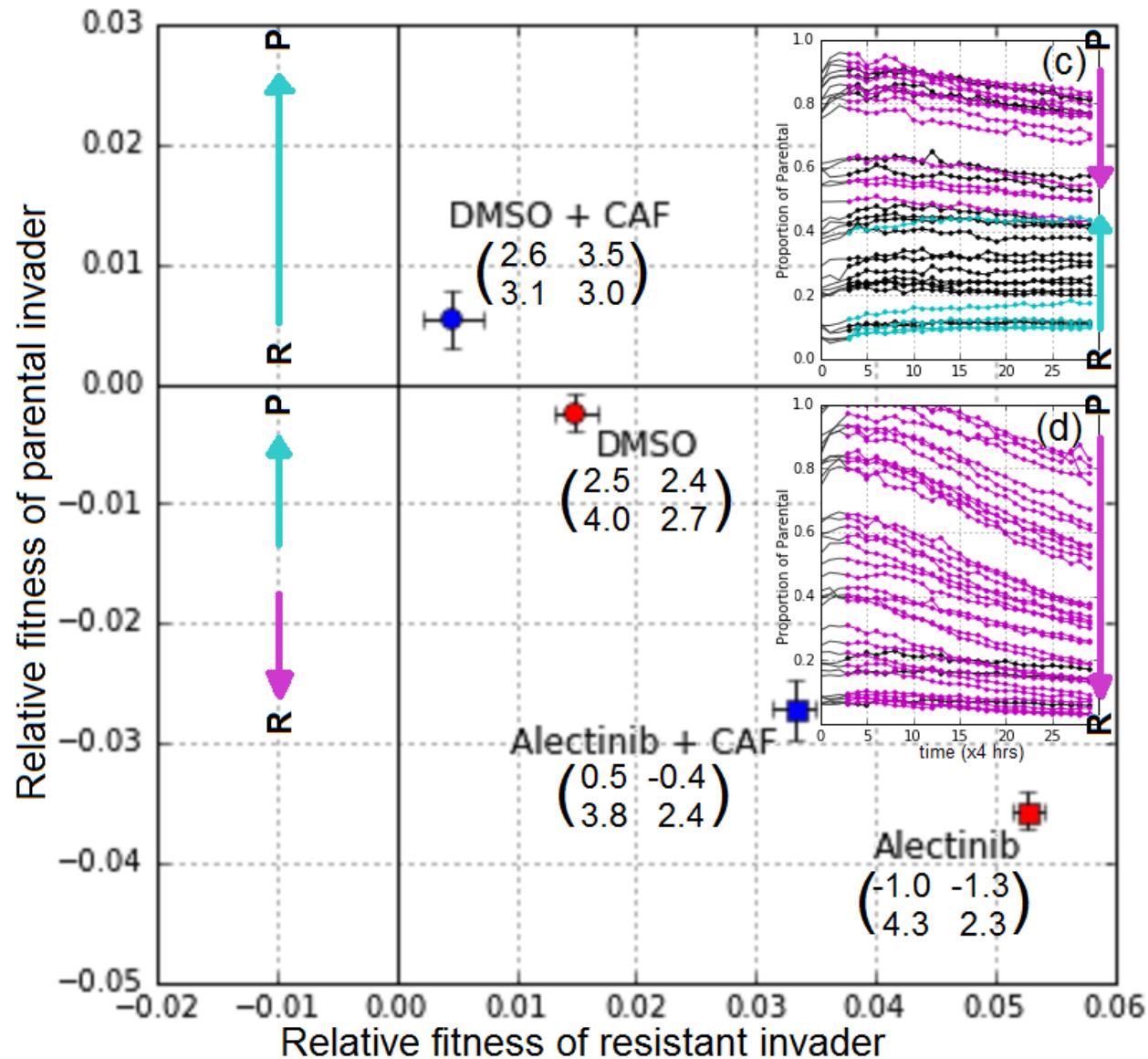
Fibroblasts and alectinib switch the evolutionary games played by non-small cell lung cancer.

*Nature Ecology & Evolution*, 3(3), 450-456.

# Evolutionary games by NSCLC

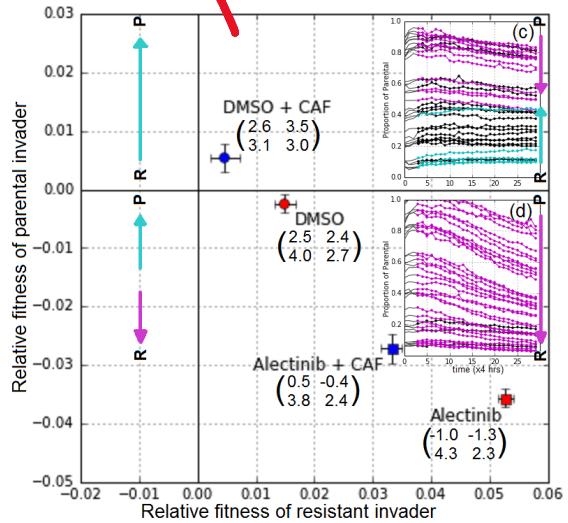


# Evolutionary games by NSCLC



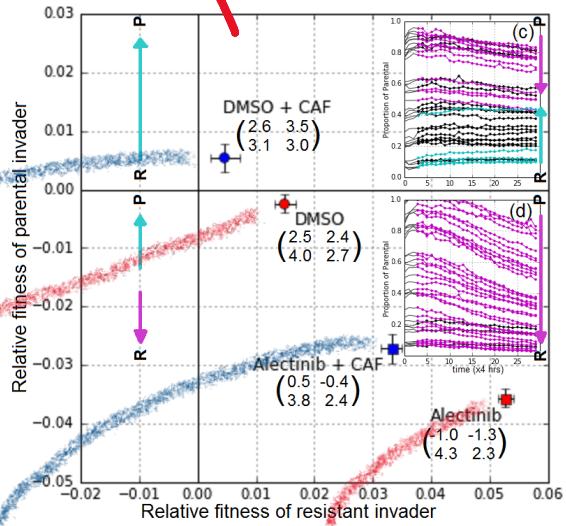
# Evolutionary games by NSCLC

$\rho^k$   $G$   $\chi^k$



# Evolutionary games by NSCLC

$P^k \subset G \chi^k$



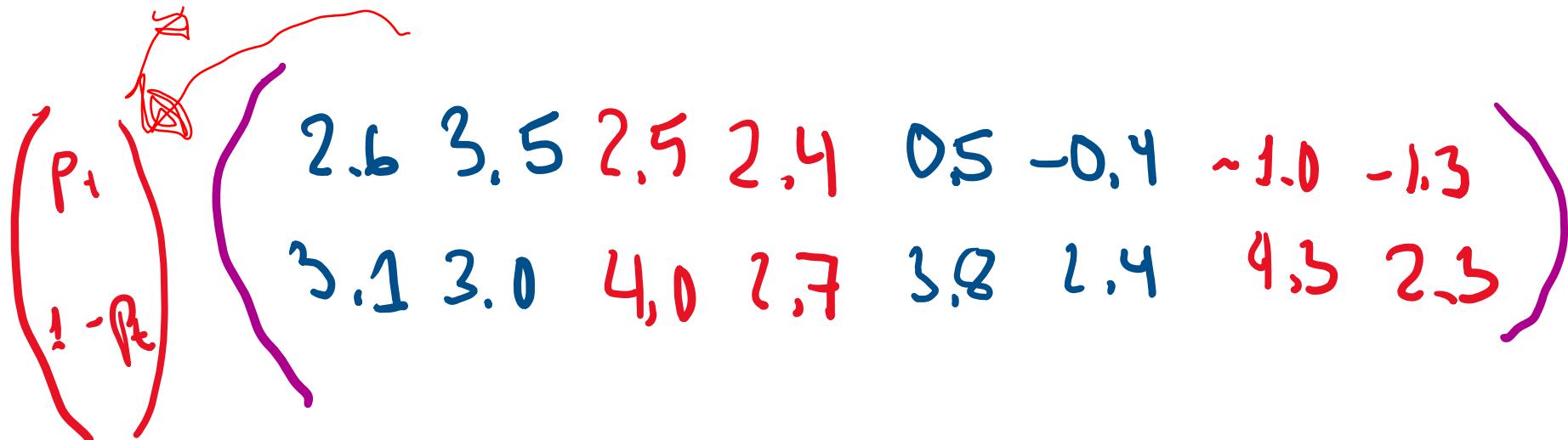
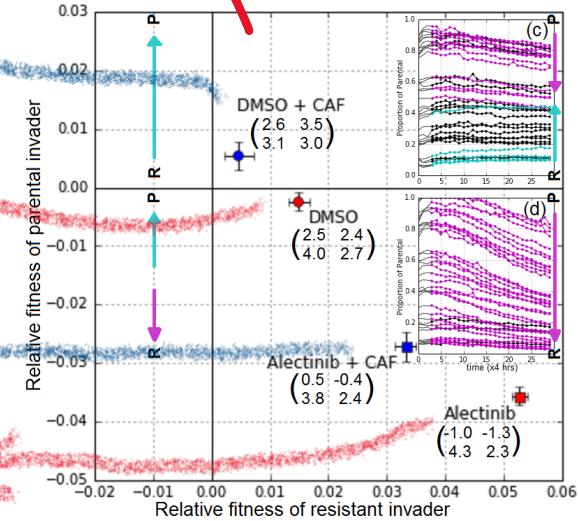
$$P^k = P_1 (1 - P_k)$$

$$\begin{matrix} 2.6 & 3.5 & 2.5 & 2.4 & 0.5 & -0.4 & \sim 1.0 & -1.3 \\ 3.1 & 3.0 & 4.0 & 2.7 & 3.8 & 2.4 & 4.3 & 2.5 \end{matrix}$$

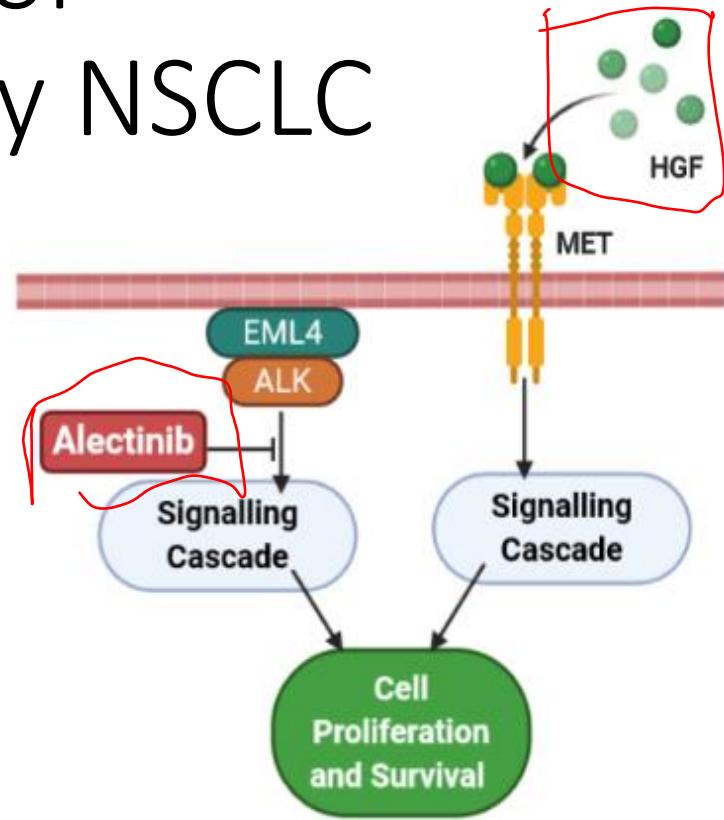
# Evolutionary games by NSCLC

$\rho^t \in \chi^t$

$$\begin{aligned} \rho^t_{D+C} &= (P_t \ 1-P_t \ 00 \ 00 \ 00) \\ \rho^t_D &= (0 \ 0 \ P_t \ 1-P_t \ 00 \ 00) \\ \rho^t_{A+C} &= (0 \ 0 \ 00 \ P_t \ 1-P_t \ 00) \\ \rho^t_A &= (0 \ 0 \ 00 \ 00 \ 00 \ P_t \ 1-P_t) \end{aligned}$$



# Hepatocyte growth factor and the games played by NSCLC



Ranjini Bhattacharya

Shiv Nadar University

# Hepatocyte growth factor and the games played by NSCLC

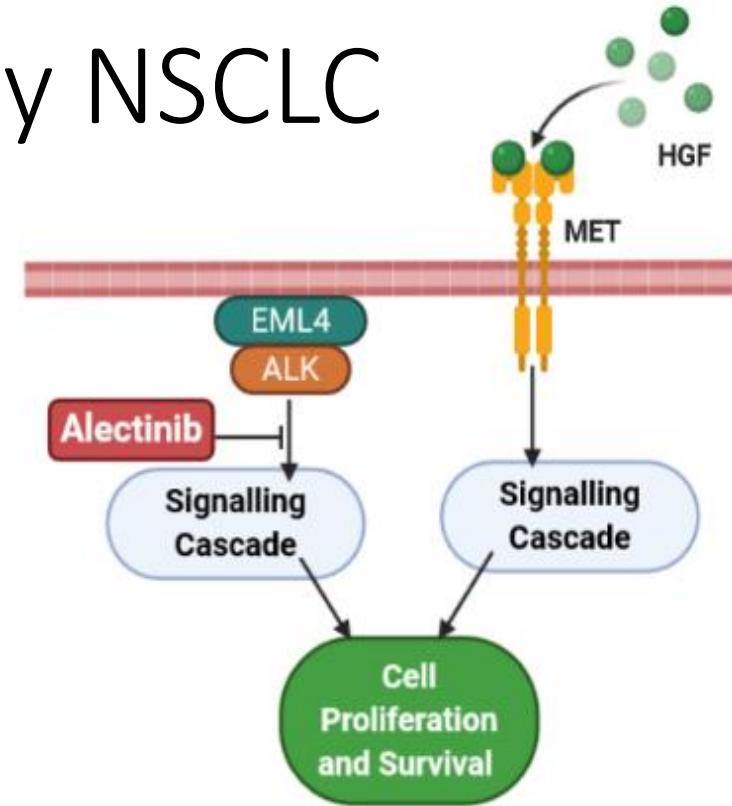


Ranjini Bhattacharya

Shiv Nadar University

$\beta^k G \chi^k$

Sensitive      Resistant       $(G_{1,1}, \dots, G_{1,m})$   
 $(G_{2,1}, \dots, G_{2,m})$



# Hepatocyte growth factor and the games played by NSCLC

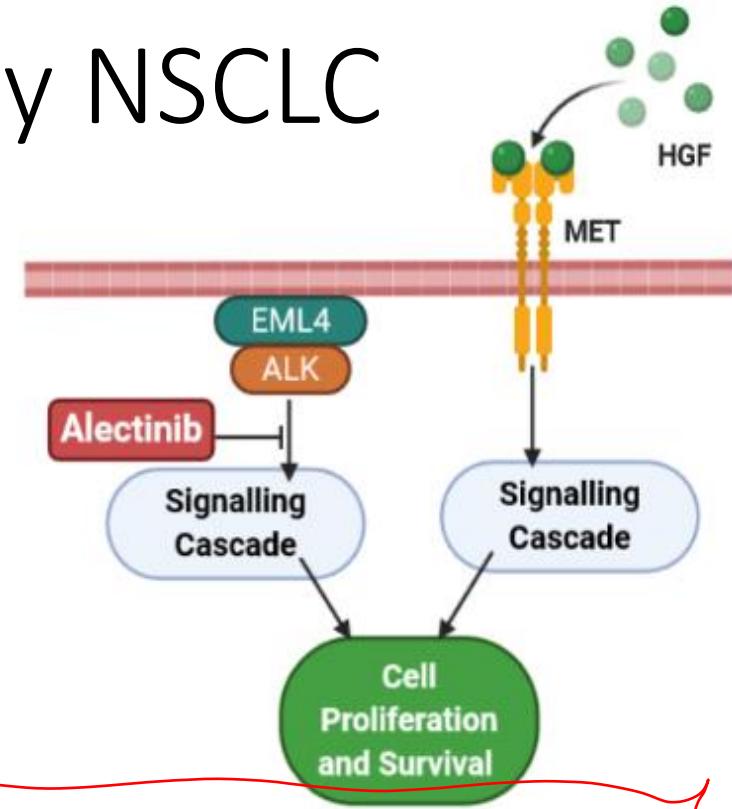
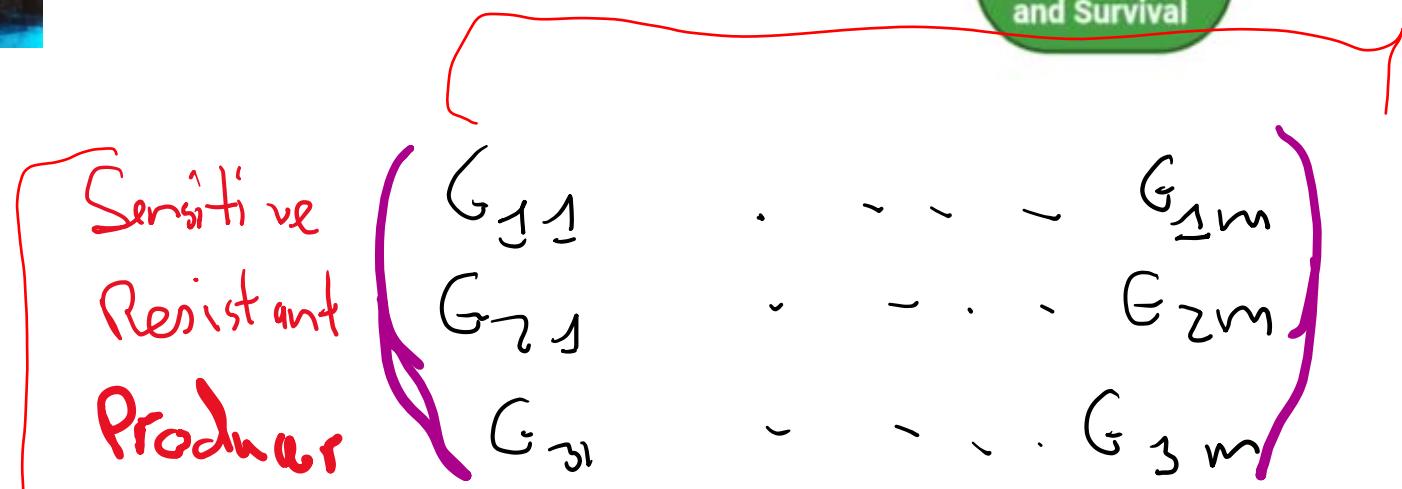


Ranjini Bhattacharya

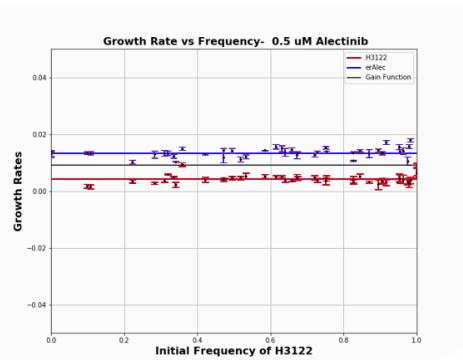
Shiv Nadar University

$\rho^t G \chi^t$

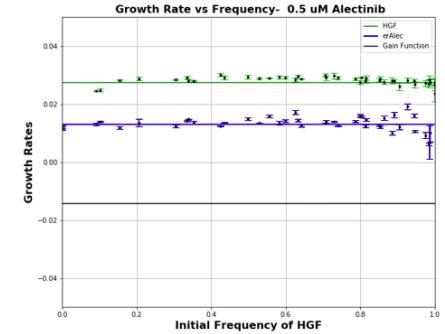
Sensitive  
Resistant  
Producer



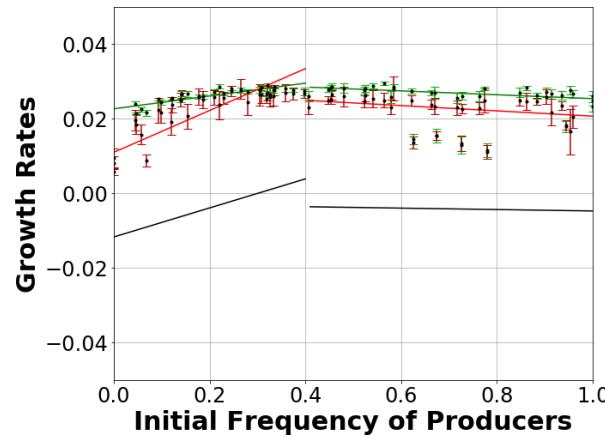
# Moving from two strategies to three



S vs R



R vs P

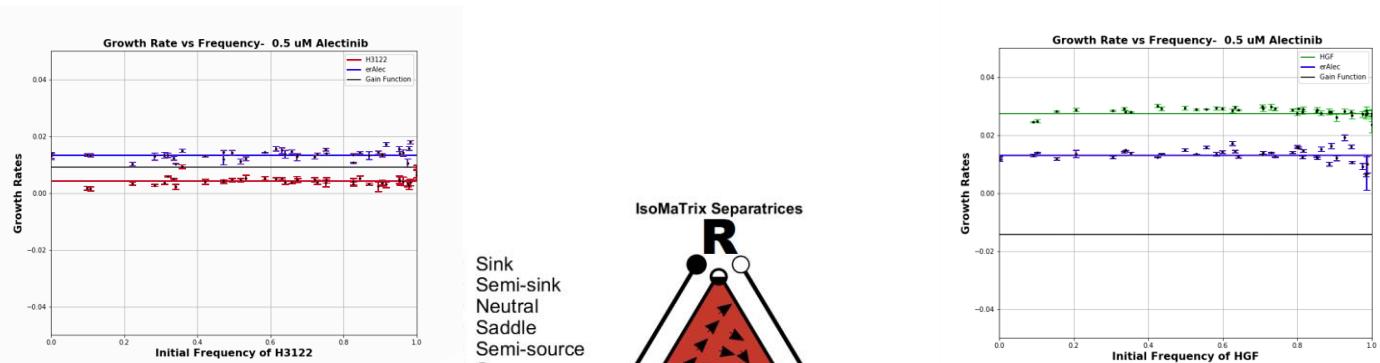


S vs P

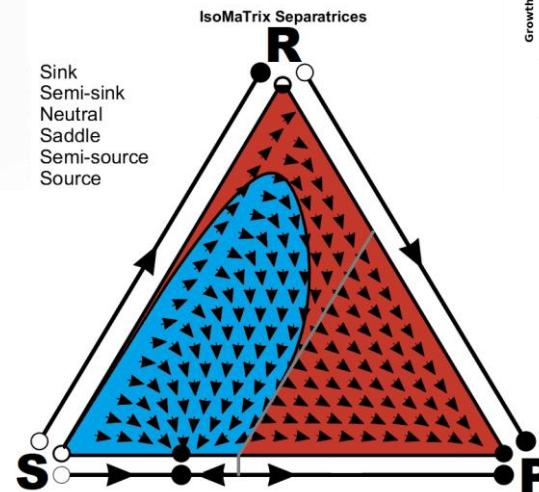
Ranjini Bhattacharya

Shiv Nadar University

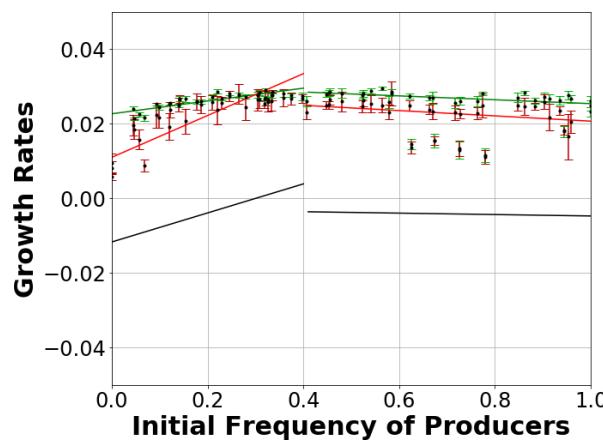
# Moving from two strategies to three



S vs R



R vs P



S vs P

# Two kinds of competitive release



Vague idea: decreasing the **sensitive** subpopulation helps the **resistant** subpopulation.

**Nathan Farrokhan**

Case Western Reserve University



# Two kinds of competitive release

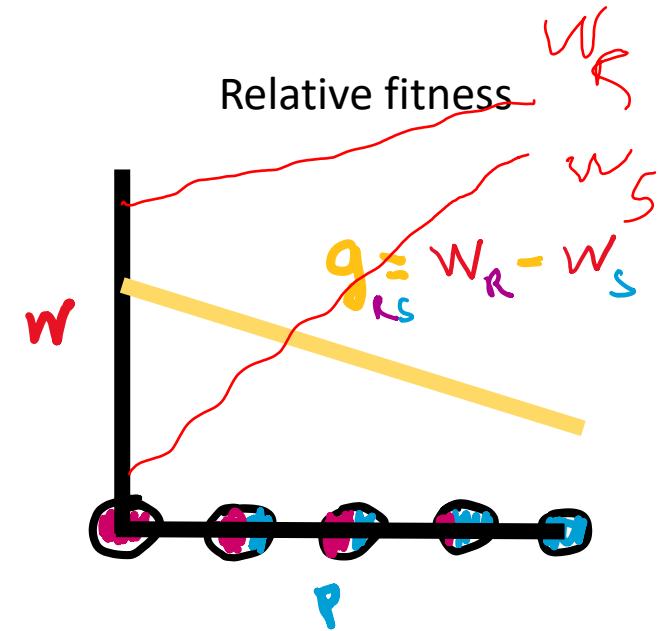
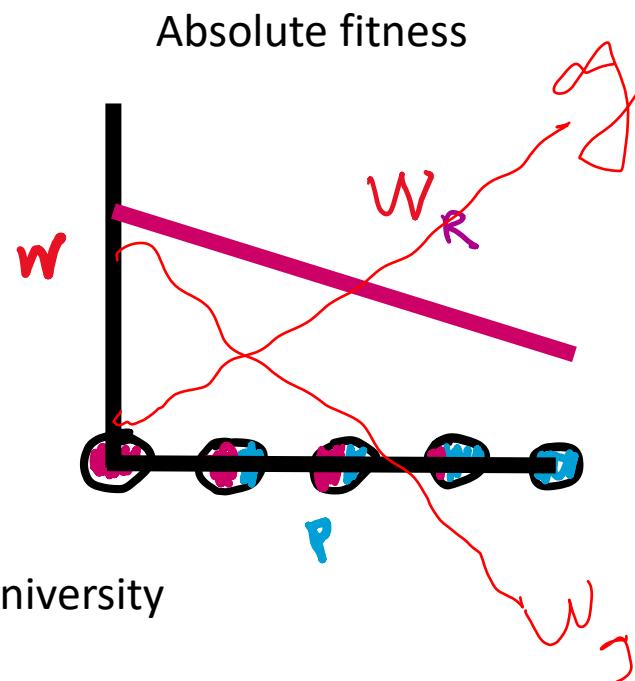


Nathan Farrokhian

Case Western Reserve University



Vague idea: decreasing the **sensitive** subpopulation helps the **resistant** subpopulation.

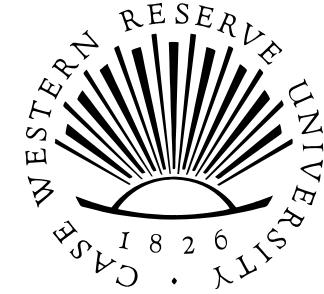


# Two kinds of competitive release

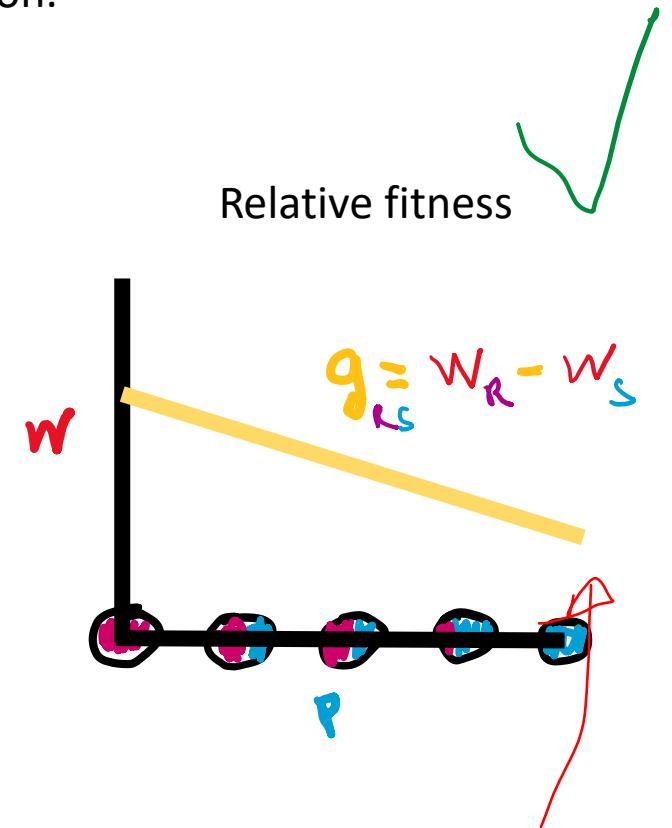
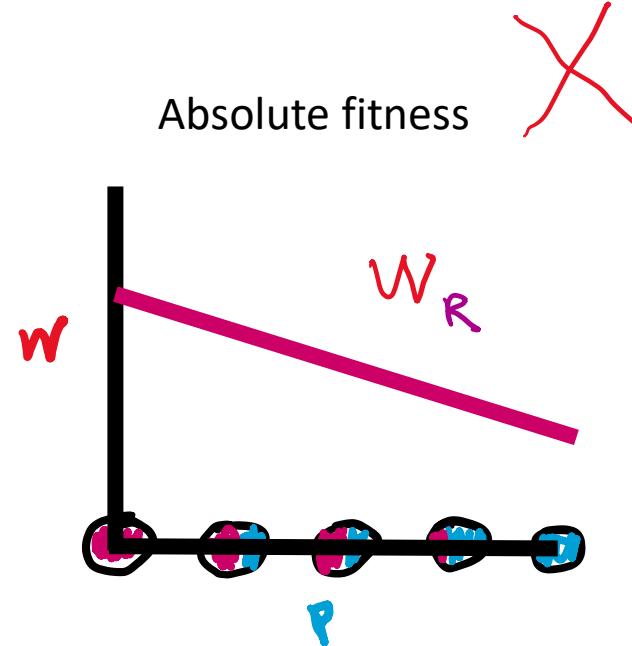


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Vague idea: decreasing the **sensitive** subpopulation helps the **resistant** subpopulation.

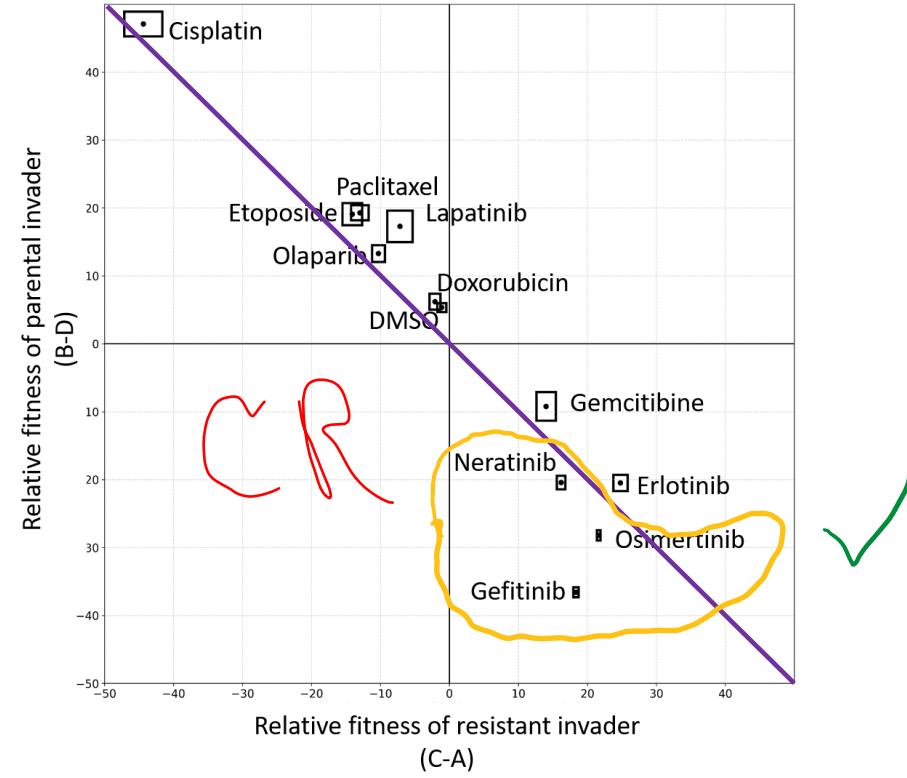


# Competitive release in the games played by NSCLC



Nathan Farrokhian

Case Western Reserve University



# Conclusion



- (1) the relative power of the two players and
- (2) the rules of the game that they are playing.