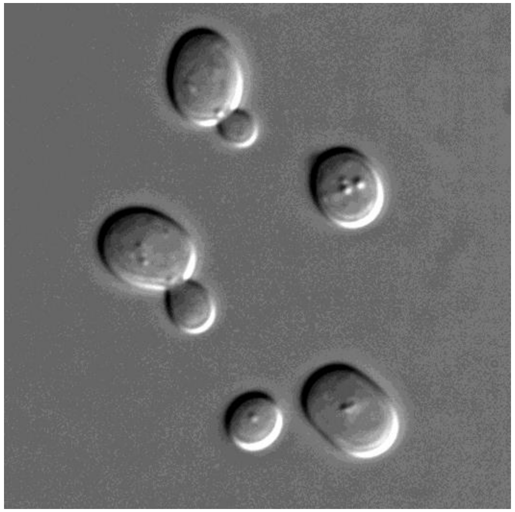
A modeling study to explore how selected traits may affect fitness in *Saccharomyces cerevisiae* batch culture

Collot Dorian

Nidelet Thibault, Dillmann Christine, Méléard Sylvie, Martin Olivier,
Sicard Delphine, Legrand Judith

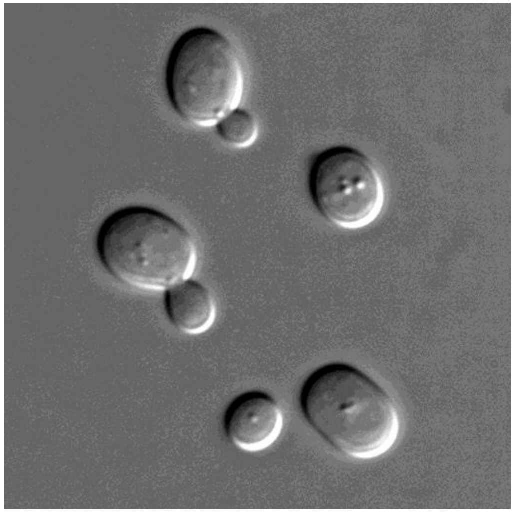
5th September 2016

Saccharomyces cerevisiae



http://fr.wikipedia.org/wiki/Saccharomyces

Saccharomyces cerevisiae



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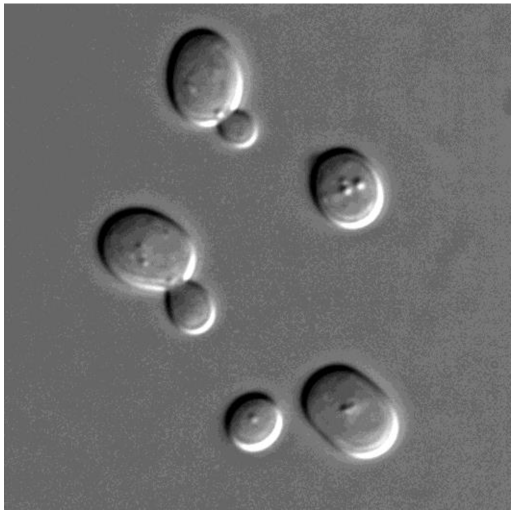

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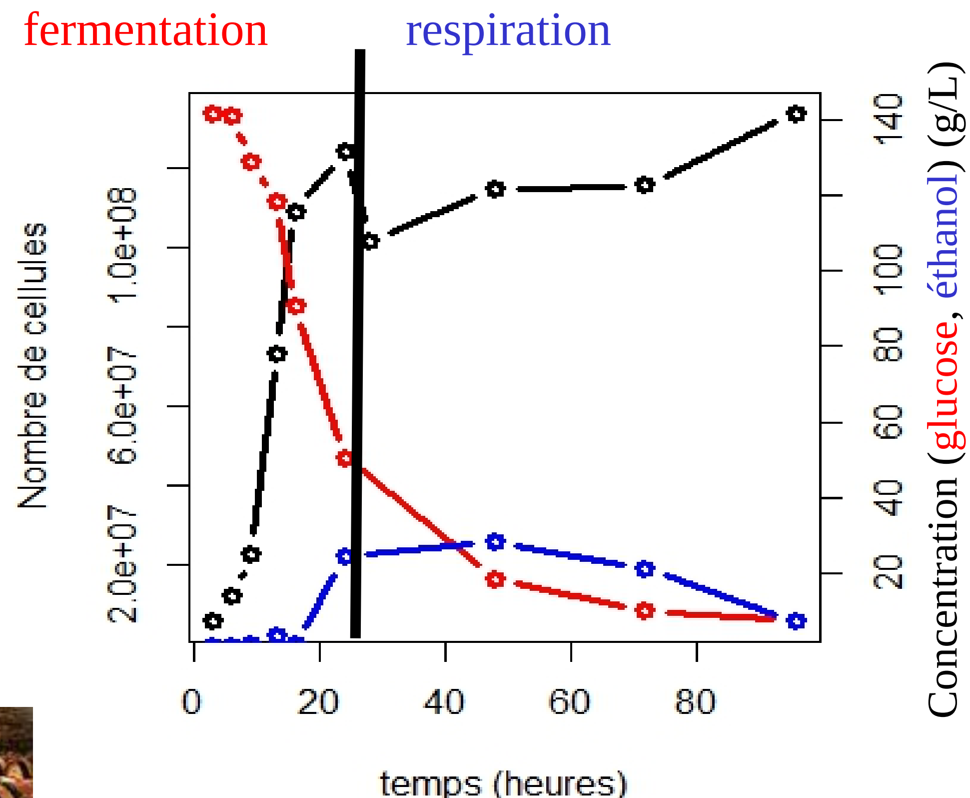


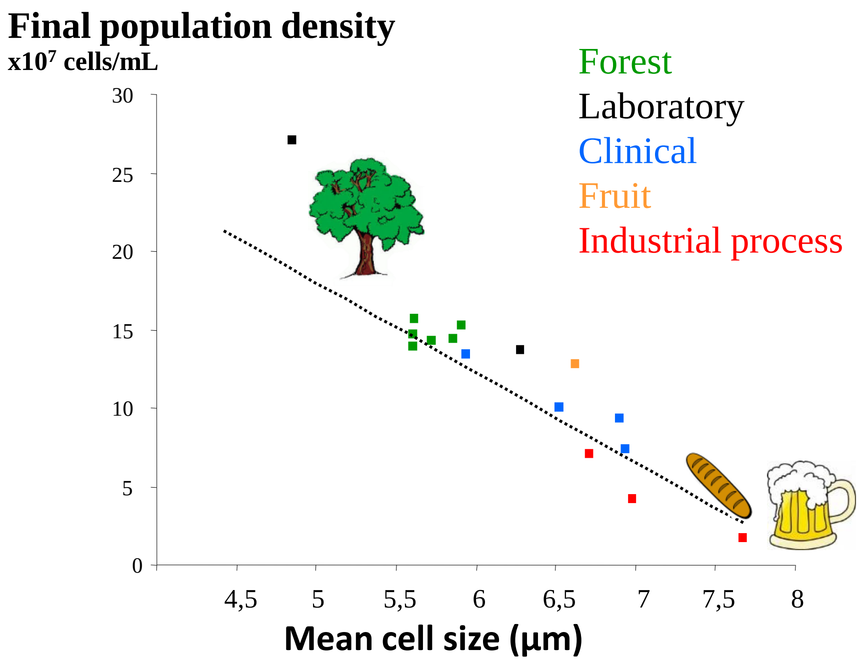
Fermentation :

Glucose $\longrightarrow$ CO_2 + Ethanol + 2 ATP

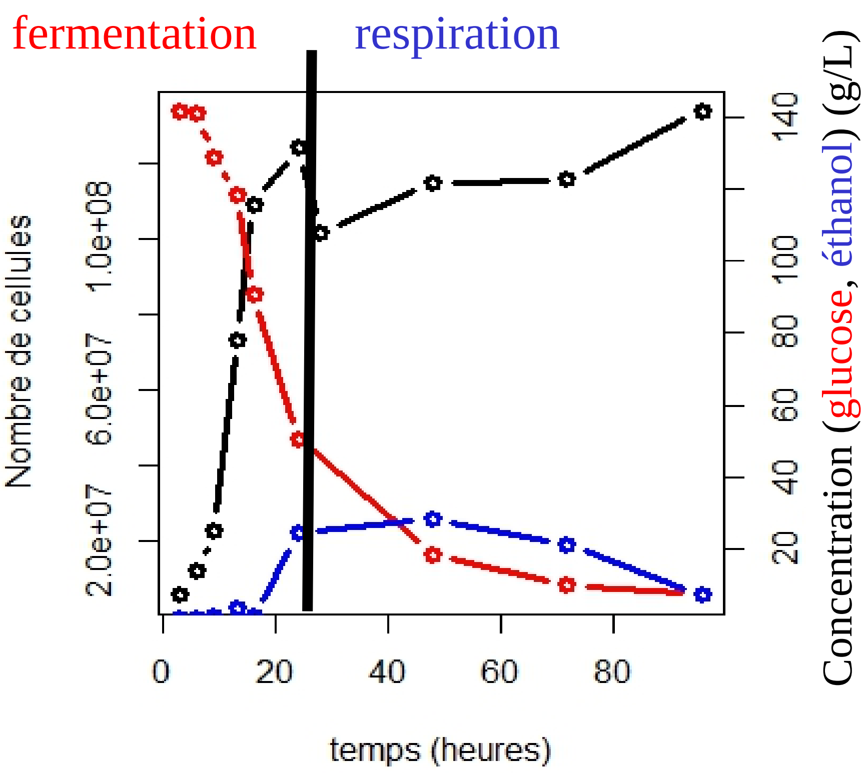
Respiration:

Ethanol + O_2 $\longrightarrow$ CO_2 + 32 ATP

Yeast adaptation



Spor et al., 2009

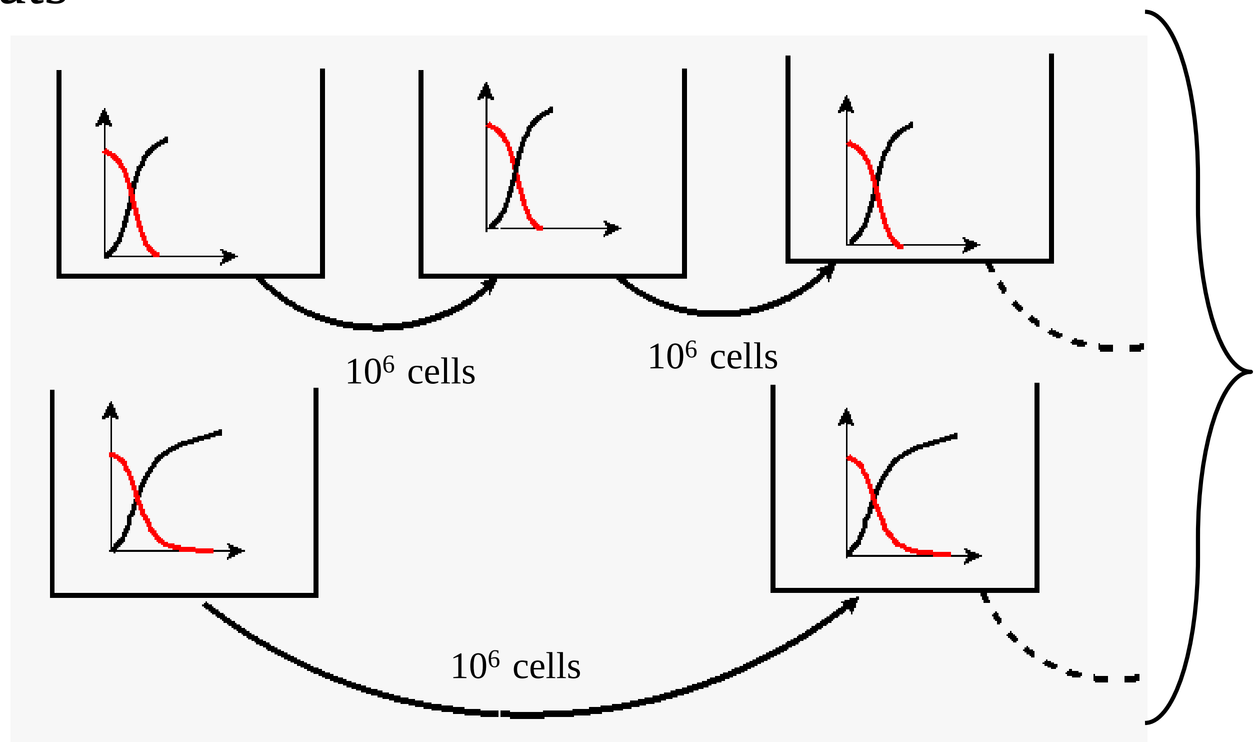


Adaptation *in vitro*

Experimental evolution: *(Spor et al., 2014)*

6 strains from different environment
4 environments
3 replicats

72 « evolved » strains



0h 48h 96h

x2 Glucose: 10 or 150g/L

Experimental evolution: *(Spor et al., 2014)*

6 strains from different environment

4 environments

3 replicats

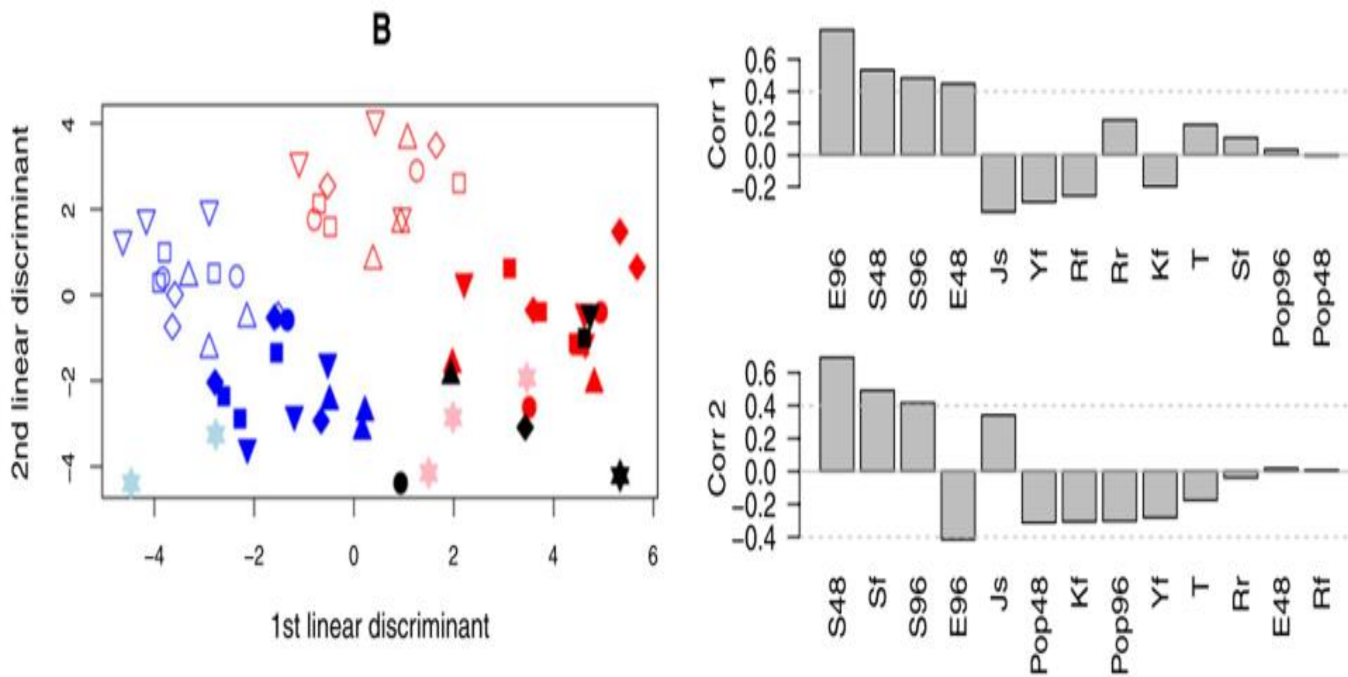
72 « evolved » strains

1%-96h

15%-96h

1%-48h

15%-48h

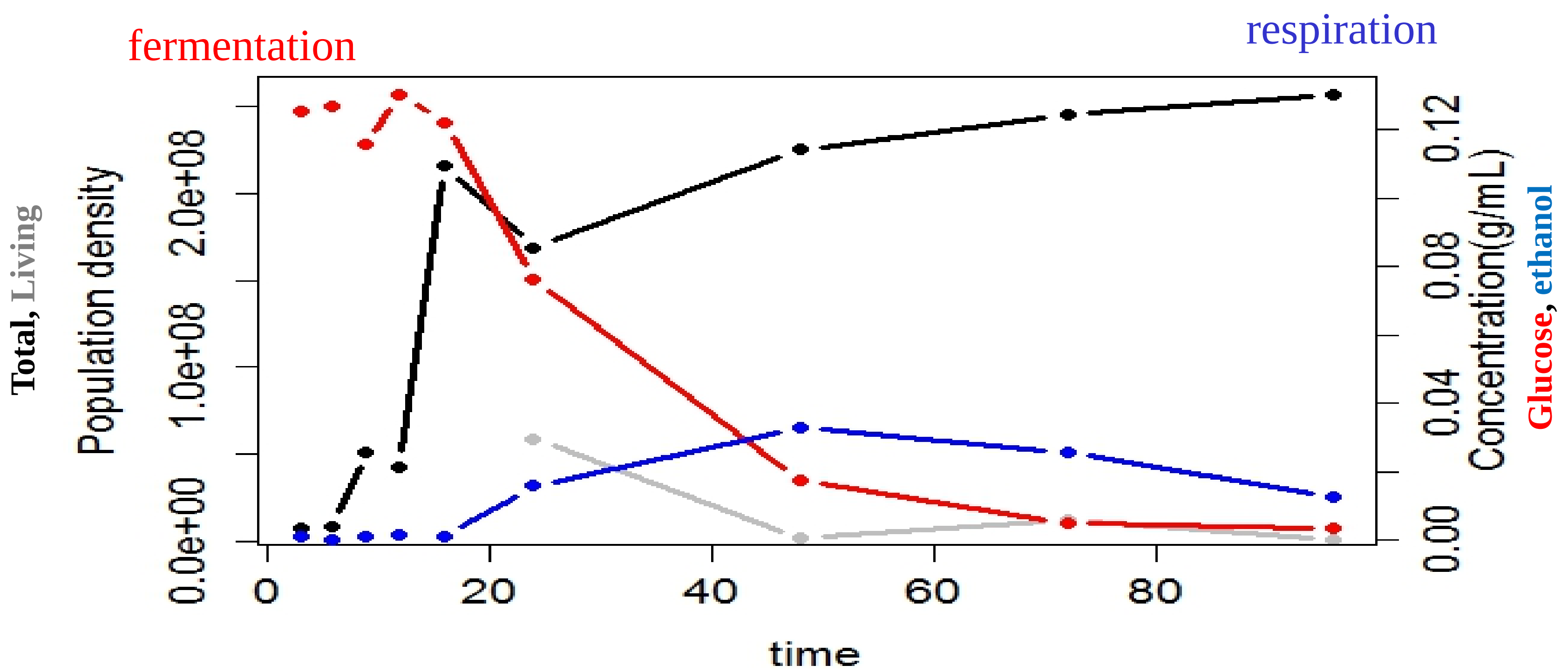


Spor et al., 2014

What are the traits which determine fitness in a seasonal environment?

What is the impact of selected traits on season length?

Batch culture model



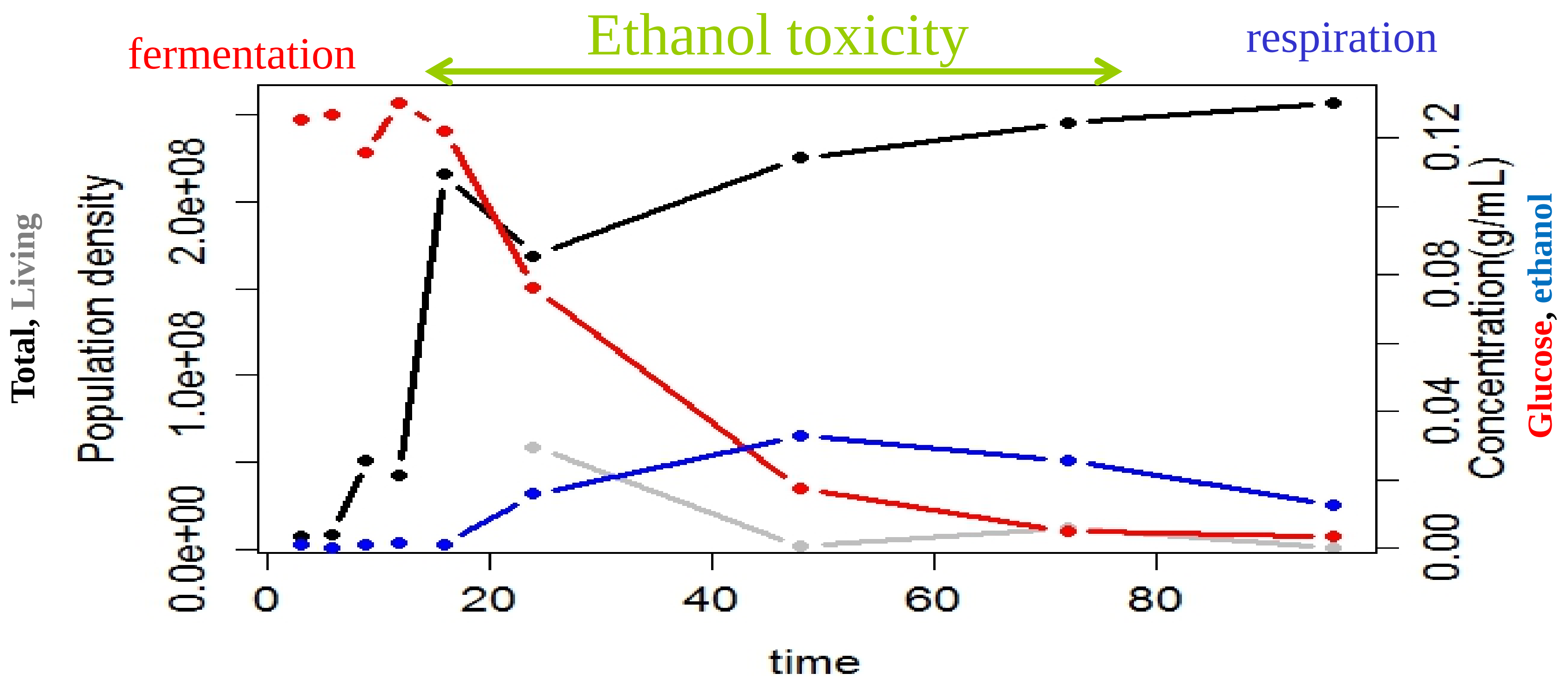
$$\frac{dG}{dt} = -\sum_i J_{fi} \frac{G}{K_f + G} N_i$$

$$\frac{dN_i}{dt} = r_{fi} \frac{G}{K_{fi}+G} . \exp\left(-\frac{E}{E_{m,i}}\right) . N_i + r_{ri} . \exp\left(-\frac{E}{E_{m,i}}\right) . \frac{E}{K_{ri}+E} \left(\frac{K_{Ci}}{K_{Ci}+G}\right) N_i - m . N_i$$

$$\frac{dE}{dt} = \sum_i J_{fi} \frac{G}{K_f + G} p_i N_i - \sum_i J_{ri} \frac{E}{K_{ri}+E} \left(\frac{K_{Ci}}{K_{Ci}+G}\right) N_i$$

Adapted from *MacLean et al., 2006*

Batch culture model



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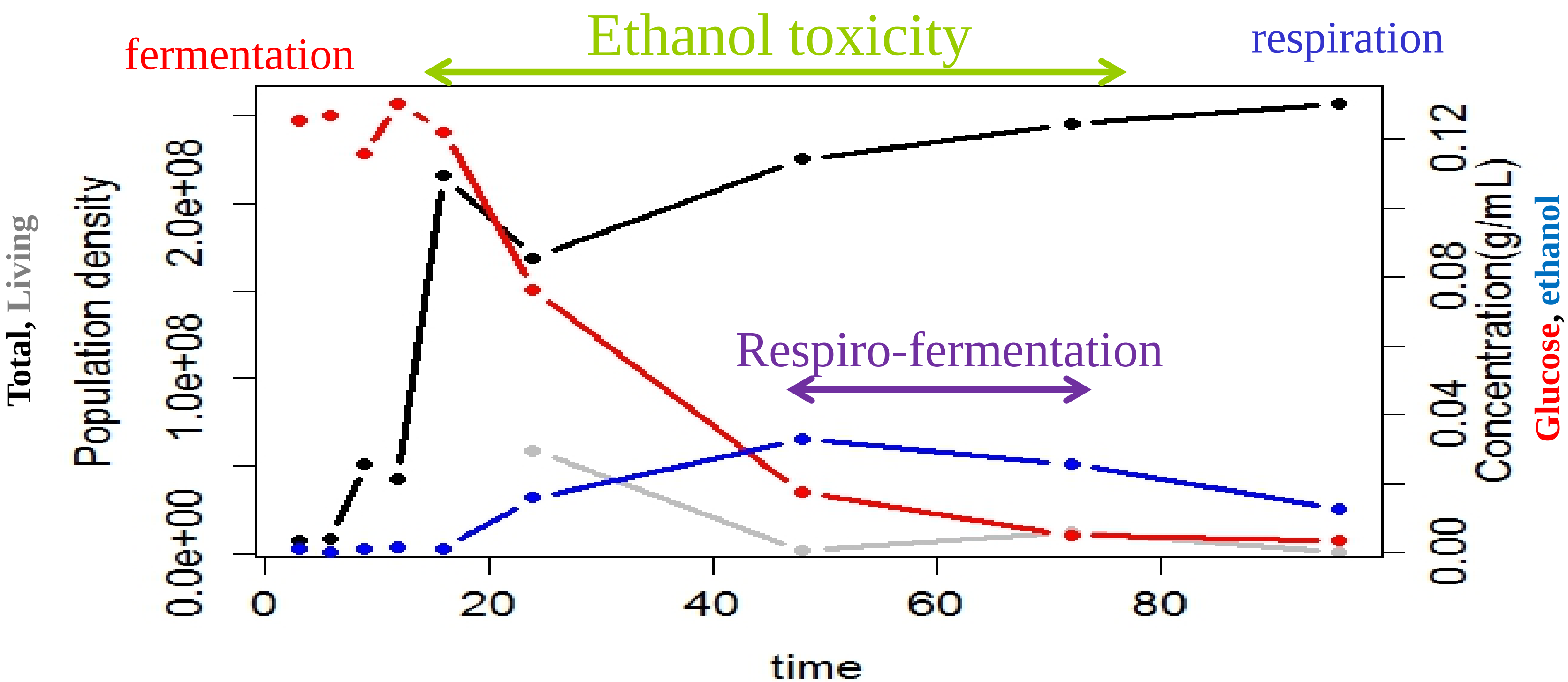

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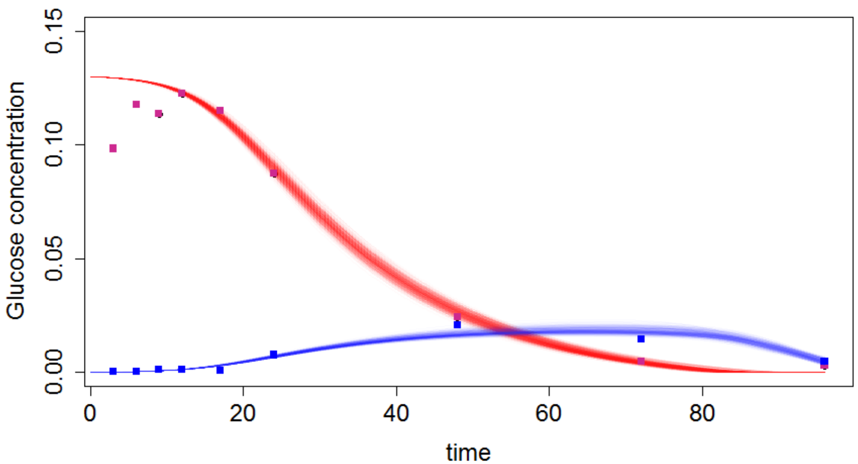
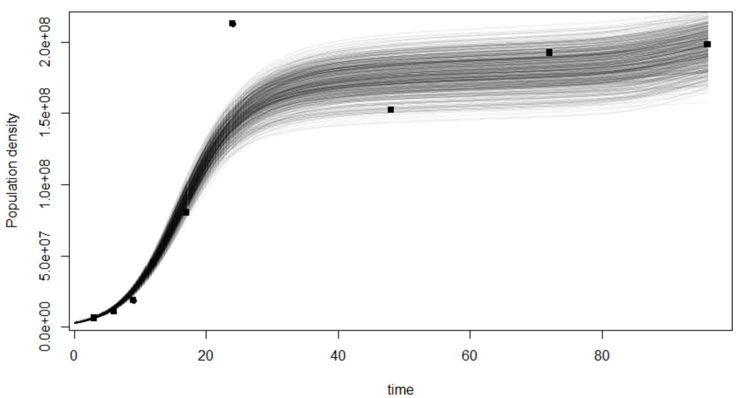
Inference of the parameters

Inference by ABC method,
Toni et al.



Parameters	Boundary set
Glucose comsuption rate J_f	10^{-11}-2.10^{-10} (g.cell^{-1}.h^{-1})
Fermentation growth rate r_f	0.2-0.6 (h^{-1})
Fermentation yield p	0-0.5
« Affinity » of the reaction K	10^{-7}-10^{-2} (g/mL)
Ethanol comsuption rate J_r	10^{-11}-10^{-9} (g.cell^{-1}.h^{-1})
Fermentation growth rate r_r	0.01-0.1 (h^{-1})
Inhibition of Glucose on resp. Kc	10^{-7}-10^{-2} (g/mL)
Mortality rate m	0.01-0.4 (h^{-1})
Toxic effect of ethanol Em	10^{-4}-10^{-2} (g/mL)



$$\frac{dG}{dt} = -\sum_i J_{fi} \frac{G}{K_f+G} N_i$$

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What are the traits which determine fitness in a seasonal environment? What is the impact of selected traits on season length?

Simplified model:

- **Links between traits and fitness**
- **Seasons and traits**

Extension to complete model & further work

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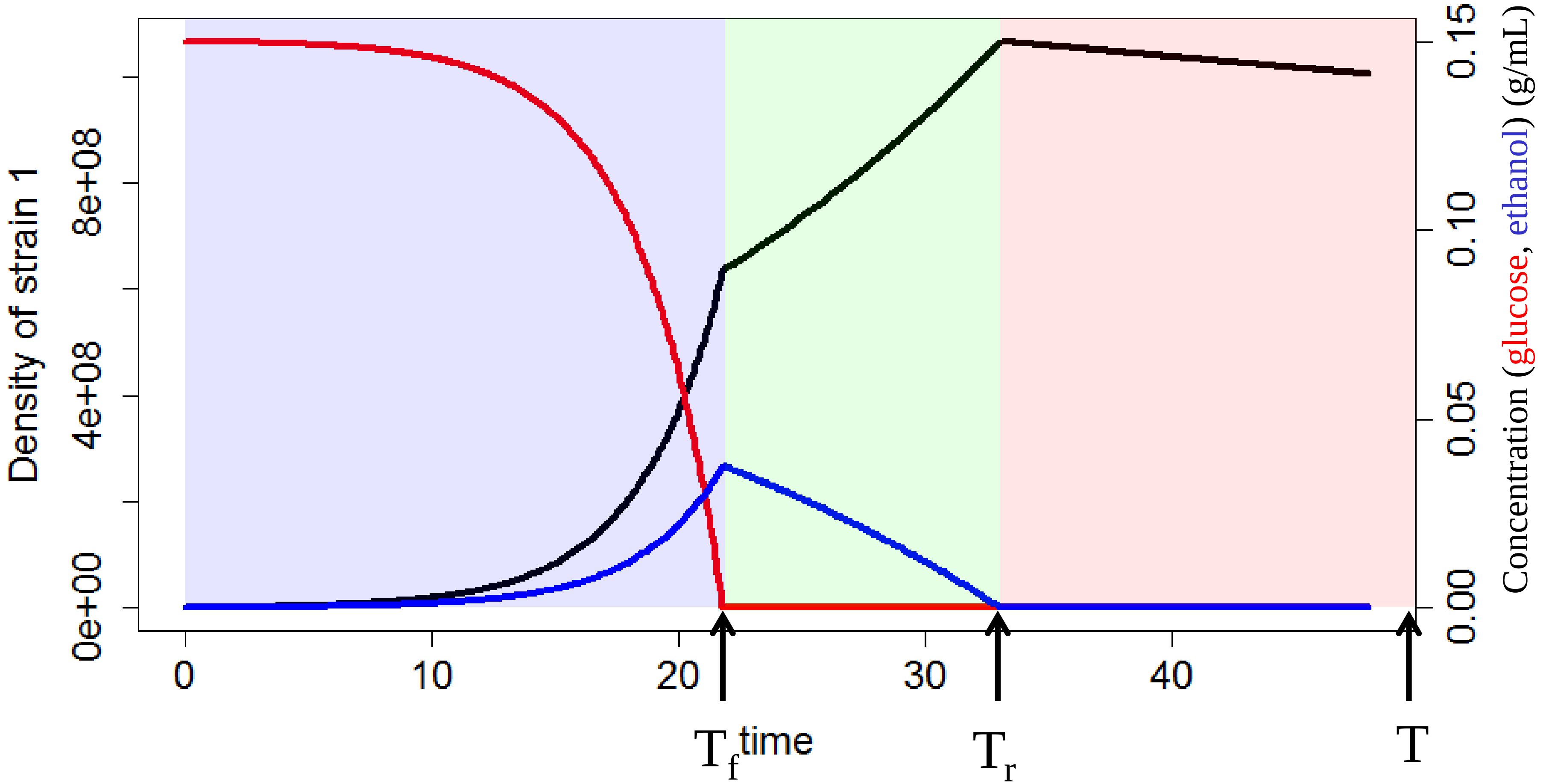
Simple model



T_f=length of the fermentation season

T_r-T_f=length of the respiration season

T= length of the batch

Link between traits and fitness

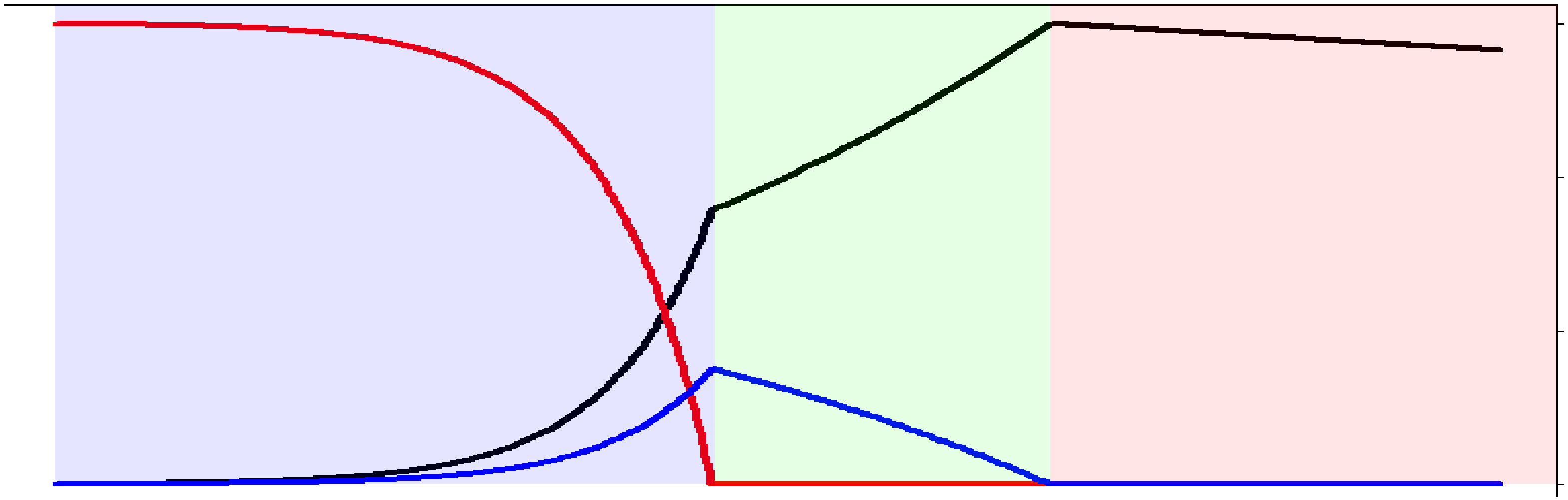
$$W_{1/2}(T) = \ln\left(\frac{N_1(T)}{N_2(T)}\right) - \ln\left(\frac{N_1(0)}{N_2(0)}\right)$$

Using the previous equations:

$$\boxed{W_{1/2}(T) = \left(r_{f,1} - r_{f,2}\right)T_f + \left(r_{r,1} - r_{r,2}\right)(T_r - T_f) - (m_1 - m_2)T}$$

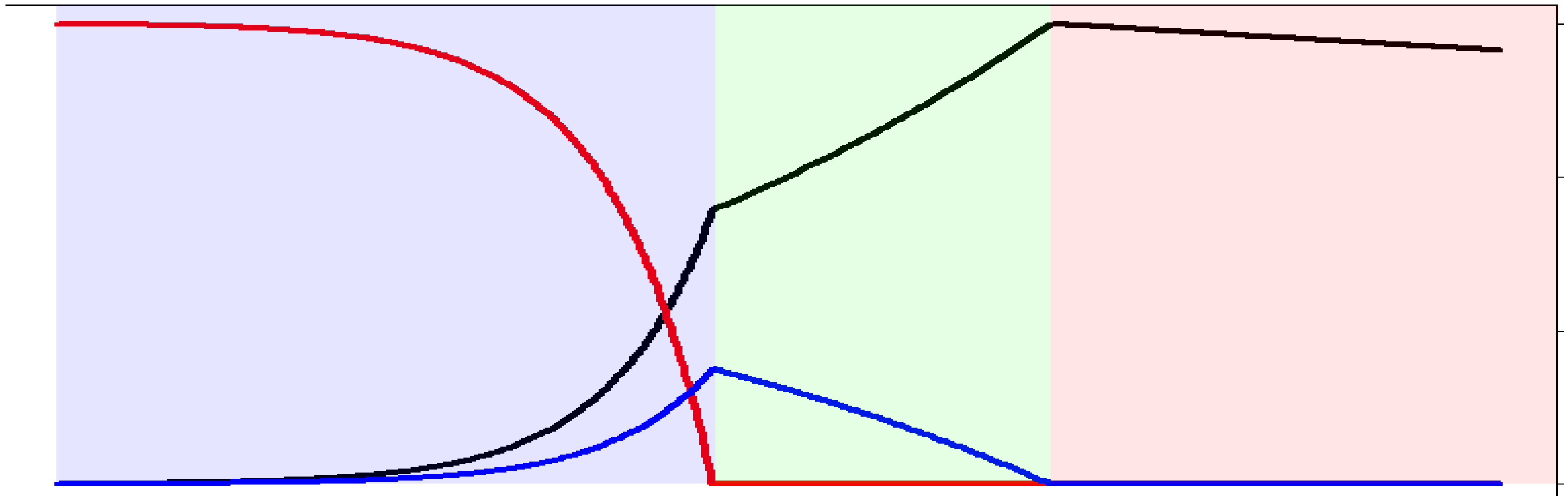
Fitness depends on:

- differences in growth rates or mortality rates
- associated season lengths



	Fermentation T_f	Respiration $(T_r\text{-}T_f)$	Mortality $(T\text{-}T_r)$
Traits selected	-High fermentation growth rate -Low mortality rates	-High respiration growth rate -Low mortality rates	-Low mortality rates

$$W_{1/2}(T) = (r_{f,1} - r_{f,2})T_f + (r_{r,1} - r_{r,2})(T_r - T_f) - (m_1 - m_2)T$$



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What are the determinants of seasons length?

What are the traits which determine fitness in a seasonal environment? What is the impact of selected traits on season length?

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Extension to complete model & further work

Seasons length and traits

Analytical solution in monoculture (resident population):

$$T_f = \frac{1}{(r_f - m)} . ln\left(\frac{y_f . G_o}{N_o} + 1\right)$$

$$(T_r - T_f) = \frac{1}{(r_r - m)} . ln\left(p . \frac{y_r . G_o}{(N_o + y_f . G_o)} + 1\right)$$

Seasons length and traits

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If $N_o \ll y_f . G_o$, i.e. the number of cells produced in fermentation is larger than the initial number of cells:

$$(T_r - T_f) = \frac{1}{(r_r - m)} . ln\left(p . \frac{y_r}{y_f} + 1\right)$$

$$T_f = \frac{1}{(\boldsymbol{r_f} - m)} . ln\left(\frac{y_f . G_o}{N_o} + 1\right)$$

	Fermentation T_f	Respiration (T_r-T_f)	Mortality (T-T_r)
Traits selected	-High fermentation growth rate -Low mortality rates	-High respiration growth rate -Low mortality rates	-Low mortality rates
Biotics components of season length	-Fermentation growth rate **(-)**		
Abiotics components of season length			

$$T_f = \frac{1}{(r_f - \boldsymbol{m})} . ln\left(\frac{y_f . G_o}{N_o} + 1\right)$$

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Abiotics components of season length	-Initial glucose concentration **(+)** -Initial cells density **(-)**		

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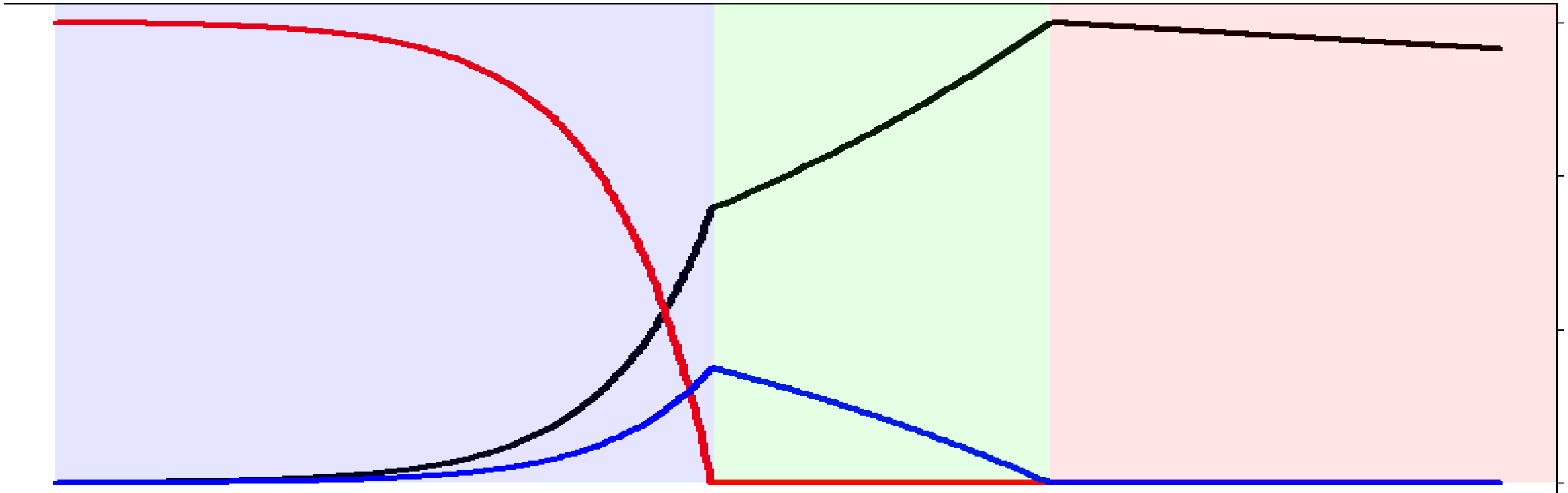

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Biotics components of season length	-Fermentation growth rate **(-)** -mortality rates **(+)** -Fermentation yield **(+)**	-Respiration growth rate **(-)** -Mortality rate -Fermentation yield **(-)** -Respiration yield **(+)** -Ethanol production **(+)**	
Abiotics components of season length	-Initial glucose concentration **(+)** -Initial cells density **(-)**		-Batch length **(+)**

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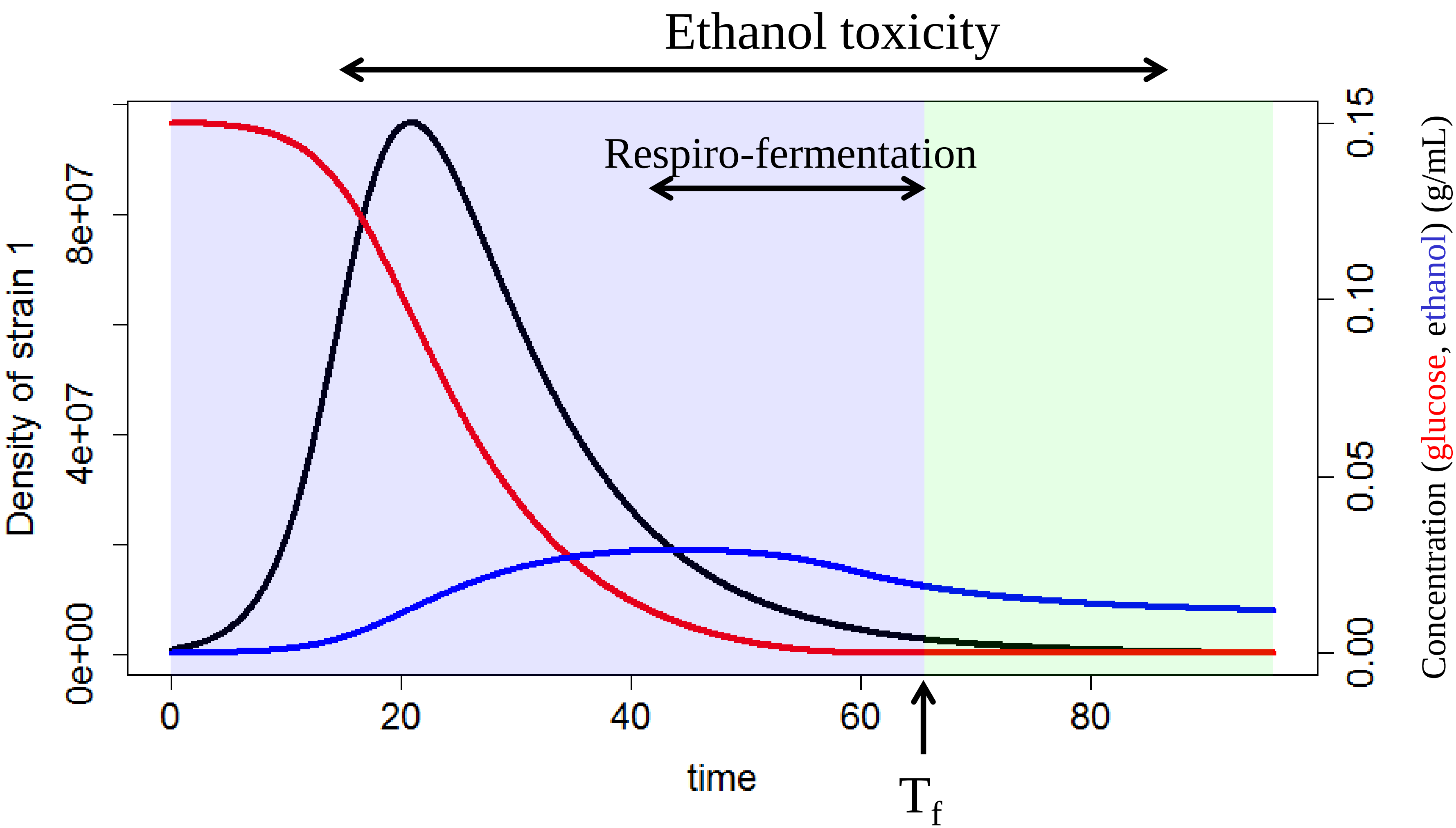
Extension to complete model & further work



Efficient season length: $$T_{ferm}^{eff} = \int_0^T exp\left(-\frac{E}{E_{m,i}}\right) . \frac{G}{K_{f,i}+G} dt$$

$$T_{resp}^{eff} = \int_0^T exp\left(-\frac{E}{E_{m,i}}\right) . \frac{K_{c,i}}{K_{c,i}+G} . \frac{E}{K_{r,i}+E} dt$$

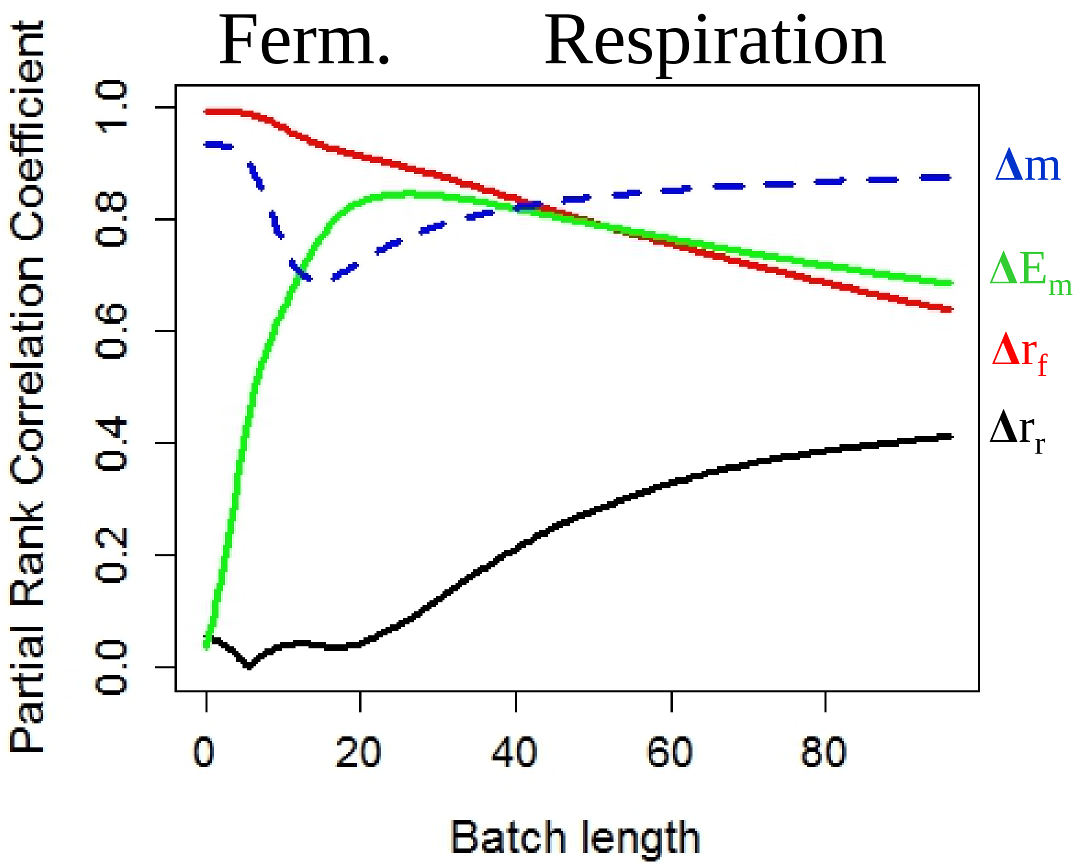
Competitions *in Silico*

- Sampling of 100 strains (Latin Hypercube Sampling)
- Initial frequency of the mutant : 0.001%
- 9 900 competitions.
- Fitness definition:

$$W_{1/2}(T) = \ln\left(\frac{N_1(T)}{N_2(T)}\right) - \ln\left(\frac{N_1(0)}{N_2(0)}\right)$$

N_i is the density of strain i.

Correlation between fitness and traits



Fermentation growth rate r_f

Mortality rate m

Respiration growth rate $\mathbf{r_r}$

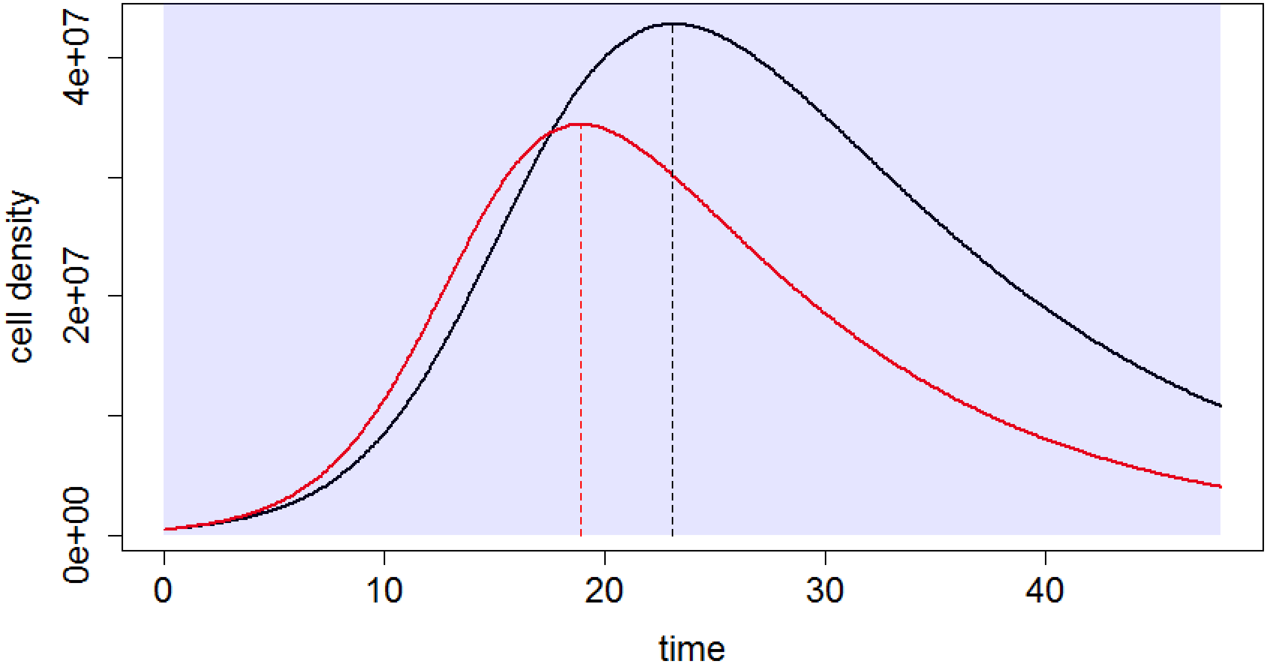
Resistance to ethanol E_m

Interseasons due to ethanol

$m_1 < m_2$

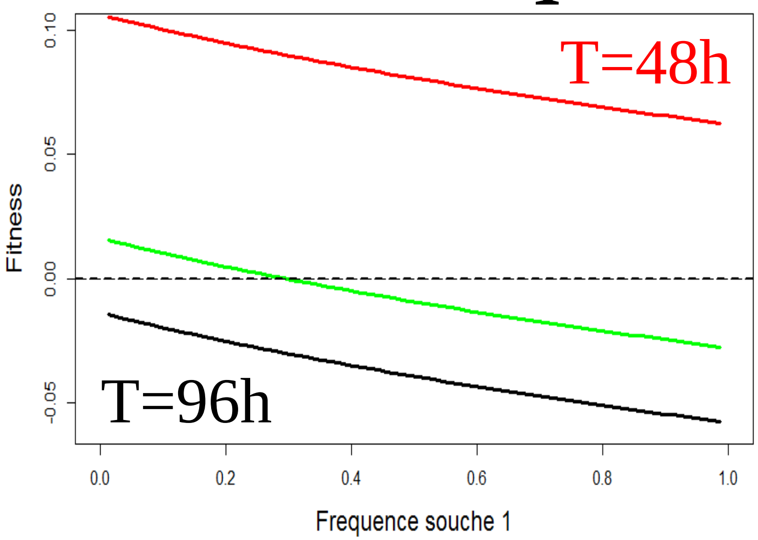
$r_{f,1} > r_{f,2}$

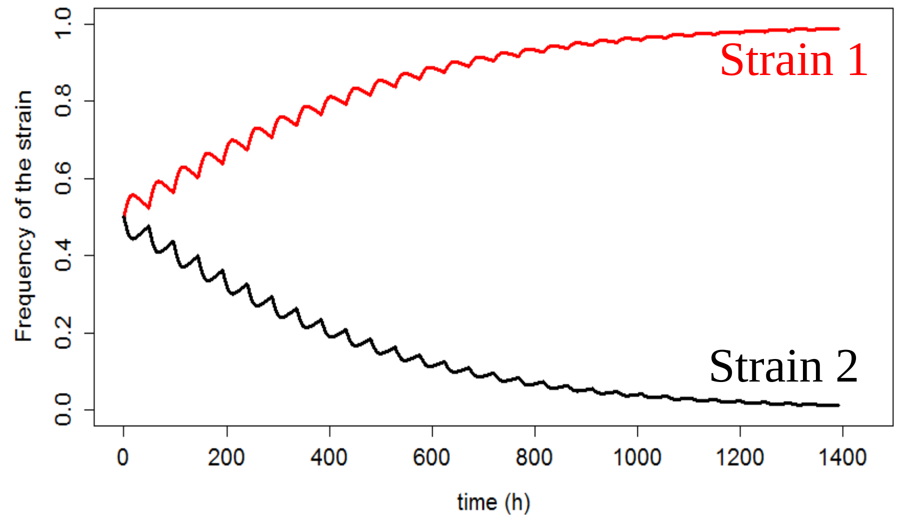
$E_{m,1} < E_{m,2}$



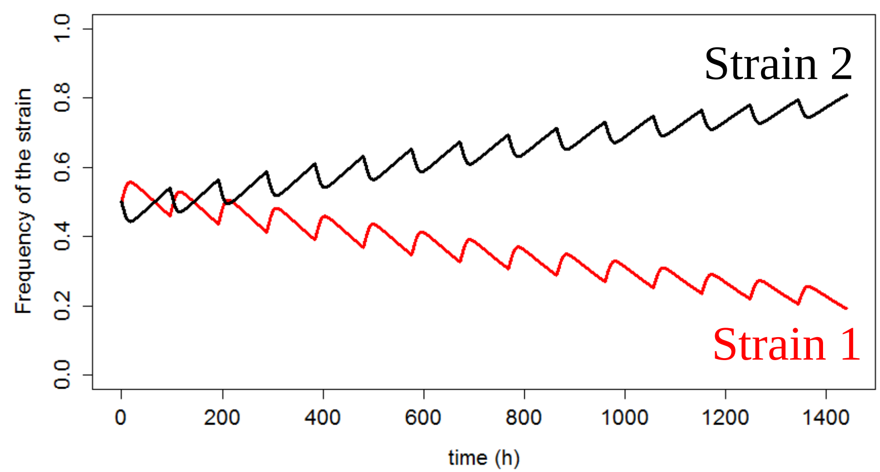
$W_{1/2}$=-0.98

Impact of batch length and frequency dependence





Parameters	Red	Black
m	0.106	0.1
J_f	7.10^{-11}	7.10^{-11}
r_f	0.43	0.4
Em	9.10^{-3}	9.10^{-3}
p	0.25	0.25
J_r	2.10^{-10}	2.10^{-10}
r_r	0.05	0.05
Kc	8.10^{-4}	8.10^{-4}
K	5.10^{-4}	5.10^{-4}



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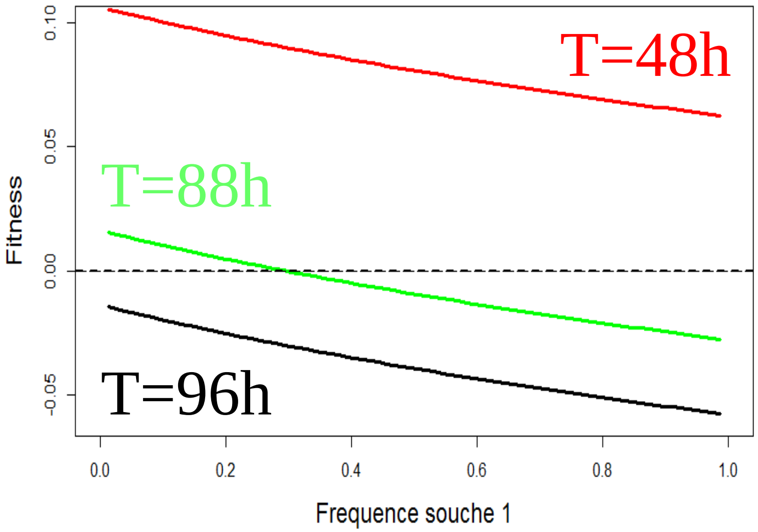

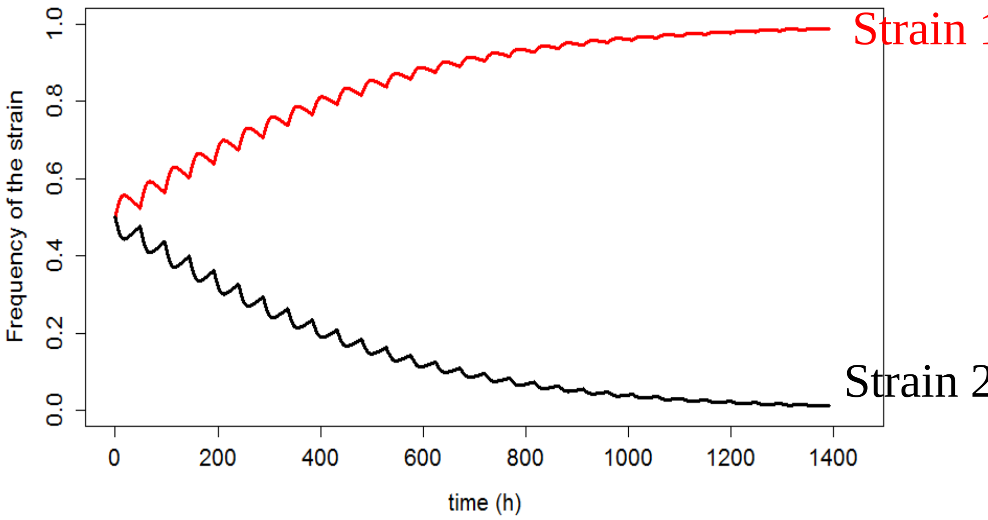

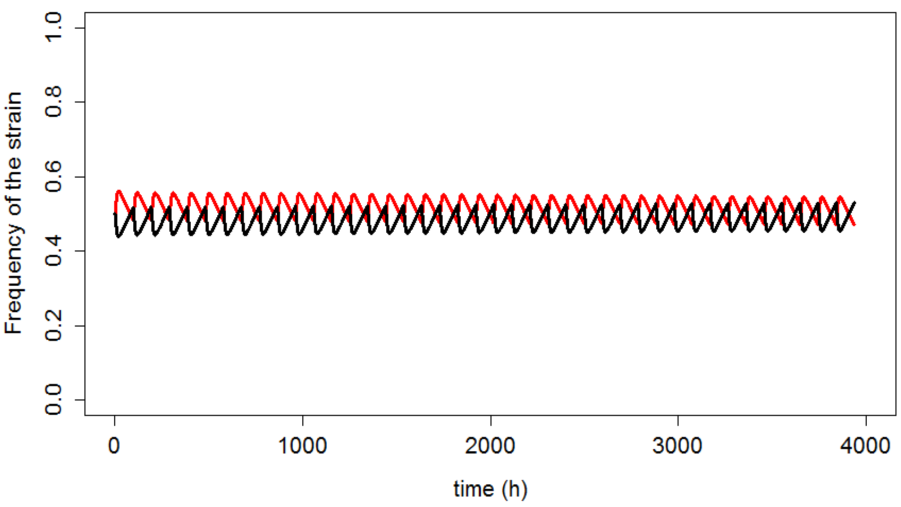

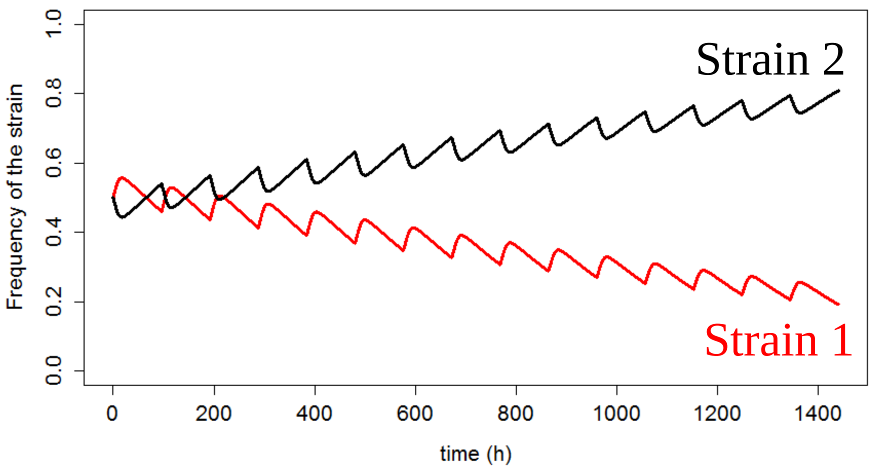

Conclusion

- The length of the seasons changes the intensity of selection on life-history traits
- Biotic conditions define the length of the seasons

→ frequency dependence

- Batch length can modify the seasons and thus which traits are selected

Thanks to:

Nidelet Thibault
Dillmann Christine
Sicard Delphine
Legrand Judith
Martin Olivier
Méléard Sylvie

Experimental evolution:
Spor Aymé
Bourgais Aurélie

And you for your attention