17/6/2020

# Tal’s reference (MED4/1A3)

note

Trying to use Tal’s culture as reference (pro co-culture metabolic, growing MED4 and 1A3 in mono- and co-cultures).

Even though Tal’s experiment is using the same growth conditions (Tal's cultures were grown in pro99 lowN (1:8), 22C, 27 uE), Tal’s experiments have lower growth. More important, the co-cultures grew less than the axenic med4, unlike Dikla’s experiment

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However, since this is the only reference I have, I decided to start by tuning to Tal’s experiment as an exercise, till we have better data. I tried to run optimization using genetic algorithm for all combinations of the parameters : gamma\_n\_p, excretion\_n\_p, v\_n\_max\_p, mu\_inf\_p, k\_n\_p, q\_n\_min\_p, q\_n\_max\_p, mortality\_p for both alt and pro and found that the parameter which yielded the best models were mortality\_p and mu\_inf\_p. Therefore, I ran the genetic algorithm twice (for ALT and PRO) tuning max growth coefficient and mortality.

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For PRO there are two main solutions, lower values of both growth and mortality or higher value for both. For ALT, all GA runs revert to the same solution. I therefore updated the values of growth and mortality parameters in the model:

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| Parameter | Existing values | New value based on GA on axenic model |
| mortality\_p | 0.1 | 0.2 |
| mortality\_a | 0.1 | 0.01 |
| mu\_inf\_p | 0.86 | 0.444825 |
| mu\_inf\_a | 0.86\*6 | 0.973535 |

\* for the mortality parameter, these are the min/max values that I allowed GA to consider, likely would be even bigger (PRO) / small (ALT) if GA was permitted to use these values.

# Gamma parameters

The relevant tuning of gamma parameters was checked by running GA on the gamma and excretion parameters: gamma\_n/c\_a/p, gamma\_refractory\_n/c\_a/p and excretion\_n/c\_a/p (12 parameters).

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The C related parameters receive the same value in all 100 GA runs, while for N parameters multiple solutions are found. Furthermore, many of solutions for C parameters are at the boundary of the allowed values. Interestingly, the C excretion and Gamma solutions for ALT are higher than the corresponding PRO values.

To check the effects of the different carbon gamma and excretion parameters, I ran sensitivity, by running the model with each C gamma and excretion parameter receiving all combinations of the values: 0, 0.05, 0.1, 0.25, 0.5, 0.75, 1. In total I ran 924 models, 516 of the models (55%) are valid (that is do not predict negative values.

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Looking at the values of the parameters in the valid models, all valid models have high excretion numbers (>=50% for ALT and >=25% for PRO), preferable low gamma (% of OC) values (25% or less), and > 25% ratio of refractory OC out of OC.

# Experiment setup

Hypothesis: the dynamic of PRO/ALT co-cultures are determined by nutrient reuse.

Setup:

* Negative control?
* Axenic PRO
* Axenic ALT
* Co-culture

Additional flavors to consider:

* Multiple strains
  + PRO + ALT, PRO+PRO (MIT0604 for N reuse), other types of heterotrophic bacteria?
* MED4, growth conditions
  + lowN, pro99, lowP, light/dark
* Measurements:
  + FL – 3 per week
  + FCM: PRO + ALT – once per week, more during exponential growth
  + DOC, DIC, DIN, DON ? (refractory?), DIP, DOP – same as FCM
  + DOC – 10-15ml, DIC – 14-16ml, DIN , DON, DIP- 10ml, DOP
  + Eddie?
  + DOC - 15ml x 2 per measurement
  + DIC – 16ml
    - alkalinity – 60ml or accurate ph meter?
  + DOC – all organic compounds. POC – particulate – all in the cell. TOC = DOC+POC – בר אילן
  + TN DON – 15ml - filter the cells – בר אילן
  + DIN – Eilat? Mike? 16ml. full. min 10ml.
  + HOOH
  + pH, alkalinity?
  + RNA SEQ?
  + growth rate, division rate, mortality rate,
  + refractory measurements, primary productivity – uptake rates exudation rates?
* ניסויי כיול
  + cell division (light/dark)
  + nano sims (nutrient recycling N15, C13)
  + DOC , refractory DOC

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| Measurement | Volume |  | Contact |
| TOC + TN | 20-30ml | Glass vial | Dina |
| DOC + DN | 20-30ml | Glass vial | Dina |
| DON ? |  |  |  |
| DOP |  |  | Mike / Anat/Tal B.E |
| DIP |  |  | Mike / Anat/Tal B.E |
| DIN | 16ml? |  | Mike / Anat/Tal B.E |
| DIC | 16ml |  | Jack Silberman |
| Alkalinity/PH | 60ml (alk) |  | Jack Silberman |
| N |  |  |  |
| P |  |  |  |

# Fitting against PNAS 11 growth curves

The goal of this experiment is to run the model of co-cultures for multiple phototroph-autotroph virtual species (generated by assigning a set of parameter values per species). The results will be clustered to see different growth dynamics. and implied physiological process. A subgoal is to suggest processes explaining the diversity of dynamics reported in the PNAS11 paper.

## Model variables:

For species *i*:

* *Xi* – number of cells
* *Bij* – species *i* biomass of nutrient *j* (do not distinguish between organic and inorganic)

(T – Inorganic / Organic)

For nutrient j:

* *ROj* – concentration of organic nutrient *j* in the media
* *RIj* – concentration of inorganic nutrient *j* in the media
* possibly can add refractory organic nutrient. Only change is in Roj

### Model parameters:

parameters per species:

General params:

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| --- | --- | --- |
| Param | Description | Value |
| u\_inf | Infinite growth rate |  |
| m | Mortality rate |  |

Params per species and nutrient

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| Param \ nutrient | Description | N | | C | |
|  |  | Organic | Inorganic | Organic | Inorganic |
| Qmin | Min quota |  | |  | |
| Qmax | Max quota |  | |  | |
| Vmax | Max uptake rate |  |  |  |  |
| K | Half saturation |  |  |  |  |
| Exudation | Exudation rate |  | |  | |
| Gamma | Fraction of inorganic matter released |  | |  | |
| Gamma refractory | Fraction of organic refractory matter (from all organic matter) |  | |  | |

Assume that exudation and mortality releases only organic matter and respiration releases inorganic matter.

marine bacteria uptake rates DOC glucose amino acid nitrate urea piruvat