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► **To cite this version:**

Anne Goelzer, Catherine Tanous-Healy, Gérard Scorletti, Vincent Fromion. Growth rate reflects a bottleneck on the resource sharing between cellular processes. Conference: Systems Biology of microorganisms, 2010, Paris, France. pp.1. <hal-02815643>

HAL Id: hal-02815643

<https://hal.inrae.fr/hal-02815643v1>

Submitted on 6 Jun 2020

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Title:

Growth rate reflects a bottleneck on the resource sharing between cellular processes

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Abstract: (Your abstract must use **Normal style** and must fit in this box. Your abstract should be no longer than 300 words. The box will 'expand' over 2 pages as you add text/diagrams into it.)

The growth rate should be a highly optimized process in bacteria since the battle for the conquest of ecological niches is tough. Understanding the main elements governing the growth rate management is crucial to further understand and predict the bacterium behaviour with respect to various environmental conditions. Constraint-based approaches integrating the whole metabolic network of an organism such as Flux Balance Analysis successfully predicted the maximum growth rate reachable in various conditions [1]. However, they fail to predict a number of commonly observed metabolic strategies.

Here we showed that the sharing of resources between the cellular processes intrinsically and structurally limits the growth rate [2]. We formalized the problem of resource repartition at the cell scale as an optimization problem and demonstrated the existence of a trade-off for the protein repartition between the translation apparatus and the metabolic network. Moreover, the resolution of this optimization problem for *Bacillus subtilis* allows the estimation for a given medium composition of (i) the maximal growth rate reachable; (ii) the concentrations of ribosomes, the concentration of proteins involved in the metabolic network and more generally the resource repartition between cell components; (iii) the flux distribution. Besides, we also predicted the induction and repression of metabolic sub-systems with respect to the environmental condition which correspond to the recently identified elementary modules of *Bacillus subtilis* [3]. Finally we also recovered the well-known evolution of ribosomes and metabolic proteins with respect to the growth rate of the Copenhagen school [4].

The proposed method, named "Resource Balance Analysis" (RBA), thus constitutes a powerful tool to explore many biological aspects such as the amino acid composition of enzymes, the codon usage or the emergence of structured genetic regulations. Moreover, RBA should be helpful to evaluate the impact of genetic modifications in the context of synthetic biology.

[1] Edwards J, Palsson BO. PNAS 2000, **97**(10):5528-5533.

[2] Goelzer A, Fromion V, Scorletti C. IEEE Conference on Decision and Control, 2009.

[3] Goelzer A. et al. BMC Syst Bio, 2008.

[4] Marr AG. Microbiol Rev. 1991. 55(2) :316-333.