Microbial biofilms are a large heterogeneous collection of cells working as a close-knit community located on a suitable substrate and held together within a matrix of polymers and other molecules that have been secreted by this heterogeneous collection. The cells in this collection have varied genetic expressions accounting for division into two fundamentally different states – planktonic and biofilm.

Matrix Of Multiple Solutions (MOMS) is a novel quantitative approach to analyze the multiple genetic expression levels. It is built over the known Flux Based Analysis (FBA) method supported by an Ordinary Differential Equation (ODE) regulatory network. The biofilm associated gene pool of about 100 non-essential genes controls the genetic expression of the Flagellar and Curli/Fimbriae modes, which are mutually exclusive and initiate, sustain and stabilize biofilms. The model is built using the known genetic annotation of the E.coli model (E.coli K12) and the additional 110 genes connected with biofilm.

The MOMS set the distribution of the solutions that encompass a large set of biofilm regulatory gene expression profiles. Specific matrix vector elements of this MOMS set correspond to possible genetic outcomes towards formation of biofilm and modulation of the Flagellar and Curli/Fimbriae pathways. The energy and nodes factors in these possible regulatory states provide a predictive method and a “what-if” analysis from simulation results to understand and look at possible drugs targets to prevent and disrupt biofilms.

Validation of model with specific examples

- An inverse correlation between csrA and the biofilm formation was established through the MOMS approach (Fig-3).
- In vitro experiment was carried out to test the same and it was found that the csrA knock out indeed produced more biofilm than the wild type. (Fig-5), validating the MOMS approach.
- Relation between Di-0-glucosyl Cyclase and ydaM gene (Fig-6) – MOMS indicated that overexpression of ydaM leads to increased c-di-GMP levels.

Conclusions

- The MOMS approach to solving biological network quantitative behavior in the presence of complex feedforward and feedback loops provides a method to estimate probability of a certain specific end point behavior of the network in the absence of exact gene expression data.
- With large computational power and the ability to handle big data, MOMS approach provides a good handle to predict behavior of a microbial population.
- The distribution of the scatter in a given area when plotted against the end point (formation of biofilm) provides a view of the possible relationship between the gene expression in consideration to the propensity of forming biofilm since the key biofilm matrix expressions converge to the formation as shown in Fig-2.
- This provides a window of opportunities to find possible gene targets for discovery of novel drugs that can prevent/disrupt biofilms.

References

- 110 references for Miranath Rajagopal et al., A Pleiotropic Gene from Escherichia coli That Affects Gluconeogenesis, Cell Size, and Surface Properties.
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