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Title : Approximate Algorithm for Finding Elementary Modes of Metabolic Networks via Low-distortion Embeddings
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<p>Report :</p> <p>With the support of ITP, I have stayed and studied at FB Mathematik und Informatik, Freie Universität Berlin for three months in 2012 summer. During the stay the climate was relatively colder than usual and the weather was rapidly changing, however, it was a very comfortable stay that quite a few people in Berlin are English-speaking and the whole city is fulfilled with artistic atmosphere, including musicians, painters and various kinds of pop-artists.</p> <p>The host research group, AG Mathematics in Life Science (Prof. Alexander Bockmayr's group) belongs to CSB (Computational Systems Biology) project Berlin, and therefore I have attended the weekly meetings of prof. Bockmayr's group together with some other CSB seminars including topics in recent experimental biology, such as RNA science. Especially, prof. Bockmayr advised me that prof. Edda Klipp (Theoretical Biophysics, Institute for Biology, Humboldt-Universität Berlin) and some of her graduate students are strongly and taking on a project on studying the use of information theory in biophysics, which is closely related to my previous research interest, and I was permitted to participate in the weekly seminars of prof. Klipp's group. As well as in prof. Bockmayr's group, some members in prof. Edda Klipp's group including the people working on information theory have finished their undergraduate or diploma studies in mathematics and so it was a nice opportunity to share our interests in theoretical biology.</p>

<p>(Left) Konzerthaus Berlin and Gendarmenmarkt. One of the most famous views among Berlin people.</p> <p>(Right) "The <math>\pi</math>-Buiding", the building of the department of mathematics, Freie Universität Berlin. The circular proportion (3.14159...) is printed on the wall.</p>

## Research Report.

Recent advances in molecular biology have revealed and enabled comprehensive studies on various kinds of biological networks such as metabolic networks, gene regulation networks and protein-protein interaction networks [1]. Among them, flux balance of the metabolic networks are well studied and understood from theoretical viewpoints that the mathematical models of their properties are well-formulated by linear equalities and inequalities [2]:

Let  $S$  be a stoichiometric matrix. The *flux cone* of  $S$  is defined as

$$C = \{v \in \mathbf{R}^n : S \cdot v = 0, v_i \geq 0 \text{ for all } i\},$$

and  $e \in C$  is called an *elementary mode* if there exists no vector  $v \in C$  s.t.  $\text{supp}(v) \subset \text{supp}(e)$ .

Recently, some members in prof. Bockmayr's group proposed an algorithm to enumerate the elementary modes [3]; however, it was a hard task for execution in that the required computational step grows exponentially according to the number of reactions included in the network.

During the stay, I have worked with Dr. Laszlo David (research associate of prof. Bockmayr group) and Aljoscha Palinkas (Ph.D. candidate) on the topic. First we have reviewed the basic notions and mathematical formulations of the key concepts, as well as some notions in high dimension geometry. Thereafter we discussed the possibility to establish an approximate algorithm for speeding up the enumeration of elementary modes: Let  $S (\in \mathbf{R}^{n \times m})$  and  $C$  as above. We can see  $S$  as a collection of  $n$  row (or  $m$  column)  $m$ -( $n$ -, resp.)dimensional vectors, and by Johnson-Lindenstrauss flattening lemma [4], there exists a good embedding of these points into  $\log n$ -( $m$ -)dimensional subspace with small distortion. Then denoting the embedded matrix by  $S'$ , we have conjectured that the geometry of resulting cone  $C'$  should be distorted within the order of  $\log n$ . While the proof for the estimation is not completed yet, the whole method give us an improvement in studying elementary modes.



(Left) A nice piece of joke on the door of our office, laughing at logical leaps, often found in mathematical proofs: “I think you should be more explicit here in step two.”-“Then a miracle occurs...” .



(Right) From the left; Aljoscha Palinkas, Laszlo David, Yuki Narita discussing in the seminar room.

## References.

- [1] KEGG: Kyoto Encyclopedia of Genes and Genomes, <http://www.kegg.jp/>
- [2] Sayed-Amir Marasi, Laszlo David and Alexander Bockmayr: On flux coupling analysis of metabolic subsystems, *Journal of Theoretical Biology*, 302 (2012) 62-69
- [3] Sayed-Amir Marasi, Laszlo David and Alexander Bockmayr: Analysis of Metabolic Subnetworks by Flux Cone Projections, *Algorithms for Molecular Biology*, 2012, 7:17
- [4] Jiří Matoušek: *Lectures on Discrete Geometry (Chapter 14-15)*, Springer, 2002



Home parties involving CSB members and some Japanese people studying in Berlin as working holidays.

## Acknowledgement.

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