network level. However, we identified two factors that might limit the evolution of these novel pathways in nature. First, underground reactions tend to introduce toxic metabolites into the network. Second, despite their seamless integration into the network, most underground activities do not provide advantage in any of a wide range of nutrient conditions.

We confirm using high-throughput experimental gene overexpression screens that amplification of underground activities rarely confers growth under novel carbon sources. However, despite their low frequency, such metabolic novelties are computationally predictable based on our knowledge of underground metabolism. Taken together, our study indicates that a large fraction of the biochemically feasible raw material have remained unexploited by adaptive evolution.

Modeling the seasonality of Lyme borreliosis in Hungary

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We found that the annual Lyme borreliosis (hence: LB) incidence doubled during a 13 year period in Hungary. Our aim was to understand the most important factors which determine the LB season in Hungary and explain the apparent contradiction between the annual unimodal LB incidence and the bimodal *Ixodes ricinus* tick activity run in Hungary by distinguishing the temperature dependent seasonal human and tick activity, the temperature-independent factors, and the multiplicative effect of human outdoor activity in summer holiday, using data from Hungary in the period of 1998–2012.

This distinction was verified by modeling the Lyme incidence based on the separated factors, and comparing the run of the observed and modeled incidence. The human outdoor activity showed a similar exponential correlation with ambient temperature to that the relative incidence did. It was proved that summer holiday has great influence on Lyme incidence.

To better understand the role of LB as indicator disease we modeled the temperature-related, mainly questing hard tick influenced spring and summer part of the Lyme season in Hungary in 1998–2010. Our model was based on the “wait and see” strategy of ticks and the probability distribution of the latency of early manifestation forms as ECM and neuroborreliosis. We found that the onset of the early symptoms show a log normal probability distribution which is in accordance with the literary data of the 3 days to 2 months latency with peak in the 2nd and 3th weeks. The model can explain the apparent contradiction between the observed April–May peak of tick season, the serological LB peak in the Hungarian population and of the distribution of the onset of the LB cases.