Intracellular Interactions

3994-Pos Board B722
Novel Viability Loss Process Induced by Electric Fields is Observed in the Extremophic Deinococcus Radiodurans Exposed to Gamma Radiation
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D. radiodurans is one of the fiercest radioresistant organisms, exhibiting a sophisticated repair mechanism responsible for its extremophilic character. Cultures of this organism were harvested during the exponential and stationary growth phases and irradiations were performed with a 60Co gamma source facility in the dose interval 0 - 12 kGy. Immediately after irradiation the cells were exposed to a 2 kV.cm^-1 static electric field (SEF) for 10 hours and the number of colonies was counted after a 36-hour period of incubation. An intriguing and significant depletion of the repairing shoulder, from 8 kGy to 4 kGy, was found when D. radiodurans is exposed to the electric field subsequent to irradiation. Furthermore, analysis of survival curves shows that at doses equal and higher than 4 kGy a mere additional dose of 0.9 kGy kills off 63% of the cells. It is concluded that SEFs are highly efficient radio-sensitizers, a finding that could be explored for therapy purposes. These first time and intriguing conclusions are based on previous work linking protein-ligand association and dissociation barriers in general to the costs of water transfer to/from binding sites. In the current study, we investigated a set of 8 carbapenems (including known drugs and antibacterials in development) for their structure-translocation kinetic relationships with OmPC using electrophysiology and microbiology methods. Taking into account the supporting electrophysiology and microbiology data, we demonstrated that these molecules likewise translocate through OmPC porin at rates that depend on their polar composition and H-bond replacement ability. The additional acidic group of ertapenem compared to other analogs promoted the highest entry rate into OmPC (kon =2x104 M^-1 s^-1). Zwitterionic compounds with highly polar groups attached to the penem-2 ring (i.e. panipenem, imipenem and doripenem) exhibited faster kon (>104 M^-1 s^-1), while those zwitterionic analogs with fewer exposed polar groups (i.e. meropenem and biapenem) exhibited slower kon (<5x103 M^-1 s^-1). Tebipenem pivoxil, a pro-dug developed for oral absorption, and razupenem with a change to thiazol-2-yl-thio moiety exhibited the slowest kon rates in to OmPC (~1.5x103 M^-1 s^-1) and also showed interaction with the phospholipid membrane. Our findings may help better understand the molecular mechanisms underlying antibiotic uptake through the outer membrane of Gram-negative bacteria, which is a key step in achieving antibiotic exposure and efficacy at intracellular targets.

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Unravelling the Impact of Obstacles in Diffusion and Kinetics of an Enzyme Catalysed Reaction
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Lattice gas automata simulations of diffusion-limited reactions in heterogeneous media exhibit fractal-like kinetics, which is a generalised mass action kinetics with time-dependent rate constants.1,2,3 We develop a two dimensional lattice gas automata simulation of the Michaelis-Menten mechanism in diffusion-limited conditions to investigate the effect of density and size of obstacles on reaction diffusion and rate coefficients. In order to simulate more physicochemical realistic conditions, reactants rotate and interact according to their specific orientation. We also model weak interaction forces between reactants and obstacles. Our results show that obstacle density and size affect diffusion, first- and second- order rates. We also find that particle rotations and weak force interactions among particles lead to a significant decay in the fractal-like kinetic exponent h. These results suggest that the effects of fractal-like kinetics disappear under less restricted conditions than previously believed in lattice based simulations.


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Growth and Motility of Gut Commensal Escherichia Coli in Health and Disease
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Despite the growth of E. coli is comparatively well investigated, there is still a lack of knowledge on growth of gut commensal E. coli in health and disease. Our previous investigations have shown that there is an obvious deviation from the norm in the gut microbiota of Armenian Crohn’s disease (CD) patients. The proportions of members of the CFB lineages were similar in the healthy and diseased individuals, while the increased numbers of Enterobacteriaceae members in fecal samples were found. It has been shown that growth of commensal E. coli isolates from the inflamed gut differed from those of E. coli in healthy individuals. In this study we inspected the effects of metronidazole (the antibiotic prescribed in CD therapy) on growth and motility of commensal E. coli from the healthy and CD volunteers.

27 patients with CD and 35 healthy individuals were enrolled in this study. The logistic differential equation of Verhulst has been used to characterize the growth of commensal E. coli isolates.
Results have demonstrated the increased numbers of E. coli isolates in feces of subjects with active CD. In vitro investigations of growth and motility of gut commensal E. coli isolates have shown that addition of metronidazole to the culture medium does not affect the growth parameters of isolates of healthy people. While statistically significant differences in growth parameters were obtained for patients’ isolates in the culture medium with metronidazole, in contrast to the medium without it. The presented data show that the chronic inflammation and drugs used during the inflammation effect on physiological characteristics of gut commensal bacteria.