Using knot theory to model the formation of minicircle networks on trypanosomatida

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Abstract. Trypanosomatida parasites, such as trypanosoma and lishmania, are the cause of deadly diseases in many third world countries. A distinctive feature of these organisms is the three dimensional organization of their mitochondrial DNA into maxi and minicircles. In some of these organisms minicircles are confined into a small disk shaped volume and are topologically linked, forming a gigantic linked network. The origins of such a network as well as of its topological properties are mostly unknown. In this paper we quantify the effects of the confinement on the topology of such a minicircle network. We introduce a simple mathematical model in which a collection of randomly oriented minicircles are spread over a rectangular grid. We present analytical and computational results showing that a positive critical percolation density exists, that the probability of formation of a highly linked network increases exponentially fast when minicircles are confined, and that the mean minicircle valence (the number of minicircles that a particular minicircle is linked to) increases linearly with density. When these results are interpreted in the context of the mitochondrial DNA of the trypanosome they suggest that confinement plays a key role on the formation of the linked network. This hypothesis is supported by the agreement of our simulations with experimental results that show that the valence grows linearly with density. Our model predicts the existence of a percolation density and that the distribution of minicircle valences is more heterogeneous than initially thought.