Molecular Dynamics Simulations of resistin and RELMβ proteins: Insight into structural dynamics

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Abstract

Diabetes mellitus and high levels of resistin are risk factors for COVID-19, suggest- ing a shared mechanism for their contribution to the increased severity of COVID-19. Resistin belongs to the family of resistin-like molecules (RELMs) whose implications for inflammatory and metabolic dysfunctions warrant its study in order to shed light on the etiology of these concerning pathologies. In this work, our objective is to char- acterize the structural dynamics of the reported crystallized resistin-like molecules. We performed molecular dynamics simulations of all-atom solvated protein at physiological and high temperatures for the three mouse structures reported so far. We found that in all the structures studied, there is a loss of helicity as a first step of protein denat- uration. There is a high stability of the globular β-sheet domain in resistin protein structures that is not conserved for RELMβ. At high temperature, we found a partial interconversion of α-helices into β-sheets in all proteins, indicating that this propensity is not only found during aggregation but also heating. We had been able to identify a largely persistent hydrogen-bond network shared by all the proteins in the interchain globular domain at room temperature. This network of hydrogen bonds is conserved considerably at high temperature in resistin structures, but not in RELMβ. These findings may guide future studies to increase our understanding of the different and shared mechanisms of action of RELMs.

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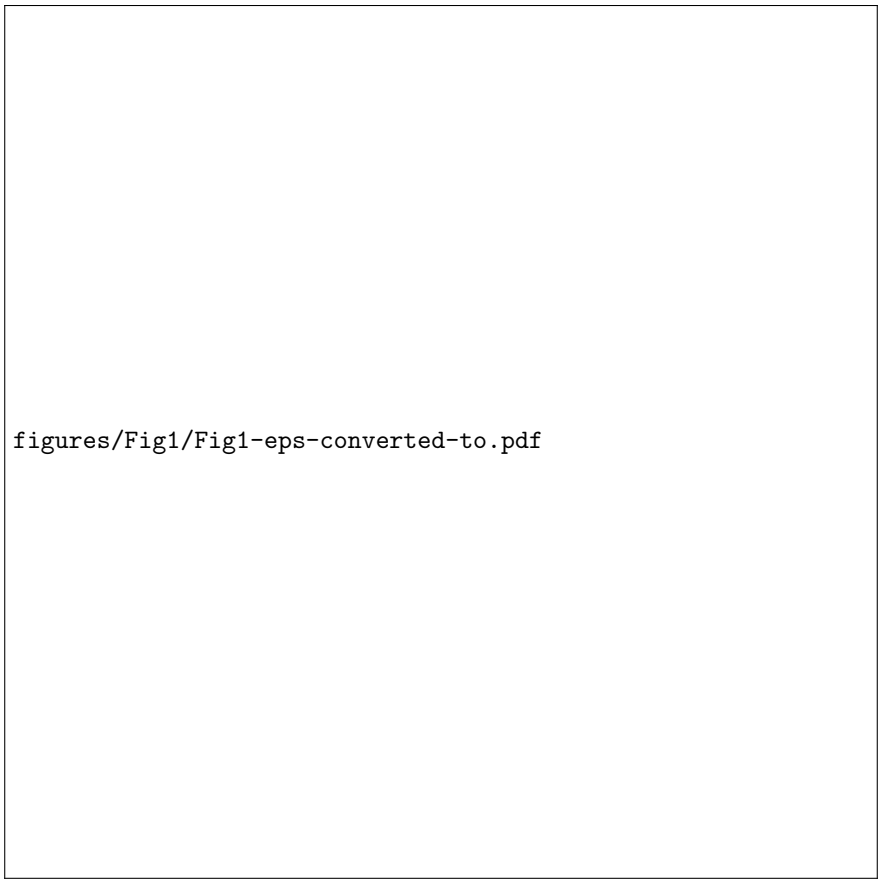

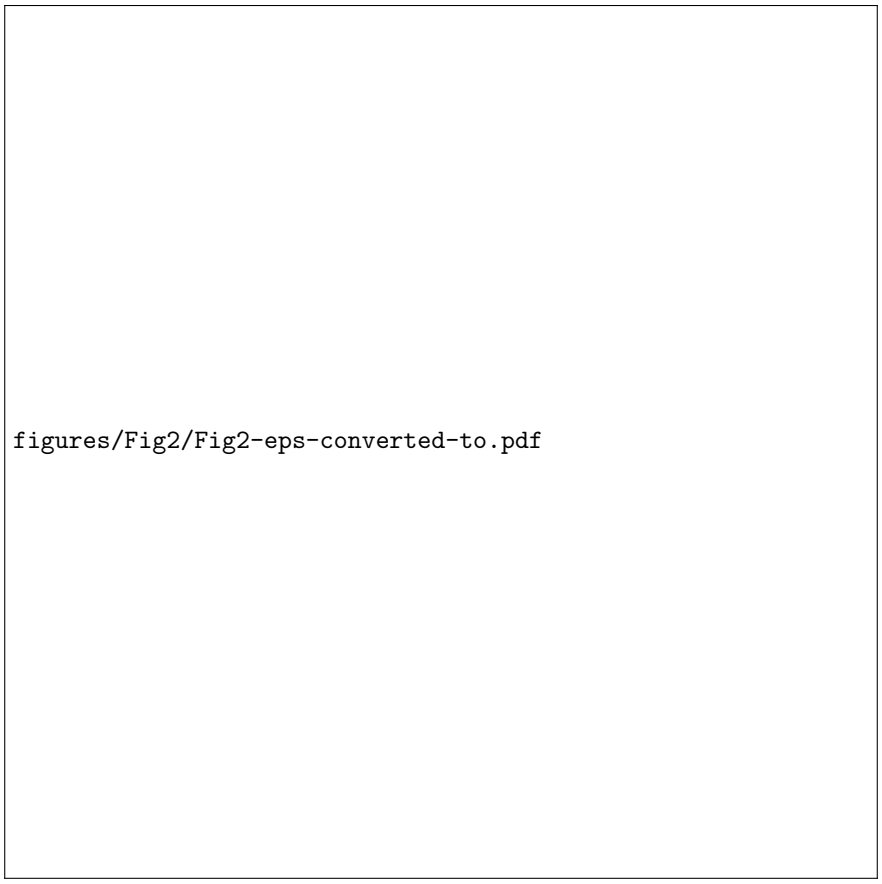

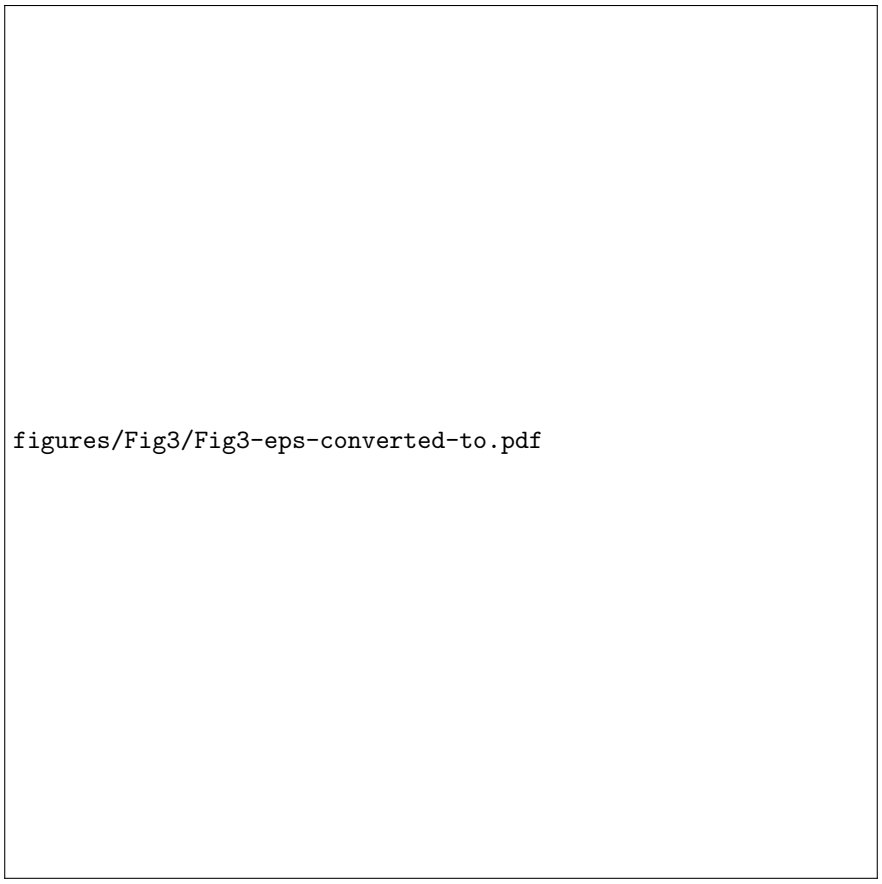

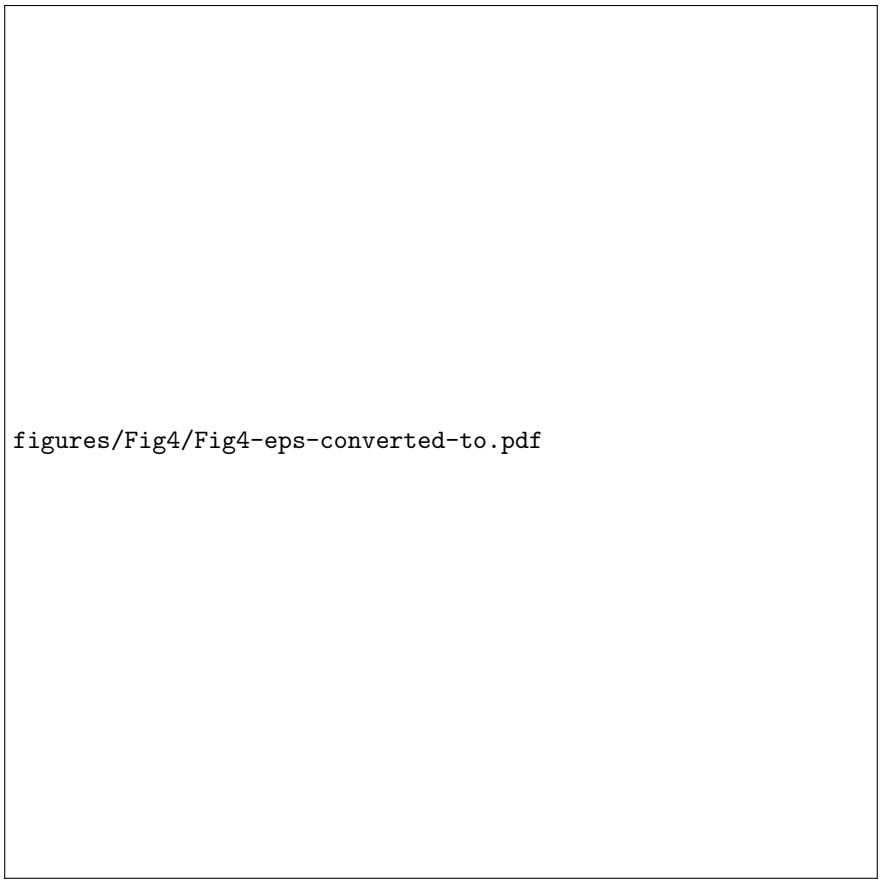

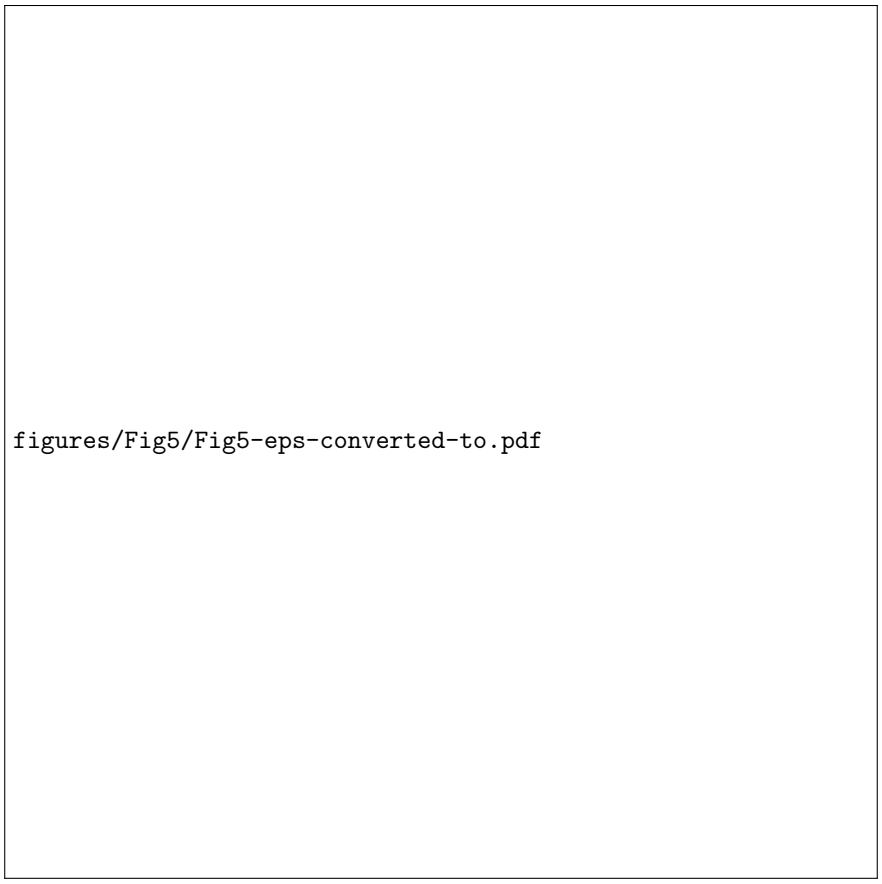

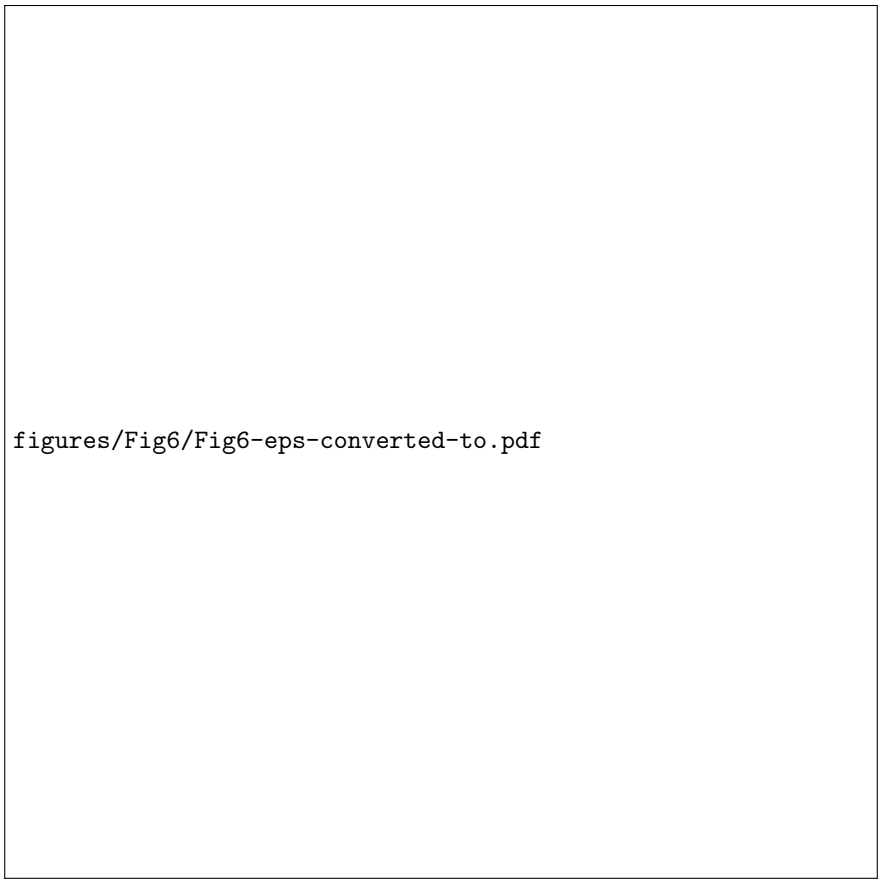

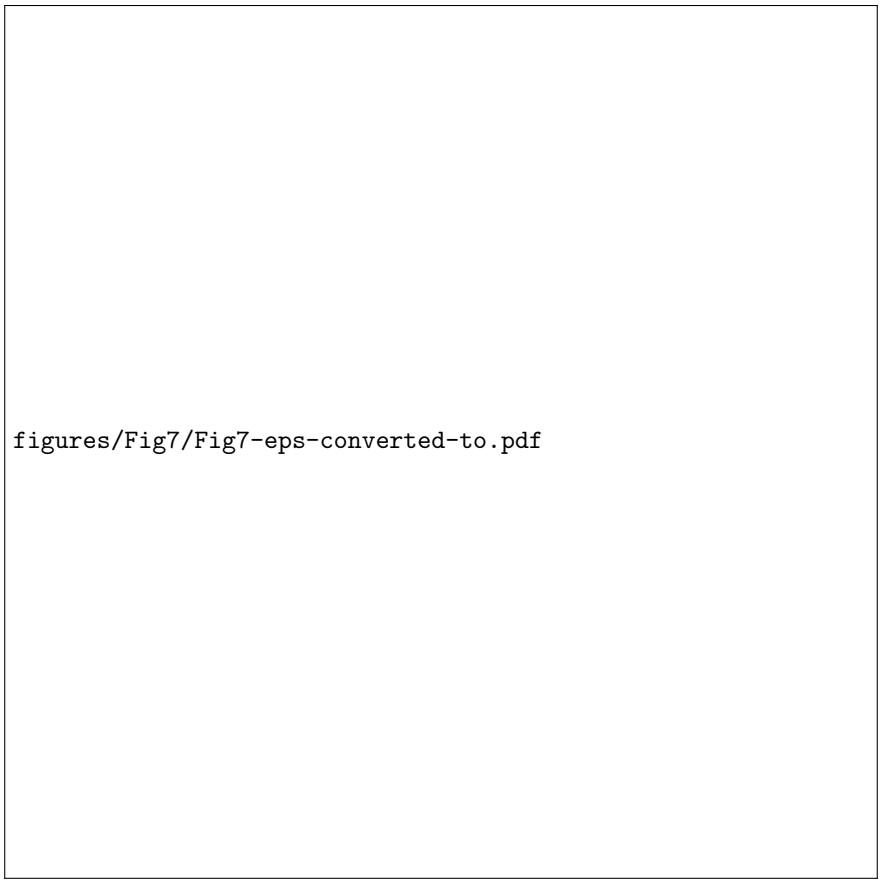

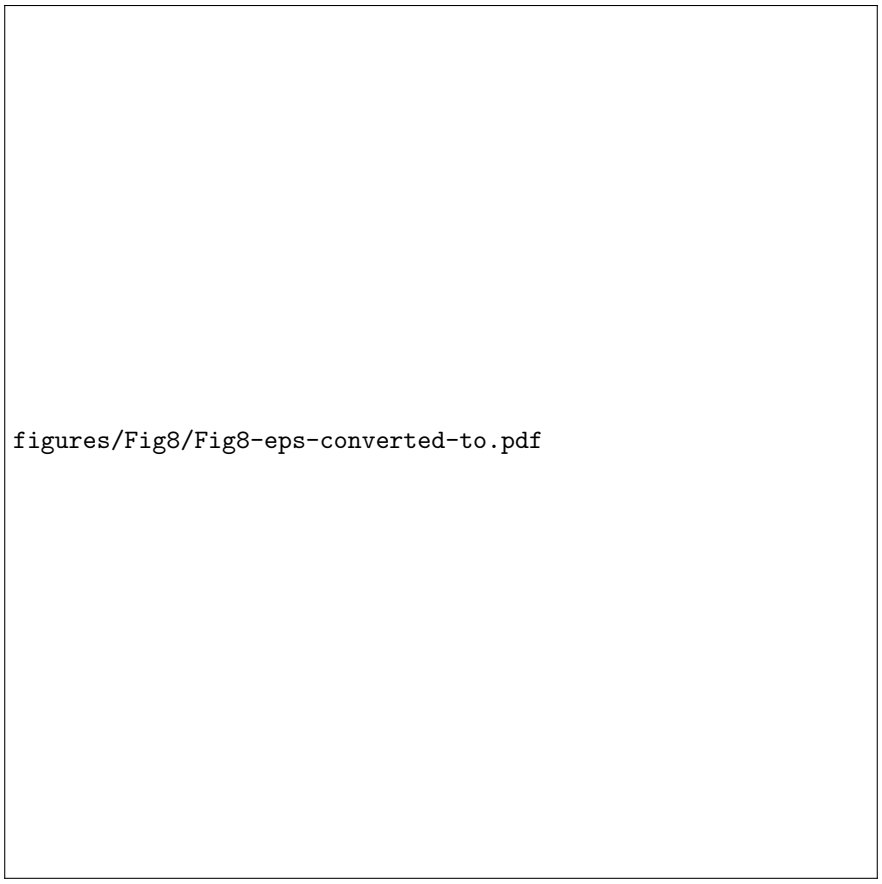

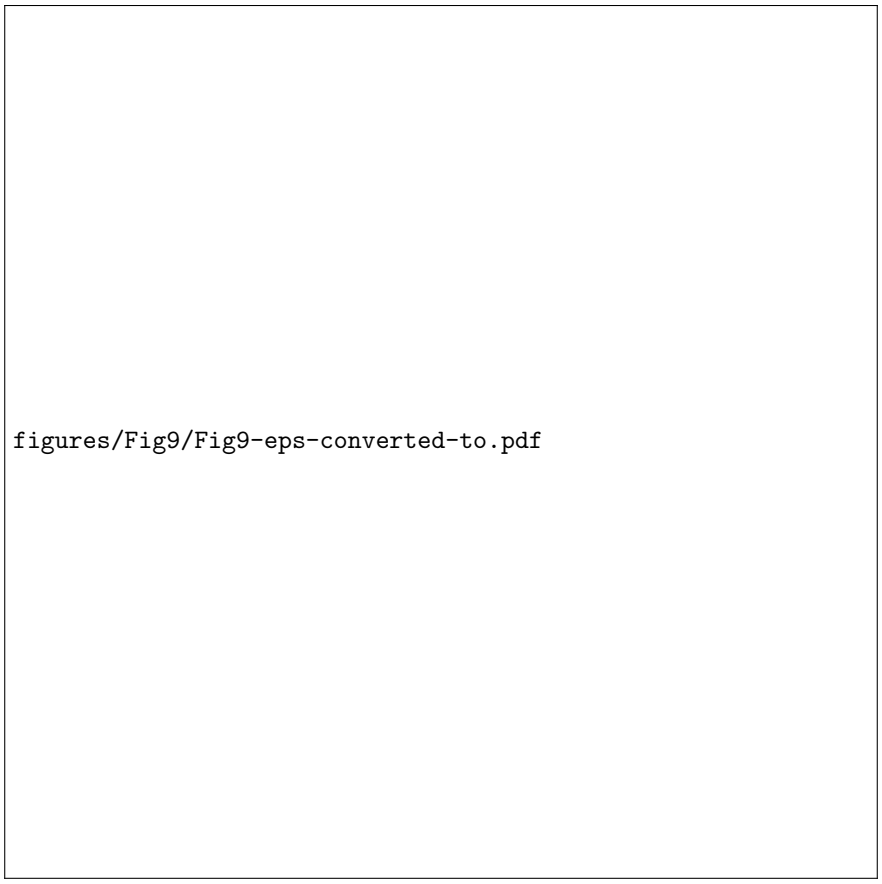

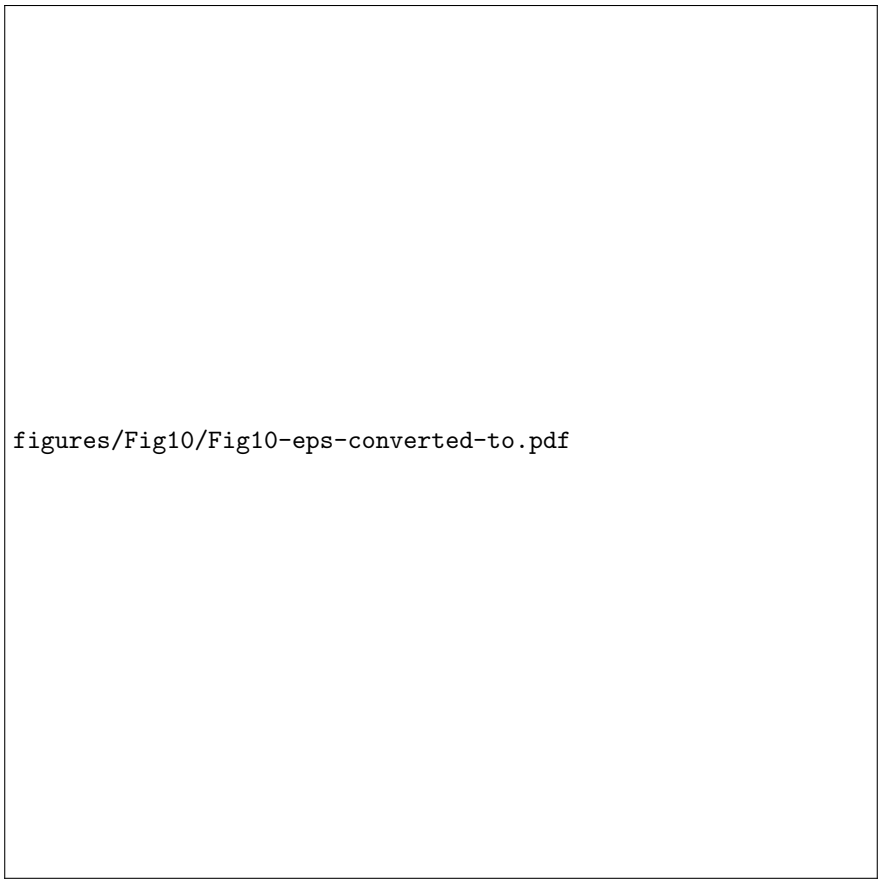

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