Abstract Submitted
for the MAR13 Meeting of
The American Physical Society

Computational studies on DNA recognition of novel organic and copper anti-tumor compounds RAFAEL R. NASCIMENTO, MARCOS B. GONÇALVES, HELENA M. PETRILLI, Instituto de Física, Universidade de São Paulo, Brazil, ANA M. D.C. FERREIRA, Instituto de Química, Universidade de São Paulo, Brazil, EMILIANO IPPOLITI, JENS DREYER, PAOLO CARLONI, German Research School for Simulation Sciences, Forschungszentrum Juelich, Germany — The ability of many organic and coordination compounds to bind to DNA and/or damage cellular structures has been largely exploited in anticancer research. Identifying DNA recognition mechanisms have thus important impact on the chemical biology of gene expression and the development of new drugs and therapies. Previous studies on copper(II) complexes with oxindole-Schiff base ligands have shown their potential anti-tumor activity towards different cells, inducing apoptosis through a preferential attack to DNA and/or mitochondria [SIL11]. The binding mechanism of the organic and copper(II) complexes [Cu(isaepy)2]2+ (1) and [Cu(isaenim)]2+ (2) and their modulation at DNA is investigated through theoretical studies. Here we adopted a multi-scale procedure to simulate this large system using molecular docking and classical molecular dynamics. Hybrid Car-Parrinello/Molecular Mechanics calculations were applied to parameterize the copper(II) complexes by using the force matching approach. Free energies of binding are investigated by metadynamics enhanced sampling methods[VAR08]. [SIL11] V. C. da Silveira et. al. JIB 105 (2011) 1692.[VAR08] A. V. Vargiu et. al. Nucl. Acids Res. 36 (2008) 5910.

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Date submitted: 07 Dec 2012 Electronic form version 1.4