

# Cisplatin under oriented external electric fields: a deeper insight into electrochemotherapy at the molecular level

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## Abstract

Electrochemotherapy is an effective strategy for the treatment of solid tumors by exposing tumor cells to electric fields to enhance the bioactivity of non-permeable or low permeable anticancer drugs, such as cisplatin. To understand the improved efficiency of cisplatin in electrochemotherapy, the effects of oriented external electric fields (OEEFs) on the geometric structures and relevant electronic properties of cisplatin have been systemically investigated by density functional theory (DFT) computations in this work. Our results reveal that the presence of positive OEEFs on cisplatin can not only weaken its Pt-Cl bonds, but also enhance the intramolecular charge transfer in it, which effectively accelerates the critical hydrolysis step involved in the mechanism of its biological activity. Moreover, the positive OEEFs can facilitate the attack of the singly aquated cis-[Pt(NH<sub>3</sub>)<sub>2</sub>(H<sub>2</sub>O)Cl]<sup>+</sup> on DNA, and enlarge the dipole moments and water solubility of cisplatin and its aquated product. Consequently, this work provides a deeper insight into the higher efficacy of electrochemotherapy than traditional chemotherapy from a molecular point of view.

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