Computational Study of SARS-CoV-2 Infection Inhibitor Hydroxychloroquine on Cardiac Toxicity

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Problem Statement

- The outbreak of coronavirus disease 2019 (COVID-19) caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2/2019-nCoV) poses a serious threat to global public health and local economies.
- With the heightened interest of the potential use of chloroquine and hydroxychloroquine for the treatment of patients with SARS-CoV2 (COVID-19 or novel coronavirus)1 it may be prudent to reflect on the risks of therapy, particularly their cardiac toxicity.
- The purpose of this study was to investigate the propensity of hydroxychloroquine (HCQ) to cause bradycardia.

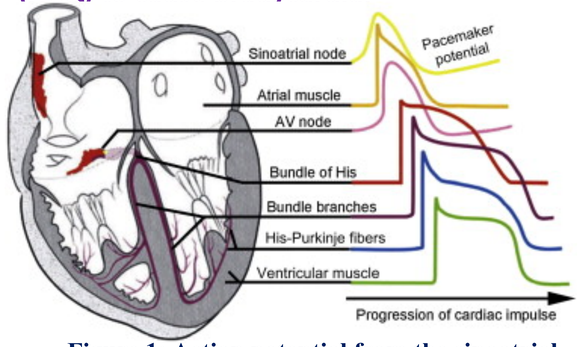

Figure 1: Action potential from the sinoatrial node

Methods

1.Computational modeling

- Physical System
  - Conceptual Model
    - Computational model

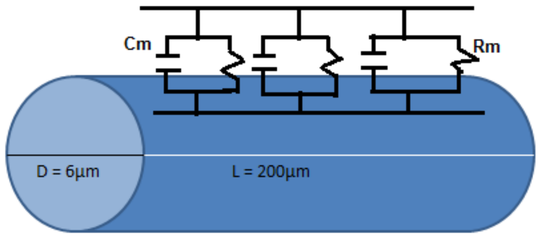

Figure 2: represents the geometrical and biophysical properties of single cell

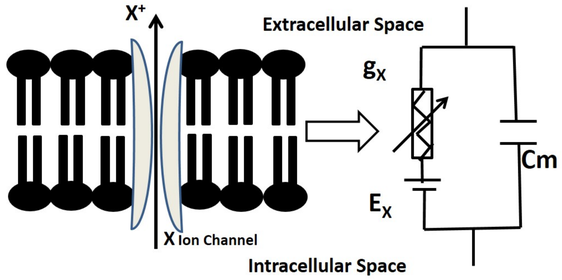

Figure 3: Parallel- Conductance model with Ion channel in Sinoatrial node mode

Results

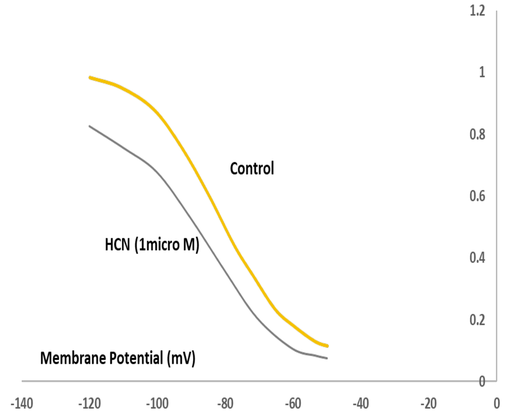

Figure 4: SA node funny current activation parameter at both controlled and HQN applied condition.

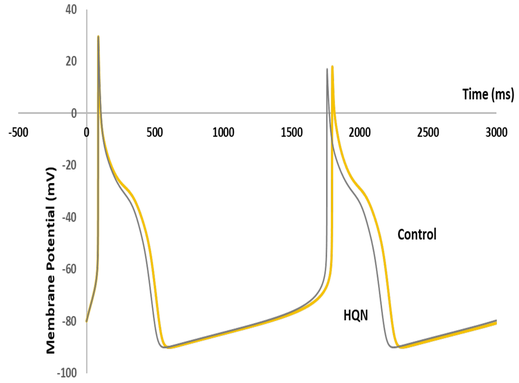

Figure 5: SA node action potential simulation in both control and applied drug conditions.

Conclusions

A modified mathematical model of the cellular electrophysiology of guniea pig SAN cell is proposed.

The model successfully reproduces both ionic currents and action potential observed in intracellular recordings from individual SAN cell.

The effects of Hydroxychloroquine drug are simulated with respect to funny current and action potential.

As Hydroxychloroquin reduces the frequency rate of the spontaneous action potential firing, it should be prevented as a potential drug against COVID-19.

References

Capel RA, Herring N, Kalla M, Yavari A, Mirams GR, Douglas G, Bub G, Channon K, Paterson DJ, Terrar DA, Burton RA. Hydroxychloroquine reduces heart rate by modulating the hyperpolarization-activated current If: Novel electrophysiological insights and therapeutic potential. Heart rhythm. 2015 Oct 1;12(10):2186-94.