

## Supplementary Materials

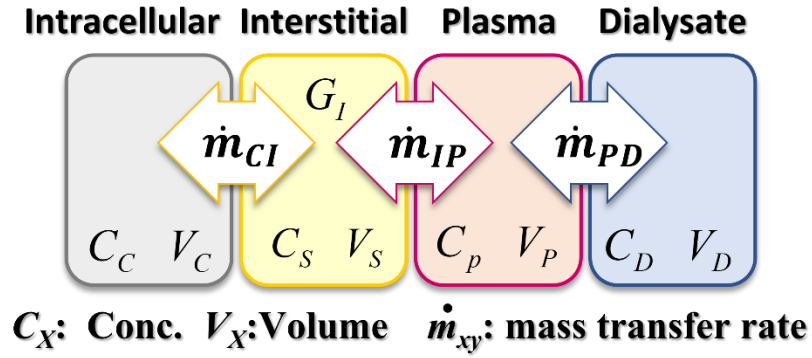


Figure S1. Schematic drawing of the 4-compartment model

ICF, IF, Plasma and DF = intracellular fluid, interstitial fluid, plasma and dialysis fluid, respectively. Mass transfer rates between those spaces are the  $\dot{m}_{CI}$ ,  $\dot{m}_{IP}$  and  $\dot{m}_{PD}$ . The electrolyte concentration and volume in each space are  $C_C$  and  $V_C$  for ICF,  $C_I$  and  $V_I$  for IF,  $C_P$  and  $V_P$  for Plasma, and  $C_D$  and  $V_D$  for DF.

The rights in the material are owned by a third party [10].

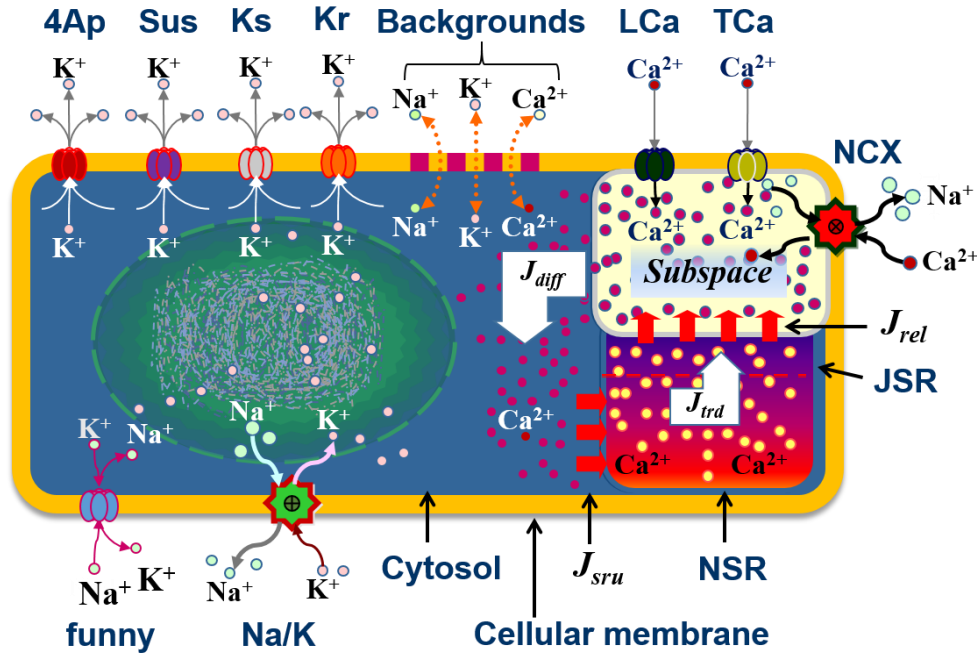


Figure S2. Schematic drawing of sinoatrial nodal cell

Proposed model represented the time courses for membrane voltage ( $V_m$ ) and membrane current ( $I_{tot}$ ) changes, based on the transition of each ion current in more than 10 types of ion channel, the pumps, and the exchanger. Moreover, since a detailed elucidation of excitation-contraction coupling required data about the intracellular local dynamics of electrolytes, the intracellular fluid in the models was divided into the following four spaces: (1) the nearest space to the cellular membrane (subspace); (2) cytosol; (3) the network sarcoplasmic reticulum (NSR); and (4) the junctional sarcoplasmic reticulum (JSR). With each cardiomyocyte beat,  $\text{Ca}^{2+}$  was released from the JSR to the subspace and transported to the JSR via the cytosol and NSR ( $\text{Ca}^{2+}$  circulation). Thus,  $\text{Ca}^{2+}$  concentration in subspace was corresponded to  $C_C$  in Fig. 1. In contrast,  $\text{Na}^+$  and  $\text{K}^+$  were transferred between the extracellular space and the cytosol. Hence,  $\text{Na}^+$  and  $\text{K}^+$  concentrations in cytosol were corresponded to  $C_C$  in Fig. 1. Transporters were abbreviated as follows: LCa = L-type  $\text{Ca}^{2+}$  channel, TCa = T-type  $\text{Ca}^{2+}$  channel, Kr = Kr channel, Ks = Ks channel, 4Ap = 4-aminopyridine-sensitive ion channel, funny = funny channel, Sus = Sustained ion channel, NCX = Na/Ca exchanger, Na/K = Na/K pump, and Backgrounds =  $\text{Na}^+$ ,  $\text{K}^+$ ,  $\text{Ca}^{2+}$  background. The  $\text{Ca}^{2+}$  fluxes were abbreviated as follows:  $J_{rel}$  = ryanodine receptors  $\text{Ca}^{2+}$  release flux,  $J_{diff}$  =  $\text{Ca}^{2+}$  transfer rate from subspace to cytosol,  $J_{sru}$  = SERCa pump  $\text{Ca}^{2+}$  uptake flux from cytosol to NSR, and  $J_{trd}$  =  $\text{Ca}^{2+}$  transfer rate from NSR to JSR. Table S3 shows mathematical equations of ion current in transporters and kinetic models for  $\text{Ca}^{2+}$  fluxes.

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- [10]. Hamada, H.; Tomo, T.; Kim, ST.; Hanai, T.; Okamoto, M.; Yamashita, A.C. Electrophysiological insights into the relationship between calcium dynamics and cardiomyocyte beating function in chronic hemodialysis treatment. *J. Artif. Organs.* **2021**, *24*, 58–64.