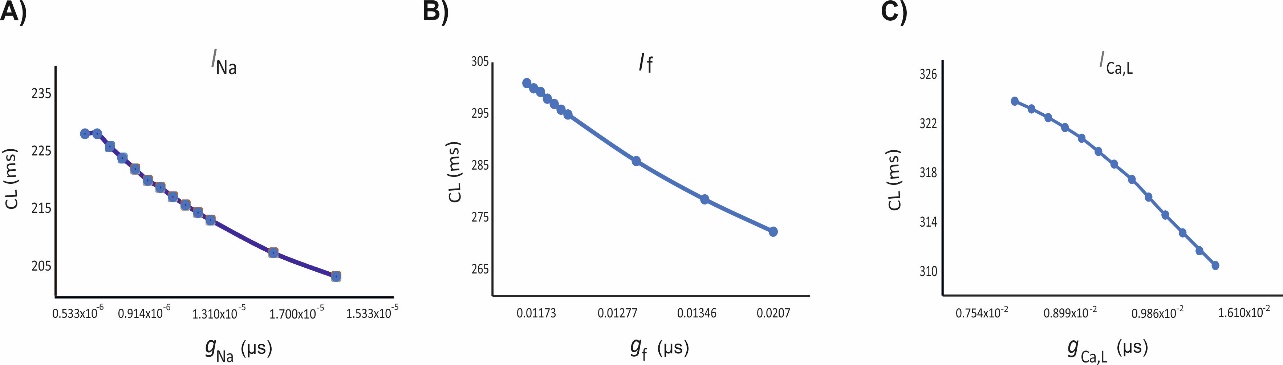
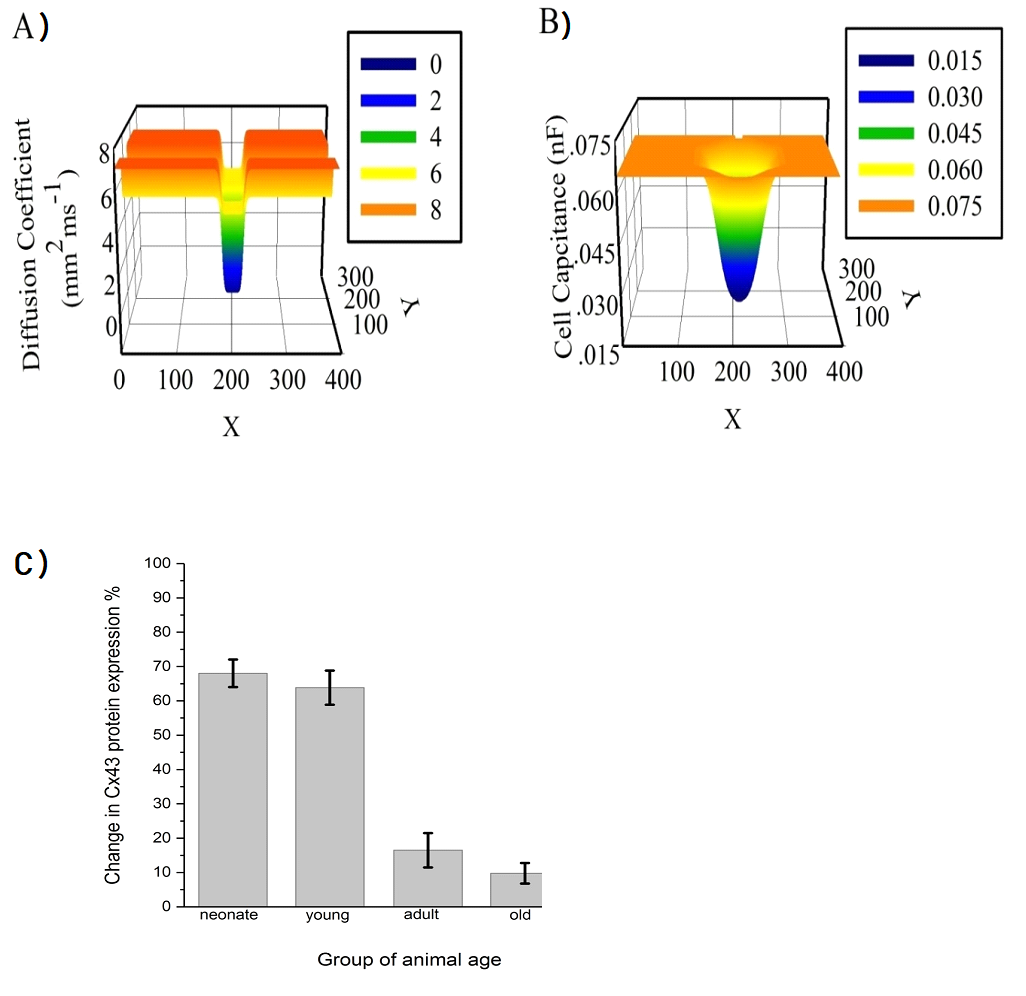
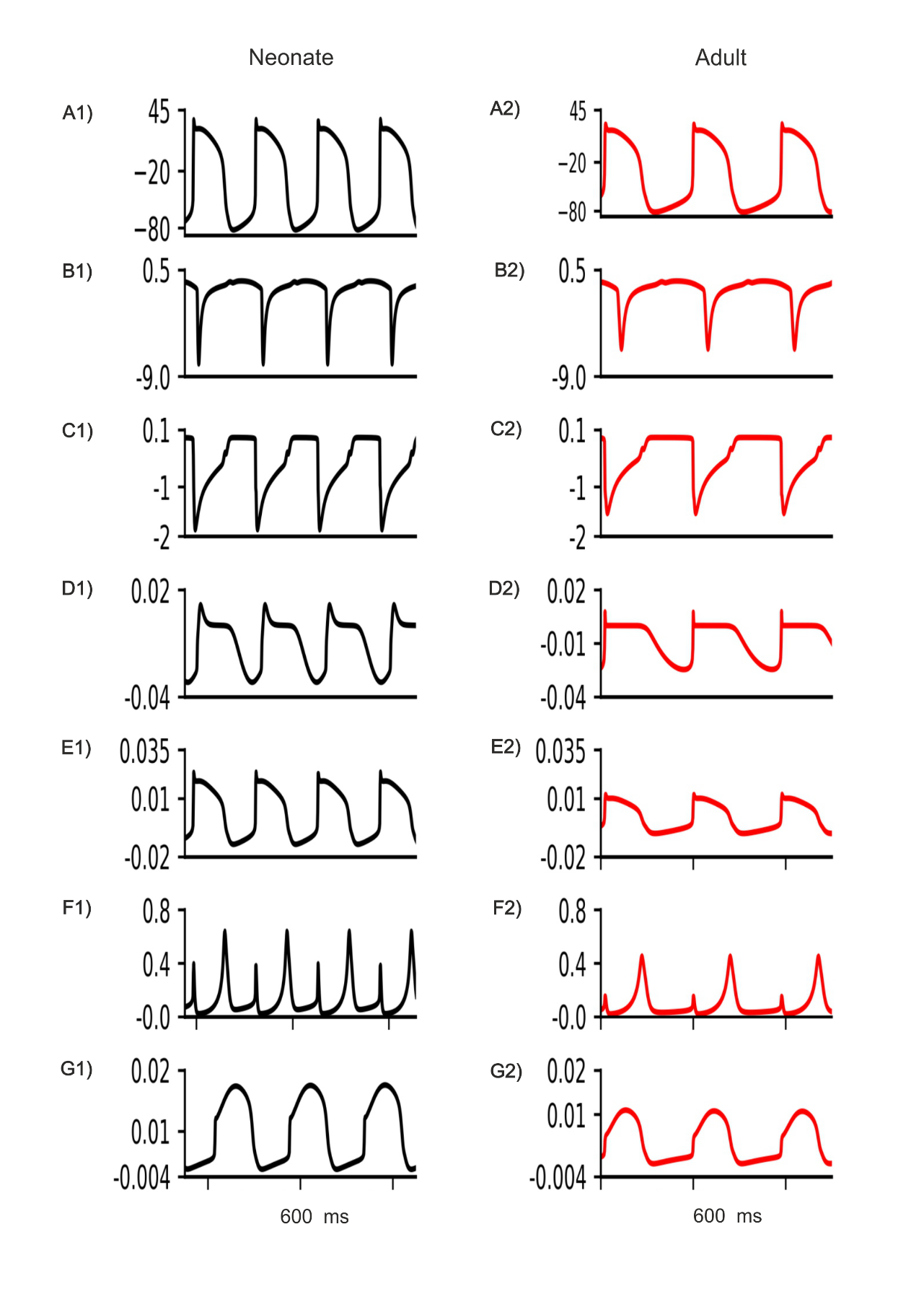
**Supplemental Figures and Table**



**Figure S1.** Sensitivity analyses of the change of the CL as a function of the conductance for *I*Na,(A) *I*Ca,L (B) and *I*f (C) .

**Figure S2.** The gradient distribution in (A) cell capacitance (*C*m) and (B) diffusion (*D*) in both longitudinal and transverse directions of the 2D tissue slice. Figure adapted from [28].The decline of the Cx43 protein expression in the SAN of rat represented as percentage during developmental maturation.(C) [22]



**Figure S3**. Simulated peripheral SAN action potentials in the neonate (black lines) as compared with the adult (red lines) (Ai-Aii) and their underlying time courses of ionic channel currents *I*Na, *I*Ca,L, *I*f, *I*NaCa, *I*Kr and *I*Ks (Bi-Gii).

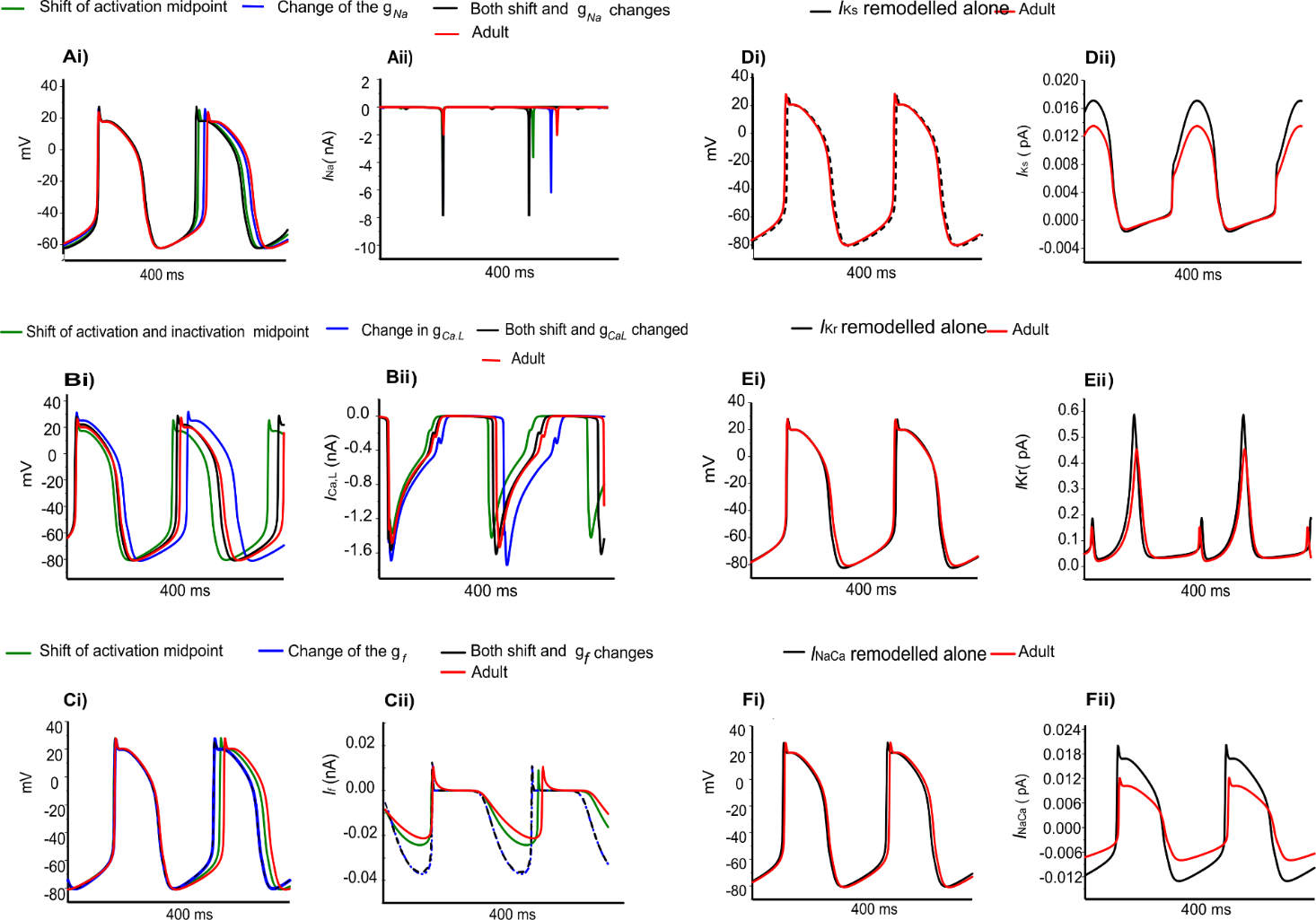
A screenshot of a cell phone

Description automatically generated

**Figure S4**. Bar chart comparison of the main AP characteristic of peripheral SAN cells: MDP (A), TOP (B), PA (C), d*V*/d*t*max (D), reduction of HR (E), and CL (F) in the neonate (grey) corresponding to the adult (red).

**Table S1**. AP characteristics of the neonate and adult peripheral SA node cell models.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | References | PA (mV) | CL (ms) | MDP (mV) | dV/dtmax (V/s) |
| Neonate | Our model | 31.69 | 156.23 | -78.45 | 72.83 |
| Adult | Zhang *et al*.[26] | 23.07 | 175.39 | -77.96 | 70.16 |



**Figure S5.** Simulated individual effects of ion-channel remodelling on central SAN action potentials in the adult and the underlying ionic currents (Ai-Aii) *I*Na, (Bi-Bii) *I*Ca,L, (Ci-Cii) *I*f, (Di-Dii) *I*Kr,(Ei-Eii) *I*Ks and (Fi-Fii) *I*NaCa

A screenshot of a cell phone

Description generated with very high confidence

**Figure S6.** ACh effect at a concentration of 3×10-8M on the propagation of the SAN and surrounding area of the neonate (A) and adult (B) rabbit 2D tissue. Snapshots of the activation pattern at various timings are shown.

A screenshot of a cell phone

Description generated with very high confidence

**Figure S7.** ACh effect at a concentration of 8×10-8M on the propagation of the SAN and surrounding area of the neonate (A) and adult (B) rabbit 2D tissue. Snapshots of the activation pattern at various times are shown.

A close up of a colorful background

Description automatically generated

**Figure S8.** Multi-leading pacemaking sites resulting from ion-channel remodelling in the absence of connexin remodelling. Snapshots of the activation pattern at various timings are shown.

## References

22. Jones SA, Lancaster MK, Boyett MR. Ageing-related changes of connexins and conduction within the sinoatrial node. J Physiol [Internet]. 2004 Oct [cited 2017 Jul 26];560(2):429–37. Available from: http://doi.wiley.com/10.1113/jphysiol.2004.072108

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