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## Understanding the effects of heart beat irregularity on ventricular function in human atrial fibrillation: simulation models may help to untie the knot—Authors' reply

We would like to thank colleagues Masè and Ravelli for their positive comments on our paper and valuable suggestions.<sup>1,2</sup> We certainly share their opinion that the combination of clinical data with computer simulations has the potential to improve our understanding of atrial fibrillation (AF) mechanisms and may help suggest novel targets for therapies.

As they rightfully point out, the model we used in our paper is based solely on the RR interval sequences measured in 10 AF patients, and despite the use of generic simulations to deepen our mechanistic understanding of left ventricular (LV) function changes in AF, the wide range of clinically observed RR sequences may not have been captured to its full extent.

Coupling our model of the heart and circulation<sup>3,4</sup> to the electrical models of atrioventricular (AV) dynamics in AF that Masè and Ravelli

highlighted<sup>5,6</sup> would indeed allow us to inform the CircAdapt model with more complex and realistic RR sequences. It would also make it possible to investigate the mechanistic link between electrical atrial dysfunction and ventricular function in various types of AF. Such a combination of electrical and mechanical computer models would open the possibility to tackle additional clinically relevant research questions such as how atrial dynamics (e.g. atrial flutters) and AV interactions (e.g. AV block) affect beat-to-beat LV haemodynamics and function in AF, or how LV diastolic dysfunction increases the risk for AF and vice versa.

**Conflict of interest:** none declared.

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