Response to Reviewer 2 Comments

**Point 1:** Line 44: the authors say that very high-frequency (VHF) components of HRV are influenced by the autonomic system. Further on, the authors say that ‘cardiac contractility’ contributes to VHF rhythms. This is not much clear, and I would expect only non-autonomic influences in this band, when it is present. Could you please clarify it?

**Response 1:** We carefully changed the physiological significance of VHF from ‘cardiac contractility’ to ‘an indicator of activity of ANS’. After doing lots of research literature, we found that the physiological significance of VHF and VLF band is still controversial. We cannot hastily attribute VHF or VLF to a specific physiological system in absence of an accurate conclusion. The ANS subsystem reflected by VHF may be able to influence ‘cardiac contractility’ (reference [7]), but we cannot assume that VHF component is equivalent to ‘cardiac contractility’. However, there is no doubt that both of them are influenced by ANS, when none of them are susceptible to a simple autonomic branch interpretation (reference [11-17]), as we highlighted in Line 45-46, 257-266 after revision.

**Point 2:** Line 227: automatic nerve system à autonomic nervous system Table 3: as the authors previously stated, VLF band may be influenced by several mechanisms, not only the peripheral nervous system. Consider looking at (Front Physiol 8:255, 2017) for a reasonable interpretation of ultra-rapid oscillations in HRV. Line 261: in general, the predictability of HRV in CHF is lower than in healthy subjects (see Phys Rev E Stat Nonlin Soft Matter Phys71:021906, 2005). Therefore, I do not believe that increased unpredictability is the reason for the diminished coupling between IMFs. The discussion section should be carefully revised, regarding the physiological interpretation. It is based on the factors presented in Table 3 and this table may not be fully correct. Line 281: PNS à SNS

**Response 2:** The spelling mistakes mentioned by the reviewer were corrected. I am really sorry for my carelessness! As mentioned in Point 1, we assumed that VLF and VHF were influenced by complex ANS mechanism, not a specific subsystem like ‘cardiac contractility’ or ‘peripheral nervous system’. The physiological significance of VHF is clarified in Response 2. Likewise, though the ANS subsystem reflected by VLF may have some influence on thermoregulatory mechanisms, renin – angiotensin system and peripheral chemoreceptors (reference [49-51]), we cannot attribute VLF power to them. We revised Table 3, and delete Column “Physiological Meaning” to avoid possible misunderstanding. The physiological significance of these frequency bands is clarified in Line 45-46, 257-266. We have carefully rethought the physiological significance and revised the discussion part according to the comments. This time we do not try to hastily understand the diminished coupling between IMFs from the perspective of unpredictability. The exact conclusion we can draw from this study is TE(*→1) and TE(3→*) is reduced in CHF subjects. We would discuss the physiological significance of this conclusion in the discussion part. The significant difference in TE(*→1) suggests a loss of information flowing from HF, LF and VLF to VHF with disease. Meanwhile, the reduced TE(3→*) value also suggests the reduced information from LF to VHF, HF and VLF. Since these 4 frequency bands represent different branches of ANS, this reduced information demonstrate a weakened coupling strength intra
ANS and thus an ANS dysfunction in CHF groups. CHF has been proved to be a cardiovascular disease along with ANS dysfunction, which is consistent with our study.

**Point 3:** Why would TE represent a marker of autonomic modulation? It should be understood from its definition: information transfer from one signal to another.

**Response 3:** TE can estimate the amount of uncertainty reduced in future values of one time series by knowing the past values of another series, and thus quantify directional coupling zones of physiological systems. Autonomic nerve system includes PNS and SNS, and the 4 frequency bands can represent different branches of ANS to some degree. The reduced TE values among IMFs in CHF groups suggests the loss of information transaction intra ANS, compared with normal controls. The significantly difference of TE values of CHF patients shows an ANS dysfunction and thus can represent a marker of autonomic modulation.