Appendix for "Spatial Correlation Between Myocyte's Repolarization Times and their Alternans Drives T-Wave Alternans on the ECG"

Massimo W. Rivolta, Juan Pablo Martínez, Roberto Sassi, Pablo Laguna*

The following sections must be considered as Appendix of the manuscript "Spatial Correlation Between Myocyte's Repolarization Times and their Alternans Drives T-Wave Alternans on the ECG" published in IEEE Journal of Biomedical and Health Informatics.

All cited sections, equations and figures refer to the original manuscript.

1 Expected value of TWA

We report the mathematical derivation of the expected value of TWA on the surface ECG, according to the second order approximation of $t_d(t)$ in (12) performed with a Taylor's expansion around $\bar{\bar{\rho}}$. TWA can be computed by the difference of the expected values of the lead factors $w_{1,k,l}$ and $w_{2,k,l}$ on consecutive beats, weighted by the beat independent $t_d(t)$ and $\dot{t}_d(t)$, respectively. The derivation is as follows

$$
\begin{aligned}
\mathbb{E}\left[w_{1,k,l}\right] &= -\sum_{m=1}^{M} A_{l,m}\mathbb{E}\left[\theta_m + \bar{\phi}_k + \phi_{k,m} + (-1)^k \frac{a_m}{2}\right] \\
&= -\sum_{m=1}^{M} A_{l,m}\left(\theta_m + (-1)^k \frac{a_m}{2}\right) \\
\mathbb{E}\left[w_{2,k,l}\right] &= \frac{1}{2}\sum_{m=1}^{M} A_{l,m}\mathbb{E}\left[\left(\theta_m + \bar{\phi}_k + \phi_{k,m} + (-1)^k \frac{a_m}{2}\right)^2\right] \\
&= \frac{1}{2}\sum_{m=1}^{M} A_{l,m}\left(\theta_m^2 + \sigma_{\bar{\phi}}^2 + \sigma_{\phi}^2 + \frac{a_m^2}{4} + (-1)^k\theta_m a_m\right).
\end{aligned}
$$

Then, since $t_d(t)$ is constant across beats, the expected value of TWA becomes

$$
\begin{aligned}
&\left|\mathbb{E}\left[\psi_{2i,l}(t) - \psi_{2i-1,l}(t)\right]\right| \\
&\approx \left| - t_d(t)\sum_{m=1}^{M} A_{l,m}a_m + \dot{t}_d(t)\sum_{m=1}^{M} A_{l,m}\theta_m a_m\right| \\
&= \left| - t_d(t)\sum_{m=1}^{M} A_{l,m}\delta_m + \dot{t}_d(t)\sum_{m=1}^{M} A_{l,m}\theta_m(\bar{\delta} + \delta_m)\right|,
\end{aligned}
$$

2 Quantification of alternating $\mathcal{V}$-index

Here, we report the mathematical derivation of the difference between the $\mathcal{V}$-index $v_{2i,l}^2$ and $v_{2i-1,l}^2$ when Taylor's expansion is performed around either $\bar{\bar{\rho}}$ or $\bar{\rho}_k$.

*M. W. R. and R. S. are with the Dipartimento di Informatica, Università degli Studi di Milano, Via Celoria 18, 20133, Milan (MI), Italy. Corresponding author's email: massimo.rivolta@unimi.it

J. P. M. and P. L. are with the BSICoS Group, Aragón Institute of Engineering Research, IIS Aragón, Universidad de Zaragoza, Zaragoza, Spain and with the CIBER en Bioingenierìa, Biomateriales y Nanomedicina (CIBER-BBN), Spain.

When considering the Taylor's expansion in $\bar{\bar{\rho}}$, following the methodology reported in sec. II.B, the $\mathcal{V}$-index is the ratio of ensemble variance $w_{2,k,l}$ and $w_{1,k,l}$ at k-th beat and l-th lead. For compactness, let us define the quantity $x_{k,m} = \bar{\phi}_k + \phi_{k,m} + b_{k,m}$ where $b_{k,m} = \theta_m + (-1)^k a_m/2$.

The variance of $w_{1,k,l}$ becomes

$$\begin{aligned}
\mathrm{var}\left[w_{1,k,l}\right] &= \mathrm{var}\left[-\sum_{m=1}^{M} A_{l,m} x_{k,m}\right] \\
&= \sum_{m=1}^{M} A_{l,m}^2 \mathrm{var}\left[x_{k,m}\right] \\
&+ \sum_{m=1}^{M} \sum_{n \neq m}^{M} A_{l,m} A_{l,n} \mathrm{cov}[x_{k,m}, x_{k,n}] \\
&= \sum_{m=1}^{M} A_{l,m}^2 \left(\sigma_{\bar{\phi}}^2 + \sigma_{\phi}^2\right) - \sigma_{\bar{\phi}}^2 \sum_{m=1}^{M} A_{l,m}^2 = \sigma_{\phi}^2 \sum_{m=1}^{M} A_{l,m}^2,
\end{aligned}$$

Differently from the original formulation of the $\mathcal{V}$-index, $\mathrm{cov}[x_{k,m}, x_{k,n}] \neq 0$ because each myocyte of a beat k shares $\bar{\phi}_k$ with all the others. In addition, $\sum_{m=1}^{M} \sum_{n \neq m}^{M} A_{l,m} A_{l,n} = -\sum_{m=1}^{M} A_{l,m}^2$ due to the fact that $\sum_{m=1}^{M} A_{l,m} = 0$.

Similarly, the variance of $w_{2,k,l}$ is

$$\begin{aligned}
\mathrm{var}\left[w_{2,k,l}\right] &= \mathrm{var}\left[\frac{1}{2} \sum_{m=1}^{M} A_{l,m} x_{k,m}^2\right] \\
&= \frac{1}{4} \sum_{m=1}^{M} A_{l,m}^2 \mathrm{var}\left[x_{k,m}^2\right] \\
&+ \frac{1}{4} \sum_{m=1}^{M} \sum_{n \neq m}^{M} A_{l,m} A_{l,n} \mathrm{cov}[x_{k,m}^2, x_{k,n}^2] \\
&= \frac{\sigma_{\phi}^4}{2} \sum_{m} A_{l,m}^2 + \sigma_{\bar{\phi}}^2 \sigma_{\phi}^2 \sum_{m} A_{l,m}^2 + \sigma_{\phi}^2 \sum_{m} A_{l,m}^2 b_{k,m}^2 \\
&+ \sigma_{\bar{\phi}}^2 \sum_{m,n} A_{l,m} A_{l,m} b_{k,n} b_{k,n}
\end{aligned}$$

The $\mathcal{V}$-index becomes

$$\begin{aligned}
v_{k,l}^2 &= \frac{\mathrm{var}[w_{2,k,l}]}{\mathrm{var}[w_{1,k,l}]} \\
&= \frac{\sigma_{\phi}^2}{2} + \sigma_{\bar{\phi}}^2 + s_{\theta\theta} + \frac{1}{4} s_{aa} + (-1)^k s_{\theta\delta} \\
&+ \eta_{\theta\theta,l} + \frac{1}{4} \eta_{aa,l} + (-1)^k \eta_{\theta a,l} \\
&+ \frac{\sigma_{\bar{\phi}}^2}{\sigma_{\phi}^2} \frac{\sum_{m,n} A_{l,m} A_{l,n} \left(\theta_m + (-1)^k \frac{a_m}{2}\right) \left(\theta_n + (-1)^k \frac{a_n}{2}\right)}{\sum_m A_{l,m}^2}
\end{aligned}$$

Finally, the difference between $v_{2i,l}^2$ and $v_{2i-1,l}^2$ is

$$|v_{2i,l}^2 - v_{2i-1,l}^2| = 2\left|s_{\theta\delta} + \eta_{\theta a,l} + f_l^2\right|$$

where f_l^2 is the one reported in (15).

When considering the Taylor's expansion in $\bar{\rho}_k$ (as in our second formulation), the terms $\bar{\phi}_k$ and $\bar{\delta}$ are absorbed, thus making the standard deviation of the former $\sigma_{\bar{\phi}}$ and the latter quantity equal to 0, obtaining

$$|v_{2i,l}^2 - v_{2i-1,l}^2| = 2\left|s_{\theta\delta} + \eta_{\theta\delta,l}\right|$$