Supporting Information: Calculating sensitivity and specificity of a parallel test

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15 March 2022

Prerequisites

As in Wang & Hanson (2019)[1], we assume that our study design comprises K binary diagnostic tests over J time points ($J, K \in \mathbb{N}_{>0}$). In the original article, $T_{ijk} = 1$ denotes a positive test result using test k on individual i on time point j, and $T_{ijk} = 0$ denotes a negative test result in the same setting. For our considerations, we can drop index i and will consider $J \times K$ matrices T containing binary test results.

Sensitivity of test k is denoted as $Se_k = \mathrm{P}(T_{jk} = 1 \mid D = 1)$ and specificity of test k is denoted as $Sp_k = \mathrm{P}(T_{jk} = 0 \mid D = 0)$ with respect to the true disease state D ($D = 1$ for presence, $D = 0$ for absence of disease) for $j \in 1, 2, \ldots, J$. As in the original article, $C^+_{k_1 k_2}$ denotes the pairwise correlation between test k_1 and k_2 ($k_1, k_2 \in \{1, \ldots, K\}$), and R^+_k denotes the correlation between repeated measurements using test k, both considering only diseased cases. In the same way, $C^-_{k_1 k_2}$ denotes the pairwise correlation between tests k_1 and k_2, and R^-_k denotes the correlation between repeats of test k, considering only non-diseased cases. All of these parameters above, sensitivity, specificity, true disease state and correlation between tests, are assumed to be static and thus independent of time point j. This applies as well to the correlation between repeated measurements, denoted by R^+_k and R^-_k, respectively, which is assumed to be independent of the two time points j_1 and $j_2 \in 1, 2, \ldots, J$, and thus the order of observations is considered exchangeable.

As presented in Wang & Hanson (2019), a parallel test refers to a combination of multiple tests and / or multiple time points. A parallel test is considered positive, if any of the included test results is positive, otherwise it is considered negative. In this way, the combination of test results yields an increase in sensitivity (see Wang & Hanson, 2019). In the original article, this interpretation is denoted using the union symbol $\cup$, which we will also use here.

We introduce set $\mathcal{J} = \{1, \ldots, J\}$ and set $\mathcal{K} = \{1, \ldots, K\}$. Let $\widetilde{J}$ denote the number of repeated measurements ($\widetilde{J} \in \mathbb{N}$, $\widetilde{J} < J$) included in the parallel test. Since repeated applications of a specific test are assumed to be exchangeable over time, the respective index set of repeats $\widetilde{\mathcal{J}}$ equals $\{1, \ldots, \widetilde{J}\}$. Let $\widetilde{\mathcal{K}}$ denote the set of diagnostic tests included in the parallel test, i.e. $\widetilde{\mathcal{K}} \subset \mathcal{K}$, and let $\widetilde{K} := |\widetilde{\mathcal{K}}|$ denote the number of diagnostic tests included in the parallel test. So the specificity of a parallel test is given by

$$\mathrm{P}\left(\bigcup_{j \in \widetilde{\mathcal{J}},\, k \in \widetilde{\mathcal{K}}} T_{jk} = 0 \mid D = 0 \right)$$

[1] Wang, C, Hanson, TE. Estimation of sensitivity and specificity of multiple repeated binary tests without a gold standard. Statistics in Medicine. 2019; 38: 2381– 2390. https://doi.org/10.1002/sim.8114

and the sensitivity of a parallel test is given by

$$\mathrm{P}\left(\bigcup_{j \in \widetilde{\mathcal{J}},\, k \in \widetilde{\mathcal{K}}} T_{jk} = 1 \mid D = 1 \right).$$

For the latter, it is more efficient to consider the complementary event, as a negative result for a parallel test implies that every single test result needs to be negative. Therefore, we will make use of the equality

$$\mathrm{P}\left(\bigcup_{j \in \widetilde{\mathcal{J}},\, k \in \widetilde{\mathcal{K}}} T_{jk} = 1 \mid D = 1 \right) = 1 - \mathrm{P}\left(\bigcup_{j \in \widetilde{\mathcal{J}},\, k \in \widetilde{\mathcal{K}}} T_{jk} = 0 \mid D = 1 \right).$$

Thus, for both sensitivity and specificity of a parallel test, we have to include all matrices of possible test results with $T_{jk} = 0$, if $j \in \widetilde{\mathcal{J}}$ and $k \in \widetilde{\mathcal{K}}$, and $T_{jk} \in \{0, 1\}$ for $j \in \mathcal{J} \setminus \widetilde{\mathcal{J}}$ or $k \in \mathcal{K} \setminus \widetilde{\mathcal{K}}$. These matrices can be visualized in the following way (with rearrangement of columns $\{1, \ldots, K\}$ to $\{\widetilde{\mathcal{K}} \cup (\mathcal{K} \setminus \widetilde{\mathcal{K}})\}$):

$$\begin{matrix} \widetilde{\mathcal{J}}\left\{\vphantom{\begin{matrix}0\\ \vdots\\ 0\end{matrix}}\right. \\ \vphantom{\begin{matrix}\bullet\\ \vdots\\ \bullet\end{matrix}} \end{matrix} \left.\underbrace{\begin{pmatrix} \overbrace{\begin{matrix}0 & \cdots & 0\\ \vdots & & \vdots\\ 0 & \cdots & 0\end{matrix}}^{\widetilde{\mathcal{K}}} & \begin{matrix}\bullet & \cdots & \bullet\\ \vdots & & \vdots\\ \bullet & \cdots & \bullet\end{matrix} \\ \begin{matrix}\bullet & \cdots & \bullet\\ \vdots & & \vdots\\ \bullet & \cdots & \bullet\end{matrix} & \begin{matrix}\bullet & \cdots & \bullet\\ \vdots & & \vdots\\ \bullet & \cdots & \bullet\end{matrix} \end{pmatrix}}_{\mathcal{K}}\right\} \mathcal{J}$$

Let $\mathcal{T}$ denote the set of such matrices T (so $|\mathcal{T}| = 2^{JK - \widetilde{J}\widetilde{K}}$). Therefore, for the sensitivity of a parallel test we have to calculate

$$\mathrm{P}\left(\bigcup_{j \in \widetilde{\mathcal{J}},\, k \in \widetilde{\mathcal{K}}} T_{jk} = 0 \mid D = 1 \right) = \sum_{t \in \mathcal{T}} \mathrm{P}(T = t \mid D = 1) = \sum_{t \in \mathcal{T}} d^{+}(1 + \widetilde{tc}^{+} + \widetilde{rc}^{+}) \tag{1}$$

with

$$d^{+} = \prod_{k \in \mathcal{K}} Se_k^{\sum_{j \in \mathcal{J}} t_{jk}} (1 - Se_k)^{J - \sum_{j \in \mathcal{J}} t_{jk}},$$

$$\widetilde{tc}^{+} = \sum_{j \in \mathcal{J}} \sum_{\substack{u, v \in \mathcal{K} \\ u < v}} C^{+}_{uv} \frac{\left(\frac{Se_u - 1}{Se_u}\right)^{t_{ju}} \left(\frac{Se_v - 1}{Se_v}\right)^{t_{jv}}}{(1 - Se_u)(1 - Se_v)},$$

and

$$\widetilde{rc}^{+} = \sum_{k \in \mathcal{K}} \sum_{\substack{u, v \in \mathcal{J} \\ u < v}} R^{+}_{k} \frac{\left(\frac{Se_k - 1}{Se_k}\right)^{t_{uk} + t_{vk}}}{(1 - Se_k)^2},$$

as given in Wang & Hanson (2019). Similarly, the specificity of a parallel test is calculated as

$$\mathrm{P}\left(\bigcup_{j \in \widetilde{\mathcal{J}},\, k \in \widetilde{\mathcal{K}}} T_{jk} = 0 \mid D = 0 \right) = \sum_{t \in \mathcal{T}} \mathrm{P}(T = t \mid D = 0) = \sum_{t \in \mathcal{T}} d^{-}(1 + \widetilde{tc}^{-} + \widetilde{rc}^{-}) \tag{2}$$

with

$$d^- = \prod_{k\in\mathcal{K}} Sp_k^{J-\sum\limits_{j\in\mathcal{J}} t_{jk}} (1-Sp_k)^{\sum\limits_{j\in\mathcal{J}} t_{jk}},$$

$$\widetilde{tc}^- = \sum_{j\in\mathcal{J}} \sum_{\substack{u,v\in\mathcal{K}\\ u<v}} C_{uv}^- \frac{\left(\frac{Sp_u}{Sp_u-1}\right)^{t_{ju}} \left(\frac{Sp_v}{Sp_v-1}\right)^{t_{jv}}}{Sp_u Sp_v},$$

and

$$\widetilde{rc}^- = \sum_{k\in\mathcal{K}} \sum_{\substack{u,v\in\mathcal{J}\\ u<v}} R_k^- \frac{\left(\frac{Sp_k}{Sp_k-1}\right)^{t_{uk}+t_{vk}}}{Sp_k^2}.$$

These formulas can be simplified for our purposes, since tests and time points not included in a parallel test do not contribute to the estimators for the parallel test. Thus, calculations reduce to the zero submatrix of dimension $\widetilde{J}\times\widetilde{K}$. We will show this in more detail in the following sections.

Sensitivity of parallel tests

We split Equation (1) into three parts:

$$\sum_{t\in\mathcal{T}} d^+(1+\widetilde{tc}^+ + \widetilde{rc}^+) = \sum_{t\in\mathcal{T}} d^+ + \sum_{t\in\mathcal{T}} d^+\widetilde{tc}^+ + \sum_{t\in\mathcal{T}} d^+\widetilde{rc}^+ \tag{3}$$

As stated above, the set $\mathcal{T}$ contains $2^{JK-\widetilde{J}\widetilde{K}}$ distinct matrices (t_{jk}) with $t_{jk}=0$, if $j\in\widetilde{\mathcal{J}}$ and $k\in\widetilde{\mathcal{K}}$, and $t_{jk}\in\{0,1\}$ otherwise. Since all elements of the matrix are either 0 or 1, the sum of column k, $\sum_{j=1}^{J} t_{jk}$, corresponds to the number of entries in column k equal to 1. Let n_k denote a fixed column sum for column k. There are $\binom{J}{n_k}$ possible configurations of n_k ones and $J-n_k$ zeros, so $\binom{J}{n_k}$ possible configurations with sum n_k exist for column $k\in\mathcal{K}\setminus\widetilde{\mathcal{K}}$. For $k\in\widetilde{\mathcal{K}}$, there are $\binom{J-\widetilde{J}}{n_k}$ possible configurations, because $\widetilde{J}$ entries of the column are set to zero. This allows to replace the sum over $t\in\mathcal{T}$ by summation over all possible combinations of column sums. We denote this as vectors $n=(n_1,\ldots,n_K)^T$, with element i of n being the column sum n_i of column i, and set $\mathcal{N}$ containing all possible vectors of column sums respective to $\mathcal{T}$, which means that $n_k\in\{0,\ldots,J-\widetilde{J}\}$ for $k\in\widetilde{\mathcal{K}}$ and $n_k\in\{0,\ldots,J\}$ for $k\in\mathcal{K}\setminus\widetilde{\mathcal{K}}$. Thus, $|\mathcal{N}|=(J-\widetilde{J}+1)^{\widetilde{K}}(J+1)^{K-\widetilde{K}}$. Each element $n\in\mathcal{N}$ relates to $\prod_{\tilde{k}\in\widetilde{\mathcal{K}}}\binom{J-\widetilde{J}}{n_{\tilde{k}}}\prod_{k'\in\mathcal{K}\setminus\widetilde{\mathcal{K}}}\binom{J}{n_{k'}}$ elements in $\mathcal{T}$.

As an abbreviation, we denote the maximum column sum as

$$m_k := \begin{cases} J, & \text{if } k\in\mathcal{K}\setminus\widetilde{\mathcal{K}},\\ J-\widetilde{J}, & \text{if } k\in\widetilde{\mathcal{K}}.\end{cases}$$

With this, we can calculate $\sum_{t\in\mathcal{T}} d^+$ as follows:

$$\begin{aligned}
\sum_{t\in\mathcal{T}} d^+ &= \sum_{t\in\mathcal{T}}\prod_{k\in\mathcal{K}} Se_k^{\sum\limits_{j\in\mathcal{J}} t_{jk}} (1-Se_k)^{J-\sum\limits_{j\in\mathcal{J}} t_{jk}}\\
&= \sum_{n\in\mathcal{N}}\left[\prod_{\tilde{k}\in\widetilde{\mathcal{K}}}\left(\binom{J-\widetilde{J}}{n_{\tilde{k}}} Se_{\tilde{k}}^{n_{\tilde{k}}}(1-Se_{\tilde{k}})^{J-n_{\tilde{k}}}\right)\prod_{k\in\mathcal{K}\setminus\widetilde{\mathcal{K}}}\left(\binom{J}{n_k} Se_k^{n_k}(1-Se_k)^{J-n_k}\right)\right]\\
&= \prod_{k'\in\widetilde{\mathcal{K}}}(1-Se_{k'})^{\widetilde{J}}\sum_{n\in\mathcal{N}}\left[\prod_{\tilde{k}\in\widetilde{\mathcal{K}}}\left(\binom{J-\widetilde{J}}{n_{\tilde{k}}} Se_{\tilde{k}}^{n_{\tilde{k}}}(1-Se_{\tilde{k}})^{J-\widetilde{J}-n_{\tilde{k}}}\right)\prod_{k\in\mathcal{K}\setminus\widetilde{\mathcal{K}}}\left(\binom{J}{n_k} Se_k^{n_k}(1-Se_k)^{J-n_k}\right)\right]
\end{aligned}$$

$$
\begin{aligned}
&= \prod_{k'\in\widetilde{\mathcal{K}}} (1-Se_{k'})^{\widetilde{J}} \sum_{n\in\mathcal{N}} \prod_{k\in\mathcal{K}} \left(\binom{m_k}{n_k} Se_k^{n_k}(1-Se_k)^{m_k-n_k}\right)\\
&= \prod_{k'\in\widetilde{\mathcal{K}}} (1-Se_{k'})^{\widetilde{J}} \sum_{n_1=0}^{m_1}\sum_{n_2=0}^{m_2}\dots\sum_{n_K=0}^{m_K} \prod_{k\in\mathcal{K}} \left(\binom{m_k}{n_k} Se_k^{n_k}(1-Se_k)^{m_k-n_k}\right)\\
&= \prod_{k'\in\widetilde{\mathcal{K}}} (1-Se_{k'})^{\widetilde{J}} \prod_{k\in\mathcal{K}} \underbrace{\sum_{n_k=0}^{m_k} \left(\binom{m_k}{n_k} Se_k^{n_k}(1-Se_k)^{m_k-n_k}\right)}_{=(Se_k+1-Se_k)^{m_k}=1}\\
&= \prod_{k'\in\widetilde{\mathcal{K}}} (1-Se_{k'})^{\widetilde{J}}
\end{aligned}
$$

This is also part of the second summand of Equation (3):

$$
\sum_{t\in\mathcal{T}} d^+\widetilde{tc}^+ = \sum_{t\in\mathcal{T}}\left[\prod_{k\in\mathcal{K}}\left(Se_k^{\sum\limits_{j\in\mathcal{J}} t_{jk}}(1-Se_k)^{J-\sum\limits_{j\in\mathcal{J}} t_{jk}}\right)\sum_{j'\in\mathcal{J}}\sum_{\substack{u,v\in\mathcal{K}\\u<v}}\left(C^+_{uv}\frac{\left(\frac{Se_u-1}{Se_u}\right)^{t_{j'u}}\left(\frac{Se_v-1}{Se_v}\right)^{t_{j'v}}}{(1-Se_u)(1-Se_v)}\right)\right] \tag{4}
$$

We focus on $\widetilde{tc}^+$ for the next steps. Let $u, v \in \mathcal{K}$, $n_u = \sum_{j=1}^J t_{ju}$, $n_v = \sum_{j=1}^J t_{jv}$. As stated before, there are $\binom{m_u}{n_u}\binom{m_v}{n_v}$ possible configurations of columns u, v yielding sums n_u, n_v. If $j \in \mathcal{J}\setminus\widetilde{\mathcal{J}}$, these can be divided into $\binom{m_u-1}{n_u}\binom{m_v-1}{n_v}$ configurations with $t_{ju} = 0, t_{jv} = 0$, $\binom{m_u-1}{n_u}\binom{m_v-1}{n_v-1}$ configurations with $t_{ju} = 0, t_{jv} = 1$, $\binom{m_u-1}{n_u-1}\binom{m_v-1}{n_v}$ configurations with $t_{ju} = 1, t_{jv} = 0$, and $\binom{m_u-1}{n_u-1}\binom{m_v-1}{n_v-1}$ configurations with $t_{ju} = 1, t_{jv} = 1$ (for $1 \le n_u < m_u$ and $1 \le n_v < m_v$, for $n_u \in \{0, m_u\}$, $n_v \in \{0, m_v\}$ see below). Otherwise, if $j \in \widetilde{\mathcal{J}}$, and $u, v \in \widetilde{\mathcal{K}}$, then $t_{ju} = 0$ and $t_{jv} = 0$ in all $\binom{m_u}{n_u}\binom{m_v}{n_v}$ cases. If $j \in \widetilde{\mathcal{J}}$, and $u \in \widetilde{\mathcal{K}}$, but $v \in \mathcal{K}\setminus\widetilde{\mathcal{K}}$, then $t_{ju} = 0, t_{jv} = 0$ in $\binom{m_u}{n_u}\binom{m_v-1}{n_v}$ configurations, and $t_{ju} = 0, t_{jv} = 1$ in $\binom{m_u}{n_u}\binom{m_v-1}{n_v-1}$ configurations. Analogously, if $j \in \widetilde{\mathcal{J}}$ and $v \in \widetilde{\mathcal{K}}$, but $u \in \mathcal{K}\setminus\widetilde{\mathcal{K}}$, then $t_{ju} = 0, t_{jv} = 0$ in $\binom{m_u-1}{n_u}\binom{m_v}{n_v}$ configurations, and $t_{ju} = 1, t_{jv} = 0$ in $\binom{m_u-1}{n_u-1}\binom{m_v}{n_v}$ configurations. Finally, if $j \in \widetilde{\mathcal{J}}$ and $u, v \in \mathcal{K}\setminus\widetilde{\mathcal{K}}$, then we obtain the same results as for $j \in \mathcal{J}\setminus\widetilde{\mathcal{J}}$.

Thus, for $j \in \mathcal{J}\setminus\widetilde{\mathcal{J}}$, $u, v \in \mathcal{K}$, $u < v$ we obtain

$$
\begin{aligned}
\sum_{t\in\mathcal{T}}\left(C^+_{uv}\frac{\left(\frac{Se_u-1}{Se_u}\right)^{t_{ju}}\left(\frac{Se_v-1}{Se_v}\right)^{t_{jv}}}{(1-Se_u)(1-Se_v)}\right) = \sum_{n\in\mathcal{N}}\Bigg(&\prod_{\substack{k\in\mathcal{K}\\k\neq u\\k\neq v}}\binom{m_k}{n_k} C^+_{uv}(1-Se_u)^{-1}(1-Se_v)^{-1}\cdot\\
&\cdot\underbrace{\left(\mathbb{1}_{\{1,\dots,m_u-1\}}(n_u)\left(\binom{m_u-1}{n_u}+\binom{m_u-1}{n_u-1}\frac{Se_u-1}{Se_u}\right)+\mathbb{1}_{\{m_u\}}(n_u)\frac{Se_u-1}{Se_u}+\mathbb{1}_{\{0\}}(n_u)\right)}_{=:\delta_u}\cdot\\
&\cdot\underbrace{\left(\mathbb{1}_{\{1,\dots,m_v-1\}}(n_v)\left(\binom{m_v-1}{n_v}+\binom{m_v-1}{n_v-1}\frac{Se_v-1}{Se_v}\right)+\mathbb{1}_{\{m_v\}}(n_v)\frac{Se_v-1}{Se_v}+\mathbb{1}_{\{0\}}(n_v)\right)}_{=:\delta_v}\Bigg),
\end{aligned}
$$

which also holds for $j \in \widetilde{\mathcal{J}}$ and $u, v \in \mathcal{K} \setminus \widetilde{\mathcal{K}}$. Considering two columns u, v in the calculation above, we see that

$$\begin{aligned}
&\sum_{n_u=0}^{m_u} \sum_{n_v=0}^{m_v} \left(C^+_{uv} (1 - Se_u)^{-1} (1 - Se_v)^{-1} \delta_u \, \delta_v \right) \\
&\quad = C^+_{uv} (1 - Se_u)^{-1} (1 - Se_v)^{-1} \left(1 + \sum_{n_u=1}^{m_u-1} \left[\binom{m_u - 1}{n_u} + \binom{m_u - 1}{n_u - 1} \frac{Se_u - 1}{Se_u} \right] + \frac{Se_u - 1}{Se_u} \right) \cdot \\
&\qquad \cdot \left(1 + \sum_{n_v=1}^{m_v-1} \left[\binom{m_v - 1}{n_v} + \binom{m_v - 1}{n_v - 1} \frac{Se_v - 1}{Se_v} \right] + \frac{Se_v - 1}{Se_v} \right).
\end{aligned}$$

Therefore, we can rephrase Equation (4) as sum over $n \in \mathcal{N}$ as follows:

$$\begin{aligned}
&\sum_{\substack{u,v \in \mathcal{K} \\ u<v}} \left(C^+_{uv} \sum_{t \in \mathcal{T}} \left[\prod_{k \in \mathcal{K}} \left(Se_k^{\sum_{j \in \mathcal{J}} t_{jk}} (1 - Se_k)^{J - \sum_{j \in \mathcal{J}} t_{jk}} \right) \sum_{j' \in \mathcal{J}} \frac{\left(\frac{Se_u - 1}{Se_u} \right)^{t_{j'u}} \left(\frac{Se_v - 1}{Se_v} \right)^{t_{j'v}}}{(1 - Se_u)(1 - Se_v)} \right] \right) \\
&\quad = \sum_{\substack{u,v \in \widetilde{\mathcal{K}} \\ u<v}} \left(C^+_{uv} \sum_{n \in \mathcal{N}} \left[\prod_{\substack{k \in \mathcal{K} \\ k \neq u \\ k \neq v}} \left(\binom{m_k}{n_k} Se_k^{n_k} (1 - Se_k)^{J - n_k} \right) \prod_{k' \in \{u,v\}} \left(Se_{k'}^{n_{k'}} (1 - Se_{k'})^{J - n_{k'} - 1} \right) \cdot \right.\right. \\
&\qquad\qquad \left.\left. \cdot \left(\sum_{j=1}^{\widetilde{J}} \binom{m_u}{n_u} \binom{m_v}{n_v} + \sum_{j=\widetilde{J}+1}^{J} \delta_u \, \delta_v \right) \right] \right) + \\
&\quad + \sum_{\substack{u \in \widetilde{\mathcal{K}} \\ v \in \mathcal{K} \setminus \widetilde{\mathcal{K}} \\ u<v}} \left(C^+_{uv} \sum_{n \in \mathcal{N}} \left[\prod_{\substack{k \in \mathcal{K} \\ k \neq u \\ k \neq v}} \left(\binom{m_k}{n_k} Se_k^{n_k} (1 - Se_k)^{J - n_k} \right) \prod_{k' \in \{u,v\}} \left(Se_{k'}^{n_{k'}} (1 - Se_{k'})^{J - n_{k'} - 1} \right) \cdot \right.\right. \\
&\qquad\qquad \left.\left. \cdot \left(\sum_{j=1}^{\widetilde{J}} \binom{m_u}{n_u} \delta_v + \sum_{j=\widetilde{J}+1}^{J} \delta_u \, \delta_v \right) \right] \right) + \\
&\quad + \sum_{\substack{u \in \mathcal{K} \setminus \widetilde{\mathcal{K}} \\ v \in \widetilde{\mathcal{K}} \\ u<v}} \left(C^+_{uv} \sum_{n \in \mathcal{N}} \left[\prod_{\substack{k \in \mathcal{K} \\ k \neq u \\ k \neq v}} \left(\binom{m_k}{n_k} Se_k^{n_k} (1 - Se_k)^{J - n_k} \right) \prod_{k' \in \{u,v\}} \left(Se_{k'}^{n_{k'}} (1 - Se_{k'})^{J - n_{k'} - 1} \right) \cdot \right.\right. \\
&\qquad\qquad \left.\left. \cdot \left(\sum_{j=1}^{\widetilde{J}} \binom{m_v}{n_v} \delta_u + \sum_{j=\widetilde{J}+1}^{J} \delta_u \, \delta_v \right) \right] \right) + \\
&\quad + \sum_{\substack{u,v \in \mathcal{K} \setminus \widetilde{\mathcal{K}} \\ u<v}} \left(C^+_{uv} \sum_{n \in \mathcal{N}} \left[\prod_{\substack{k \in \mathcal{K} \\ k \neq u \\ k \neq v}} \left(\binom{m_k}{n_k} Se_k^{n_k} (1 - Se_k)^{J - n_k} \right) \prod_{k' \in \{u,v\}} \left(Se_{k'}^{n_{k'}} (1 - Se_{k'})^{J - n_{k'} - 1} \right) \sum_{j=1}^{J} \delta_u \, \delta_v \right] \right)
\end{aligned}$$

$$
\begin{aligned}
&= \sum_{\substack{u,v\in\widetilde{\mathcal{K}}\\u<v}} \left(C^+_{uv} \underbrace{\prod_{\substack{k\in\mathcal{K}\\k\neq u\\k\neq v}} \sum_{n_k=0}^{m_k} \left(\binom{m_k}{n_k} Se_k^{n_k} (1-Se_k)^{J-n_k} \right)}_{=1 \text{ for } k\in\mathcal{K}\setminus\widetilde{\mathcal{K}}} \sum_{n_u=0}^{m_u} \sum_{n_v=0}^{m_v} \left[\prod_{k'\in\{u,v\}} \left(Se_{k'}^{n_{k'}} (1-Se_{k'})^{J-n_{k'}-1} \right) \cdot \right.\right. \\
&\quad \left.\left. \cdot \left(\widetilde{J} \binom{m_u}{n_u} \binom{m_v}{n_v} + \left(J-\widetilde{J}\right) \delta_u\, \delta_v \right) \right] \right) + \sum_{\substack{u\in\widetilde{\mathcal{K}}\\v\in\mathcal{K}\setminus\widetilde{\mathcal{K}}\\u<v}} \left(C^+_{uv} \underbrace{\prod_{\substack{k\in\mathcal{K}\\k\neq u\\k\neq v}} \sum_{n_k=0}^{m_k} \left(\binom{m_k}{n_k} Se_k^{n_k} (1-Se_k)^{J-n_k} \right)}_{=1 \text{ for } k\in\mathcal{K}\setminus\widetilde{\mathcal{K}}} \cdot \right. \\
&\quad \left. \cdot \sum_{n_u=0}^{m_u} \sum_{n_v=0}^{m_v} \left[\prod_{k'\in\{u,v\}} \left(Se_{k'}^{n_{k'}} (1-Se_{k'})^{J-n_{k'}-1} \right) \left(\widetilde{J} \binom{m_u}{n_u} \delta_v + \left(J-\widetilde{J}\right) \delta_u\, \delta_v \right) \right] \right) + \\
&\quad + \sum_{\substack{u\in\mathcal{K}\setminus\widetilde{\mathcal{K}}\\v\in\widetilde{\mathcal{K}}\\u<v}} \left(C^+_{uv} \underbrace{\prod_{\substack{k\in\mathcal{K}\\k\neq u\\k\neq v}} \sum_{n_k=0}^{m_k} \left(\binom{m_k}{n_k} Se_k^{n_k} (1-Se_k)^{J-n_k} \right)}_{=1 \text{ for } k\in\mathcal{K}\setminus\widetilde{\mathcal{K}}} \sum_{n_u=0}^{m_u} \sum_{n_v=0}^{m_v} \left[\prod_{k'\in\{u,v\}} \left(Se_{k'}^{n_{k'}} (1-Se_{k'})^{J-n_{k'}-1} \right) \cdot \right.\right. \\
&\quad \left.\left. \cdot \left(\widetilde{J} \binom{m_v}{n_v} \delta_u + \left(J-\widetilde{J}\right) \delta_u\, \delta_v \right) \right] \right) + \sum_{\substack{u,v\in\mathcal{K}\setminus\widetilde{\mathcal{K}}\\u<v}} \left(C^+_{uv} \underbrace{\prod_{\substack{k\in\mathcal{K}\\k\neq u\\k\neq v}} \sum_{n_k=0}^{m_k} \left(\binom{m_k}{n_k} Se_k^{n_k} (1-Se_k)^{J-n_k} \right)}_{=1 \text{ for } k\in\mathcal{K}\setminus\widetilde{\mathcal{K}}} + \right. \\
&\quad \left. + \sum_{n_u=0}^{m_u} \sum_{n_v=0}^{m_v} \left[\prod_{k'\in\{u,v\}} \left(Se_{k'}^{n_{k'}} (1-Se_{k'})^{J-n_{k'}-1} \right) J\, \delta_u\, \delta_v \right] \right) \qquad (5)
\end{aligned}
$$

For $u, v \in \mathcal{K} \setminus \widetilde{\mathcal{K}}$, we can further conclude that

$$
\begin{aligned}
&\sum_{n_u=0}^{m_u} \sum_{n_v=0}^{m_v} \left[\prod_{k'\in\{u,v\}} \left(Se_{k'}^{n_{k'}} (1-Se_{k'})^{J-n_{k'}-1} \right) J\, \delta_u\, \delta_v \right] \\
&\qquad = J \sum_{n_u=0}^{m_u} \left(Se_u^{n_u} (1-Se_u)^{J-n_u-1} \delta_u \right) \sum_{n_v=0}^{m_v} \left(Se_v^{n_v} (1-Se_v)^{J-n_v-1} \delta_v \right)
\end{aligned}
$$

with

$$
\begin{aligned}
&\sum_{n_u=0}^{m_u} Se_u^{n_u} (1-Se_u)^{J-n_u-1} \delta_u \\
&= (1-Se_u)^{J-1} + \sum_{n_u=1}^{m_u-1} \left[Se_u^{n_u} (1-Se_u)^{J-n_u-1} \left(\binom{m_u-1}{n_u} + \binom{m_u-1}{n_u-1} \frac{Se_u-1}{Se_u} \right) \right] + Se_u^{m_u} (1-Se_u)^{J-m_u-1} \frac{Se_u-1}{Se_u} \\
&= (1-Se_u)^{J-1} + \sum_{n_u=1}^{J-1} \left[Se_u^{n_u} (1-Se_u)^{J-n_u-1} \left(\binom{J-1}{n_u} + \binom{J-1}{n_u-1} \frac{Se_u-1}{Se_u} \right) \right] + Se_u^{J-1} (1-Se_u)^{-1} (Se_u-1) \\
&= (1-Se_u)^{J-1} + \sum_{n_u=1}^{J-1} \left[\binom{J-1}{n_u} Se_u^{n_u} (1-Se_u)^{J-n_u-1} + \binom{J-1}{n_u-1} Se_u^{n_u-1} (1-Se_u)^{J-n_u-1} (Se_u-1) \right] - Se_u^{J-1} \\
&= (1-Se_u)^{J-1} - Se_u^{J-1} + \sum_{n_u=1}^{J-1} \binom{J-1}{n_u} Se_u^{n_u} (1-Se_u)^{J-1-n_u} - \sum_{n_u=1}^{J-1} \binom{J-1}{n_u-1} Se_u^{n_u-1} (1-Se_u)^{J-n_u}
\end{aligned}
$$

$$= (1 - Se_u)^{J-1} - Se_u^{J-1} - (1 - Se_u)^{J-1} + \sum_{n_u=0}^{J-1} \binom{J-1}{n_u} Se_u^{n_u} (1 - Se_u)^{J-1-n_u} - \sum_{n_u=0}^{J-2} \binom{J-1}{n_u} Se_u^{n_u} (1 - Se_u)^{J-n_u-1}$$

$$= -Se_u^{J-1} + Se_u^{J-1}$$

$$= 0.$$

This holds also for δ_v and reduces our calculations for Equation (5) considerably to

$$\sum_{\substack{u,v \in \widetilde{\mathcal{K}} \\ u<v}} \left(C_{uv}^{+} \prod_{\substack{k \in \widetilde{\mathcal{K}} \\ k \neq u \\ k \neq v}} \sum_{n_k=0}^{m_k} \left(\binom{m_k}{n_k} Se_k^{n_k} (1 - Se_k)^{J-n_k} \right) \sum_{n_u=0}^{m_u} \sum_{n_v=0}^{m_v} \left[\prod_{k' \in \{u,v\}} \left(Se_{k'}^{n_{k'}} (1 - Se_{k'})^{J-n_{k'}-1} \right) \widetilde{J} \binom{m_u}{n_u} \binom{m_v}{n_v} \right] \right)$$

$$= \sum_{\substack{u,v \in \widetilde{\mathcal{K}} \\ u<v}} \left(C_{uv}^{+} \prod_{\substack{\tilde{k} \in \widetilde{\mathcal{K}} \\ \tilde{k} \neq u \\ \tilde{k} \neq v}} (1 - Se_{\tilde{k}})^{\widetilde{J}} \prod_{\substack{k \in \widetilde{\mathcal{K}} \\ k \neq u \\ k \neq v}} \underbrace{\sum_{n_k=0}^{m_k} \left(\binom{m_k}{n_k} Se_k^{n_k} (1 - Se_k)^{m_k-n_k} \right)}_{=1} \cdot \right.$$

$$\left. \cdot \widetilde{J} \prod_{k' \in \{u,v\}} \sum_{n_{k'}=0}^{m_{k'}} \left(\binom{m_{k'}}{n_{k'}} Se_{k'}^{n_{k'}} (1 - Se_{k'})^{J-n_{k'}-1} \right) \right)$$

$$= \sum_{\substack{u,v \in \widetilde{\mathcal{K}} \\ u<v}} \left(C_{uv}^{+} \prod_{\substack{\tilde{k} \in \widetilde{\mathcal{K}} \\ \tilde{k} \neq u \\ \tilde{k} \neq v}} (1 - Se_{\tilde{k}})^{\widetilde{J}} \widetilde{J} (1 - Se_u)^{-1} (1 - Se_v)^{-1} \prod_{k' \in \{u,v\}} \sum_{n_{k'}=0}^{m_{k'}} \left(\binom{m_{k'}}{n_{k'}} Se_{k'}^{n_{k'}} (1 - Se_{k'})^{J-n_{k'}} \right) \right)$$

$$= \prod_{\tilde{k} \in \widetilde{\mathcal{K}}} (1 - Se_{\tilde{k}})^{\widetilde{J}} \sum_{\substack{u,v \in \widetilde{\mathcal{K}} \\ u<v}} \left(C_{uv}^{+} \widetilde{J} (1 - Se_u)^{-1} (1 - Se_v)^{-1} \prod_{k' \in \{u,v\}} \underbrace{\sum_{n_{k'}=0}^{m_{k'}} \left(\binom{m_{k'}}{n_{k'}} Se_{k'}^{n_{k'}} (1 - Se_{k'})^{m_{k'}-n_{k'}} \right)}_{=1} \right)$$

$$= \prod_{\tilde{k} \in \widetilde{\mathcal{K}}} (1 - Se_{\tilde{k}})^{\widetilde{J}} \widetilde{J} \sum_{\substack{u,v \in \widetilde{\mathcal{K}} \\ u<v}} C_{uv}^{+} (1 - Se_u)^{-1} (1 - Se_v)^{-1}.$$

Finally, we turn to

$$\sum_{t \in \mathcal{T}} d^{+} \widetilde{rc}^{+} = \sum_{t \in \mathcal{T}} \left[\prod_{k \in \mathcal{K}} \left(Se_k^{\sum_{j \in \mathcal{J}} t_{jk}} (1 - Se_k)^{J - \sum_{j \in \mathcal{J}} t_{jk}} \right) \sum_{k' \in \mathcal{K}} \sum_{\substack{u,v \in \mathcal{J} \\ u<v}} \left(R_{k'}^{+} \frac{\left(\frac{Se_{k'}-1}{Se_{k'}} \right)^{t_{uk'}+t_{vk'}}}{(1 - Se_{k'})^2} \right) \right]. \tag{6}$$

Let $k \in \mathcal{K}$, $n_k = \sum_{j=1}^{J} t_{jk}$. There are $\frac{1}{2}J(J-1)$ pairs (t_{uk}, t_{vk}) for $u, v \in \mathcal{J}$ with $u < v$, of which $\binom{J-n_k}{2} = \frac{1}{2}(J - n_k)(J - n_k - 1)$ pairs equal $(0, 0)$ (for $0 \leq n_k \leq J - 2$), $n_k(J - n_k)$ pairs equal $(0, 1)$ or $(1, 0)$ (for $1 \leq n_k \leq J - 1$), and $\binom{n_k}{2} = \frac{1}{2}n_k(n_k - 1)$ pairs equal $(1, 1)$ (for $2 \leq n_k \leq J$). Therefore, we can rephrase

Equation (6) as follows:

$$
\begin{aligned}
&\sum_{t\in\mathcal{T}}\left[\prod_{k\in\mathcal{K}}\left(Se_k^{\sum\limits_{j\in\mathcal{J}}t_{jk}}(1-Se_k)^{J-\sum\limits_{j\in\mathcal{J}}t_{jk}}\right)\sum_{k'\in\mathcal{K}}\sum_{\substack{u,v\in\mathcal{J}\\u<v}}\left(R^+_{k'}\frac{\left(\frac{Se_{k'}-1}{Se_{k'}}\right)^{t_{uk'}+t_{vk'}}}{(1-Se_{k'})^2}\right)\right]\\
&=\sum_{n\in\mathcal{N}}\left[\prod_{k\in\mathcal{K}}\left(\binom{m_k}{n_k}Se_k^{n_k}(1-Se_k)^{J-n_k}\right)\sum_{k'\in\mathcal{K}}\left(R^+_{k'}\left[\mathbb{1}_{\{0,\ldots,J-2\}}(n_{k'})\frac{(J-n_{k'})(J-n_{k'}-1)}{2(1-Se_{k'})^2}+\right.\right.\right.\\
&\quad\left.\left.\left.+\ \mathbb{1}_{\{1,\ldots,J-1\}}(n_{k'})\frac{n_{k'}(J-n_{k'})(Se_{k'}-1)}{Se_{k'}(1-Se_{k'})^2}+\mathbb{1}_{\{2,\ldots,J\}}(n_{k'})\frac{n_{k'}(n_{k'}-1)}{2Se_{k'}^2}\right]\right)\right]\\
&=\prod_{\tilde{k}\in\widetilde{\mathcal{K}}}(1-Se_{\tilde{k}})^{\widetilde{J}}\sum_{n\in\mathcal{N}}\left[\prod_{k\in\mathcal{K}}\left(\binom{m_k}{n_k}Se_k^{n_k}(1-Se_k)^{m_k-n_k}\right)\sum_{k'\in\mathcal{K}}\left(R^+_{k'}\left[\mathbb{1}_{\{0,\ldots,J-2\}}(n_{k'})\frac{(J-n_{k'})(J-n_{k'}-1)}{2(1-Se_{k'})^2}+\right.\right.\right.\\
&\quad\left.\left.\left.-\ \mathbb{1}_{\{1,\ldots,J-1\}}(n_{k'})\frac{n_{k'}(J-n_{k'})}{Se_{k'}(1-Se_{k'})}+\mathbb{1}_{\{2,\ldots,J\}}(n_{k'})\frac{n_{k'}(n_{k'}-1)}{2Se_{k'}^2}\right]\right)\right]\\
&=\prod_{\tilde{k}\in\widetilde{\mathcal{K}}}(1-Se_{\tilde{k}})^{\widetilde{J}}\sum_{n\in\mathcal{N}}\sum_{k'\in\mathcal{K}}\left(R^+_{k'}\binom{m_{k'}}{n_{k'}}\left[\mathbb{1}_{\{0,\ldots,J-2\}}(n_{k'})\frac{(J-n_{k'})(J-n_{k'}-1)}{2}Se_{k'}^{n_{k'}}(1-Se_{k'})^{m_{k'}-n_{k'}-2}+\right.\right.\\
&\quad-\mathbb{1}_{\{1,\ldots,J-1\}}(n_{k'})n_{k'}(J-n_{k'})Se_{k'}^{n_{k'}-1}(1-Se_{k'})^{m_{k'}-n_{k'}-1}+\\
&\quad\left.\left.+\ \mathbb{1}_{\{2,\ldots,J\}}(n_{k'})\frac{n_{k'}(n_{k'}-1)}{2}Se_{k'}^{n_{k'}-2}(1-Se_{k'})^{m_{k'}-n_{k'}}\right]\prod_{\substack{k\in\mathcal{K}\\k\neq k'}}\left(\binom{m_k}{n_k}Se_k^{n_k}(1-Se_k)^{m_k-n_k}\right)\right)\\
&=\prod_{\tilde{k}\in\widetilde{\mathcal{K}}}(1-Se_{\tilde{k}})^{\widetilde{J}}\sum_{k'\in\mathcal{K}}\left[R^+_{k'}\sum_{n_{k'}=0}^{m_{k'}}\left(\binom{m_{k'}}{n_{k'}}\left[\mathbb{1}_{\{0,\ldots,J-2\}}(n_{k'})\frac{(J-n_{k'})(J-n_{k'}-1)}{2}Se_{k'}^{n_{k'}}(1-Se_{k'})^{m_{k'}-n_{k'}-2}+\right.\right.\right.\\
&\quad-\mathbb{1}_{\{1,\ldots,J-1\}}(n_{k'})n_{k'}(J-n_{k'})Se_{k'}^{n_{k'}-1}(1-Se_{k'})^{m_{k'}-n_{k'}-1}+\\
&\quad\left.\left.\left.+\ \mathbb{1}_{\{2,\ldots,J\}}(n_{k'})\frac{n_{k'}(n_{k'}-1)}{2}Se_{k'}^{n_{k'}-2}(1-Se_{k'})^{m_{k'}-n_{k'}}\right]\right)\prod_{\substack{k\in\mathcal{K}\\k\neq k'}}\underbrace{\sum_{n_k=0}^{m_k}\left(\binom{m_k}{n_k}Se_k^{n_k}(1-Se_k)^{m_k-n_k}\right)}_{=1}\right]\\
&=\prod_{\tilde{k}\in\widetilde{\mathcal{K}}}(1-Se_{\tilde{k}})^{\widetilde{J}}\sum_{k'\in\mathcal{K}}\left[R^+_{k'}\left(\sum_{n_{k'}=0}^{\min\{m_{k'},J-2\}}\left(\binom{m_{k'}}{n_{k'}}\frac{(J-n_{k'})(J-n_{k'}-1)}{2}Se_{k'}^{n_{k'}}(1-Se_{k'})^{m_{k'}-n_{k'}-2}\right)+\right.\right.\\
&\quad-\sum_{n_{k'}=1}^{\min\{m_{k'},J-1\}}\left(\binom{m_{k'}}{n_{k'}}n_{k'}(J-n_{k'})Se_{k'}^{n_{k'}-1}(1-Se_{k'})^{m_{k'}-n_{k'}-1}\right)+\\
&\quad\left.\left.+\sum_{n_{k'}=2}^{m_{k'}}\left(\binom{m_{k'}}{n_{k'}}\frac{n_{k'}(n_{k'}-1)}{2}Se_{k'}^{n_{k'}-2}(1-Se_{k'})^{m_{k'}-n_{k'}}\right)\right)\right]\\
&=\prod_{\tilde{k}\in\widetilde{\mathcal{K}}}(1-Se_{\tilde{k}})^{\widetilde{J}}\sum_{k'\in\mathcal{K}}\left[R^+_{k'}\left(\sum_{n_{k'}=0}^{m_{k'}-2}\left[Se_{k'}^{n_{k'}}(1-Se_{k'})^{m_{k'}-n_{k'}-2}\left(\binom{m_{k'}}{n_{k'}}\frac{(J-n_{k'})(J-n_{k'}-1)}{2}+\right.\right.\right.\right.\\
&\quad\left.\left.-\binom{m_{k'}}{n_{k'}+1}(n_{k'}+1)(J-n_{k'}-1)+\binom{m_{k'}}{n_{k'}+2}\frac{(n_{k'}+2)(n_{k'}+1)}{2}\right)\right]+\\
&\quad+\mathbb{1}_{\widetilde{\mathcal{K}}}(k')\left[Se_{k'}^{m_{k'}-1}(1-Se_{k'})^{-1}\left(m_{k'}\frac{(J-m_{k'}+1)(J-m_{k'})}{2}-m_{k'}(J-m_{k'})\right)+\right.\\
&\quad\left.\left.\left.+\ Se_{k'}^{m_{k'}}(1-Se_{k'})^{-2}\frac{(J-m_{k'})(J-m_{k'}-1)}{2}\right]\right)\right]
\end{aligned}
$$

We see that

$$
\begin{aligned}
&\binom{m_{k'}}{n_{k'}}\frac{(J-n_{k'})(J-n_{k'}-1)}{2}-\binom{m_{k'}}{n_{k'}+1}(n_{k'}+1)(J-n_{k'}-1)+\binom{m_{k'}}{n_{k'}+2}\frac{(n_{k'}+2)(n_{k'}+1)}{2}\\
&=\frac{m_{k'}!\,(J-n_{k'})(J-n_{k'}-1)}{n_{k'}!\,(m_{k'}-n_{k'})!\,2}-\frac{m_{k'}!\,(n_{k'}+1)(J-n_{k'}-1)}{(n_{k'}+1)!\,(m_{k'}-n_{k'}-1)!}+\frac{m_{k'}!\,(n_{k'}+2)(n_{k'}+1)}{(n_{k'}+2)!\,(m_{k'}-n_{k'}-2)!\,2}\\
&=\frac{m_{k'}!\,(J-n_{k'})(J-n_{k'}-1)}{n_{k'}!\,(m_{k'}-n_{k'})!\,2}-\frac{m_{k'}!\,(J-n_{k'}-1)}{n_{k'}!\,(m_{k'}-n_{k'}-1)!}+\frac{m_{k'}!}{n_{k'}!\,(m_{k'}-n_{k'}-2)!\,2}\\
&=\binom{m_{k'}}{n_{k'}}\left(\frac{(J-n_{k'})(J-n_{k'}-1)}{2}-(J-n_{k'}-1)(m_{k'}-n_{k'})+\frac{(m_{k'}-n_{k'}-1)(m_{k'}-n_{k'})}{2}\right)\\
&=\begin{cases}0, & \text{if } m_{k'}=J \quad (\Leftrightarrow k'\in\mathcal{K}\setminus\widetilde{\mathcal{K}}),\\ \binom{J-\widetilde{J}}{n_{k'}}\frac{1}{2}(\widetilde{J}-1)\widetilde{J}, & \text{if } m_{k'}=J-\widetilde{J} \quad (\Leftrightarrow k'\in\widetilde{\mathcal{K}}),\end{cases}
\end{aligned}
$$

and for $k'\in\widetilde{\mathcal{K}}$

$$
m_{k'}\frac{(J-m_{k'}+1)(J-m_{k'})}{2}-m_{k'}(J-m_{k'})=m_{k'}(J-m_{k'})\left(\frac{J-m_{k'}+1}{2}-1\right)=\frac{1}{2}(J-\widetilde{J})\,\widetilde{J}\,(\widetilde{J}-1)
$$

and

$$
\frac{(J-m_{k'})(J-m_{k'}-1)}{2}=\frac{1}{2}\widetilde{J}\,(\widetilde{J}-1).
$$

Thus, we can conclude

$$
\begin{aligned}
\sum_{t\in\mathcal{T}}d^+\widetilde{rc}^+&=\prod_{\tilde{k}\in\widetilde{\mathcal{K}}}(1-Se_{\tilde{k}})^{\widetilde{J}}\sum_{k'\in\widetilde{\mathcal{K}}}\Bigg[R^+_{k'}\frac{1}{2}\widetilde{J}\,(\widetilde{J}-1)\Bigg(Se_{k'}^{J-\widetilde{J}}(1-Se_{k'})^{-2}+Se_{k'}^{J-\widetilde{J}-1}(1-Se_{k'})^{-1}(J-\widetilde{J})+\\
&\quad+\sum_{n_{k'}=0}^{J-\widetilde{J}-2}\binom{J-\widetilde{J}}{n_{k'}}Se_{k'}^{n_{k'}}(1-Se_{k'})^{J-\widetilde{J}-n_{k'}-2}\Bigg)\Bigg]\\
&=\prod_{\tilde{k}\in\widetilde{\mathcal{K}}}(1-Se_{\tilde{k}})^{\widetilde{J}}\sum_{k'\in\widetilde{\mathcal{K}}}\Bigg[R^+_{k'}\frac{1}{2}\widetilde{J}\,(\widetilde{J}-1)\Bigg(Se_{k'}^{J-\widetilde{J}}(1-Se_{k'})^{-2}+Se_{k'}^{J-\widetilde{J}-1}(1-Se_{k'})^{-1}(J-\widetilde{J})+\\
&\quad+\ (1-Se_{k'})^{-2}\Bigg[-Se_{k'}^{J-\widetilde{J}}-(J-\widetilde{J})Se_{k'}^{J-\widetilde{J}-1}(1-Se_{k'})+\underbrace{\sum_{n_{k'}=0}^{J-\widetilde{J}}\binom{J-\widetilde{J}}{n_{k'}}Se_{k'}^{n_{k'}}(1-Se_{k'})^{J-\widetilde{J}-n_{k'}}}_{=1}\Bigg]\Bigg)\Bigg]\\
&=\prod_{\tilde{k}\in\widetilde{\mathcal{K}}}(1-Se_{\tilde{k}})^{\widetilde{J}}\sum_{k'\in\widetilde{\mathcal{K}}}R^+_{k'}\frac{1}{2}\widetilde{J}\,(\widetilde{J}-1)(1-Se_{k'})^{-2}.
\end{aligned}
$$

Combining all three parts, the sensitivity of a parallel test over $\widetilde{J}$ out of J repeats and $\widetilde{K}$ out of K diagnostic tests can be computed as

$$
\begin{aligned}
&1-\sum_{t\in\mathcal{T}}d^+(1+\widetilde{tc}^++\widetilde{rc}^+)\\
&\quad=1-\prod_{\tilde{k}\in\widetilde{\mathcal{K}}}(1-Se_{\tilde{k}})^{\widetilde{J}}\left(1+\widetilde{J}\sum_{\substack{u,v\in\widetilde{\mathcal{K}}\\u<v}}C^+_{uv}(1-Se_u)^{-1}(1-Se_v)^{-1}+\frac{1}{2}\widetilde{J}\,(\widetilde{J}-1)\sum_{k'\in\widetilde{\mathcal{K}}}R^+_{k'}(1-Se_{k'})^{-2}\right).\quad(7)
\end{aligned}
$$

Specificity of parallel tests

In order to compute the specificity of a parallel test over $\widetilde{J}$ out of J repeats and $\widetilde{K}$ out of K diagnostic tests, we consider

$$\sum_{t\in\mathcal{T}} d^-(1+\widetilde{tc}^- + \widetilde{rc}^-) = \sum_{t\in\mathcal{T}} d^- + \sum_{t\in\mathcal{T}} d^-\widetilde{tc}^- + \sum_{t\in\mathcal{T}} d^-\widetilde{rc}^-.$$

Similar to previous calculations, we see that

$$\begin{aligned}
\sum_{t\in\mathcal{T}} d^- &= \sum_{t\in\mathcal{T}} \prod_{k\in\mathcal{K}} Sp_k^{J-\sum\limits_{j\in\mathcal{J}} t_{jk}} (1-Sp_k)^{\sum\limits_{j\in\mathcal{J}} t_{jk}} \\
&= \sum_{n\in\mathcal{N}} \left[\prod_{\tilde{k}\in\widetilde{\mathcal{K}}} \left(\binom{J-\widetilde{J}}{n_{\tilde{k}}} Sp_{\tilde{k}}^{J-n_{\tilde{k}}} (1-Sp_{\tilde{k}})^{n_{\tilde{k}}} \right) \prod_{k\in\mathcal{K}\setminus\widetilde{\mathcal{K}}} \left(\binom{J}{n_k} Sp_k^{J-n_k} (1-Sp_k)^{n_k} \right) \right] \\
&= \prod_{k'\in\widetilde{\mathcal{K}}} Sp_{k'}^{\widetilde{J}} \sum_{n\in\mathcal{N}} \prod_{k\in\mathcal{K}} \left(\binom{m_k}{n_k} (1-Sp_k)^{n_k} Sp_k^{m_k-n_k} \right) \\
&= \prod_{k'\in\widetilde{\mathcal{K}}} Sp_{k'}^{\widetilde{J}}.
\end{aligned}$$

Analogously to previous calculations, we obtain

$$\begin{aligned}
\sum_{t\in\mathcal{T}} d^-\widetilde{tc}^- &= \sum_{t\in\mathcal{T}} \left[\prod_{k\in\mathcal{K}} \left(Sp_k^{J-\sum\limits_{j\in\mathcal{J}} t_{jk}} (1-Sp_k)^{\sum\limits_{j\in\mathcal{J}} t_{jk}} \right) \sum_{j\in\mathcal{J}} \sum_{\substack{u,v\in\mathcal{K}\\ u<v}} \left(C_{uv}^- \frac{\left(\frac{Sp_u}{Sp_u-1}\right)^{t_{ju}} \left(\frac{Sp_v}{Sp_v-1}\right)^{t_{jv}}}{Sp_u Sp_v} \right) \right] \\
&= \prod_{k'\in\widetilde{\mathcal{K}}} Sp_{k'}^{\widetilde{J}} \sum_{\substack{u,v\in\widetilde{\mathcal{K}}\\ u<v}} C_{uv}^- Sp_u^{-1} Sp_v^{-1} \widetilde{J},
\end{aligned}$$

and

$$\begin{aligned}
\sum_{t\in\mathcal{T}} d^-\widetilde{rc}^- &= \sum_{t\in\mathcal{T}} \left[\prod_{k\in\mathcal{K}} \left(Sp_k^{J-\sum_{j\in\mathcal{J}} t_{jk}} (1-Sp_k)^{\sum_{j\in\mathcal{J}} t_{jk}} \right) \sum_{k'\in\mathcal{K}} \sum_{\substack{u,v\in\mathcal{J}\\ u<v}} \left(R_{k'}^- \frac{\left(\frac{Sp_{k'}}{Sp_{k'}-1}\right)^{t_{uk'}+t_{vk'}}}{Sp_{k'}^2} \right) \right] \\
&= \prod_{\tilde{k}\in\widetilde{\mathcal{K}}} Sp_{\tilde{k}}^{\widetilde{J}} \sum_{k'\in\widetilde{\mathcal{K}}} R_{k'}^- Sp_{k'}^{-2} \frac{1}{2} \widetilde{J}(\widetilde{J}-1).
\end{aligned}$$

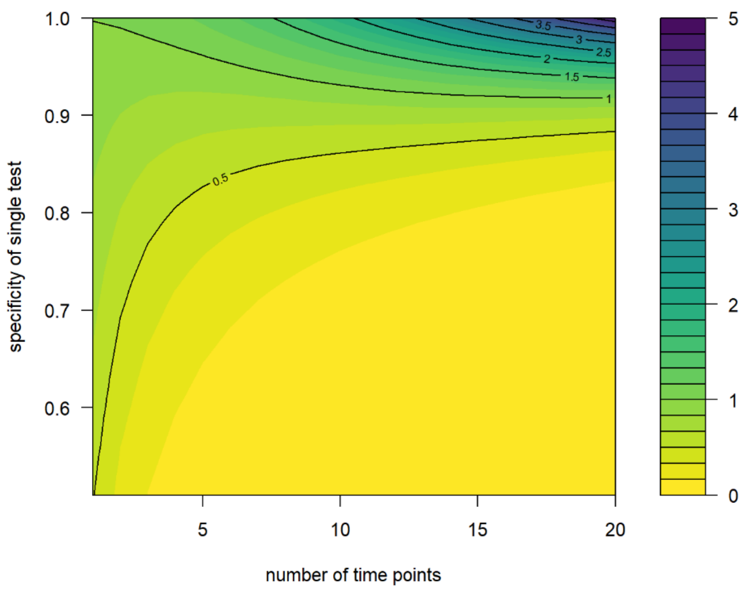
Thus, the specificity of a parallel test over $\widetilde{J}$ out of J repeats and $\widetilde{K}$ out of K tests is calculated as

$$\sum_{t\in\mathcal{T}} d^-(1+\widetilde{tc}^- + \widetilde{rc}^-) = \prod_{\tilde{k}\in\widetilde{\mathcal{K}}} Sp_{\tilde{k}}^{\widetilde{J}} \left(1 + \widetilde{J} \sum_{\substack{u,v\in\widetilde{\mathcal{K}}\\ u<v}} C_{uv}^- Sp_u^{-1} Sp_v^{-1} + \frac{1}{2}\widetilde{J}(\widetilde{J}-1) \sum_{k'\in\widetilde{\mathcal{K}}} R_{k'}^- Sp_{k'}^{-2} \right). \quad (8)$$

Remarks

Parallel testing generally leads to an increase in sensitivity and a decrease in specificity. However, we observed an unexpected curvature in specificity of a parallel test over an increasing number of time points. For simplicity, we consider here a parallel test consisting of a single test over an increasing number of time points. In this case, Equation (8) is equivalent to $Sp_k^{\widetilde{J}} \left(1 + \frac{1}{2}\widetilde{J}(\widetilde{J}-1)\, R_k^-\, Sp_k^{-2}\right)$. Considering this as a function of $\widetilde{J}$, it consists of a product of an exponential and a quadratic function, which explains the observed curvature. Figure 1 shows contour plots for the specificity of a single test evaluated as a parallel test over repeated applications, depending on the number of time points and the basic specificity of the test, for two selected values for R^{-}. Similar considerations apply to the sensitivity of a parallel test over an increasing number of time points.

(a)



(b)

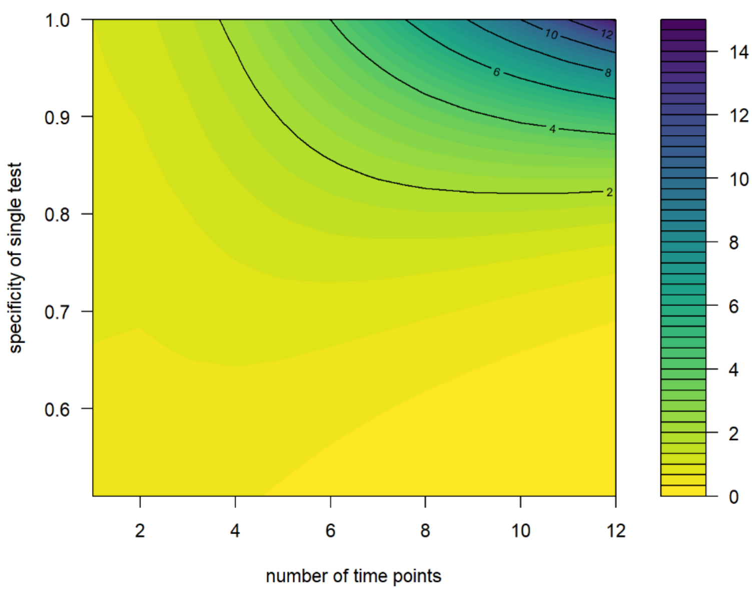


Figure 1: Values of the estimator for specificity of a parallel test consisting of a single test repeated at multiple time points, with (a) $R^{-} = 0.02$, (b) $R^{-} = 0.2$.