Topics of today:

1. Formalizing the number of occurrences (ϕ) of families/adjacencies/telomeres
2. Revisiting breakpoint and SCJ double distances
3. SCJ median, halving and guided halving
4. Breakpoint median, halving and guided halving

Occurrences of families

Given a family f and a genome $\mathbb{G}$, let $\phi(f, \mathbb{G})$ be the number of occurrences of family f in $\mathbb{G}$.

If $\mathbb{S}$ is singular, then $\phi(f, \mathbb{S}) = 1$ for each $f \in \mathcal{F}(\mathbb{S})$.

If $\mathbb{D}$ is duplicated, then $\phi(f, \mathbb{D}) = 2$ for each $f \in \mathcal{F}(\mathbb{D})$.

If $\mathbb{C}_1$ and $\mathbb{C}_2$ are canonical, then $\mathcal{F}_\star = \mathcal{F}(\mathbb{C}_1) = \mathcal{F}(\mathbb{C}_2)$ and $\phi(f, \mathbb{C}_1) = \phi(f, \mathbb{C}_2) = 1$ for each $f \in \mathcal{F}_\star$.

If $\mathbb{B}_1$ and $\mathbb{B}_2$ are balanced, then $\mathcal{F}_\star = \mathcal{F}(\mathbb{B}_1) = \mathcal{F}(\mathbb{B}_2)$ and $\phi(f, \mathbb{B}_1) = \phi(f, \mathbb{B}_2)$ for each $f \in \mathcal{F}_\star$.

Occurrences of adjacencies

Given an adjacency xy and a canonical genome $\mathbb{C}$, let $\phi(xy, \mathbb{C}) = \begin{cases} 1, & xy \in \alpha(\mathbb{C}), \\ 0, & xy \notin \alpha(\mathbb{C}). \end{cases}$

Given an adjacency xy and a duplicated genome $\mathbb{D}$,

let $\phi(xy, \mathbb{D})$ be the number of occurrences of adjacencies of type $x_i y_j$ in $\alpha(\mathbb{D})$.

Note that $\phi(xy, \mathbb{D}) \in \{0, 1, 2\}$.

Given an adjacency xy and k genomes $\mathbb{G}_1, \mathbb{G}_2, \ldots, \mathbb{G}_k$,

let $\phi(xy, \mathbb{G}_1, \mathbb{G}_2, \ldots, \mathbb{G}_k) = \phi(xy, \mathbb{G}_{1..k}) = \sum_{i=1}^{k} \phi(xy, \mathbb{G}_i)$.

Occurrences of telomeres

Given a telomere x and a canonical genome $\mathbb{C}$, let $\phi(x, \mathbb{C}) = \begin{cases} 1, & x \in \gamma(\mathbb{C}), \\ 0, & x \notin \gamma(\mathbb{C}). \end{cases}$

Given a telomere x and a duplicated genome $\mathbb{D}$,

let $\phi(x, \mathbb{D})$ be the number of occurrences of telomeres of type $x_{[i]}$ in $\gamma(\mathbb{D})$.

Note that $\phi(x, \mathbb{D}) \in \{0, 1, 2\}$.

Given a telomere x and k genomes $\mathbb{G}_1, \mathbb{G}_2, \ldots, \mathbb{G}_k$,

let $\phi(x, \mathbb{G}_1, \mathbb{G}_2, \ldots, \mathbb{G}_k) = \phi(x, \mathbb{G}_{1..k}) = \sum_{i=1}^{k} \phi(x, \mathbb{G}_i)$.

Quiz 1

Given genomes $\mathbb{D} = (1\,2\,3\,4)\ [1\,\bar{5}\,\bar{4}\,5\,\bar{3}\,\bar{2}]$, $\mathbb{C}_1 = [1\,2\,3\,4\,5]$ and $\mathbb{C}_2 = [\bar{2}\,\bar{1}]\ [\bar{4}\,\bar{3}\,5]$:

1 Which are the values of $\phi(3^h5^t,\mathbb{D})$, $\phi(2^h3^t,\mathbb{D})$, $\phi(4^h1^t,\mathbb{D})$, $\phi(1^t,\mathbb{D})$?

A 1, 1, 2, 0

B 0, 2, 0, 2

C 0, 2, 1, 1

D 1, 2, 0, 2

2 Which are the values of $\phi(3^h5^t,\mathbb{C}_1,\mathbb{C}_2)$, $\phi(2^h3^t,\mathbb{C}_1,\mathbb{C}_2)$, $\phi(1^h2^t,\mathbb{C}_1,\mathbb{C}_2)$, $\phi(1^t,\mathbb{C}_1,\mathbb{C}_2)$?

A 0, 1, 1, 2

B 0, 1, 2, 2

C 1, 1, 2, 0

D 1, 2, 0, 2

Breakpoint model - distance and double distance

Breakpoint distance of canonical genomes $\mathbb{C}_1$ and $\mathbb{C}_2$, with $n = |\mathcal{G}_\star|$, $a = |\alpha_\star|$ and $t = |\gamma_\star|$:

$$\mathrm{d}_{\mathrm{BP}}(\mathbb{C}_1, \mathbb{C}_2) \;=\; n \;-\; a \;-\; \frac{t}{2}\,.$$

Breakpoint double distance of sing-dup-canonical genomes $\mathbb{S}$ and $\mathbb{D}$, with $\mathcal{G}_\star = \mathcal{G}(\mathbb{S}) \cap \mathcal{G}(\mathbb{D})$ and $n = |\mathcal{G}_\star|$:

$$\mathrm{d}^2_{\mathrm{BP}}(\mathbb{S}, \mathbb{D}) \;=\; \mathrm{d}_{\mathrm{BP}}(2{\cdot}\mathbb{S}, \mathbb{D}) \;=\; n' \;-\; a' \;-\; \frac{t'}{2} \;=\; 2n \;-\; a' \;-\; \frac{t'}{2}\,,$$

where $n' = |\mathcal{G}(2{\cdot}\mathbb{S}) \cap \mathcal{G}(\mathbb{D})| = 2|\mathcal{G}_\star| = 2n$, $a' = |\alpha(2{\cdot}\mathbb{S}) \cap \alpha(\mathbb{D})|$ and $t' = |\gamma(2{\cdot}\mathbb{S}) \cap \gamma(\mathbb{D})|$.

Since it is possible to find a matching that fulfills each candidate adjacency/telomere between $2{\cdot}\mathbb{S}$ and $\mathbb{D}$:

$$a' = \sum_{xy \in \alpha(\mathbb{S})} \phi(xy, \mathbb{D}) \quad \text{and}$$

$$t' = \sum_{x \in \gamma(\mathbb{S})} \phi(x, \mathbb{D})$$

SCJ model - distance and double distance

SCJ distance of canonical genomes $\mathbb{C}_1$ and $\mathbb{C}_2$, with $n = |\mathcal{G}_\star|$ and $a = |\alpha_\star|$:

$$d_{\text{SCJ}}(\mathbb{C}_1, \mathbb{C}_2) \;=\; 2n \;-\; 2a \;-\; \kappa(\mathbb{C}_1) \;-\; \kappa(\mathbb{C}_2)\,.$$

SCJ double distance of sing-dup-canonical genomes $\mathbb{S}$ and $\mathbb{D}$, with $\mathcal{G}_\star = \mathcal{G}(\mathbb{S}) \cap \mathcal{G}(\mathbb{D})$ and $n = |\mathcal{G}_\star|$:

$$d^2_{\text{SCJ}}(\mathbb{S}, \mathbb{D}) \;=\; d_{\text{SCJ}}(2{\cdot}\mathbb{S}, \mathbb{D}) \;=\; 2n' \;-\; 2a' \;-\; \kappa(2{\cdot}\mathbb{S}) \;-\; \kappa(\mathbb{D}) \;=\; 4n \;-\; 2a' \;-\; 2\kappa(\mathbb{S}) \;-\; \kappa(\mathbb{D})$$

where $n' = |\mathcal{G}(2{\cdot}\mathbb{S}) \cap \mathcal{G}(\mathbb{D})| = 2|\mathcal{G}_\star| = 2n$ and $a' = |\alpha(2{\cdot}\mathbb{S}) \cap \alpha(\mathbb{D})|$.

Since it is possible to find a matching that fulfills each candidate adjacency between $2{\cdot}\mathbb{S}$ and $\mathbb{D}$:

$$a' = \sum_{xy \in \alpha(\mathbb{S})} \phi(xy, \mathbb{D})$$

SCJ median of canonical genomes

Given three canonical genomes $\mathbb{C}_1$, $\mathbb{C}_2$ and $\mathbb{C}_3$, find another canonical genome $\mathbb{M}$ that minimizes the sum:

$$s_{SCJ}(\mathbb{M}) = d_{SCJ}(\mathbb{M}, \mathbb{C}_1) + d_{SCJ}(\mathbb{M}, \mathbb{C}_2) + d_{SCJ}(\mathbb{M}, \mathbb{C}_3)$$

Recall that:

$$\begin{aligned} d_{SCJ}(\mathbb{M}, \mathbb{C}_i) &= |\alpha(\mathbb{M}) \setminus \alpha(\mathbb{C}_i)| + |\alpha(\mathbb{C}_i) \setminus \alpha(\mathbb{M})| \\ &= \sum_{xy \in \alpha(\mathbb{M})} (1 - \phi(xy, \mathbb{C}_i)) + \sum_{xy \notin \alpha(\mathbb{M})} \phi(xy, \mathbb{C}_i) \end{aligned}$$

Therefore:

$$\begin{aligned} s_{SCJ}(\mathbb{M}) &= \sum_{xy \in \alpha(\mathbb{M})} [(1 - \phi(xy, \mathbb{C}_1)) + (1 - \phi(xy, \mathbb{C}_2)) + (1 - \phi(xy, \mathbb{C}_3))] \\ &\quad + \sum_{xy \notin \alpha(\mathbb{M})} [\phi(xy, \mathbb{C}_1) + \phi(xy, \mathbb{C}_2) + \phi(xy, \mathbb{C}_3)] \\ &= \sum_{xy \in \alpha(\mathbb{M})} (3 - \phi(xy, \mathbb{C}_{1..3})) + \sum_{xy \notin \alpha(\mathbb{M})} \phi(xy, \mathbb{C}_{1..3}) \\ &= \sum_{xy} [\phi(xy, \mathbb{M}) \cdot (3 - \phi(xy, \mathbb{C}_{1..3})) + (1 - \phi(xy, \mathbb{M})) \cdot \phi(xy, \mathbb{C}_{1..3})] \\ &= \sum_{xy} [3 \cdot \phi(xy, \mathbb{M}) - \phi(xy, \mathbb{M}) \cdot \phi(xy, \mathbb{C}_{1..3}) + \phi(xy, \mathbb{C}_{1..3}) - \phi(xy, \mathbb{M}) \cdot \phi(xy, \mathbb{C}_{1..3})] \\ &= |\alpha(\mathbb{C}_1)| + |\alpha(\mathbb{C}_2)| + |\alpha(\mathbb{C}_3)| + \sum_{xy} [\phi(xy, \mathbb{M})(3 - 2 \cdot \phi(xy, \mathbb{C}_{1..3}))] \\ &= |\alpha(\mathbb{C}_1)| + |\alpha(\mathbb{C}_2)| + |\alpha(\mathbb{C}_3)| + \sum_{xy \in \alpha(\mathbb{M})} (3 - 2 \cdot \phi(xy, \mathbb{C}_{1..3})) \end{aligned}$$

SCJ median of canonical genomes

$$\begin{aligned} s_{SCJ}(\mathbb{M}) &= |\alpha(\mathbb{C}_1)| + |\alpha(\mathbb{C}_2)| + |\alpha(\mathbb{C}_3)| + \sum_{xy \in \alpha(\mathbb{M})} (3 - 2 \cdot \phi(xy, \mathbb{C}_{1..3})) \\ &= |\alpha(\mathbb{C}_1)| + |\alpha(\mathbb{C}_2)| + |\alpha(\mathbb{C}_3)| + \omega(\mathbb{M}) \end{aligned}$$

Since $|\alpha(\mathbb{C}_1)| + |\alpha(\mathbb{C}_2)| + |\alpha(\mathbb{C}_3)|$ is given (does not depend on $\mathbb{M}$), for minimizing $s_{SCJ}(\mathbb{M})$ we need to minimize:

$$\omega(\mathbb{M}) = \sum_{xy \in \alpha(\mathbb{M})} \omega(xy) = \sum_{xy \in \alpha(\mathbb{M})} (3 - 2 \cdot \phi(xy, \mathbb{C}_{1..3}))$$

where $\omega(xy) = 3 - 2 \cdot \phi(xy, \mathbb{C}_{1..3}) \in \{-3, -1, +1, +3\}$.

For minimizing $\omega(\mathbb{M})$:

- Do not add to $\mathbb{M}$ any adjacency xz that have $\omega(xz) > 0$:
  this happens when $\phi(xz, \mathbb{C}_{1..3}) \leq 1$ (xz occurs in at most one genome among $\mathbb{C}_1$, $\mathbb{C}_2$ and $\mathbb{C}_3$).
- Add to $\mathbb{M}$ any adjacency xy that have $\omega(xy) < 0$:
  this happens when $\phi(xy, \mathbb{C}_{1..3}) \geq 2$ (xy occurs in at least two genomes among $\mathbb{C}_1$, $\mathbb{C}_2$ and $\mathbb{C}_3$).
- For $z \neq y$: $\omega(xz) > 0 \Leftrightarrow \omega(xy) < 0$.

There is no adjacency xy with $\omega(xy) = 0$. Therefore, the SCJ median problem has a unique solution:

$$\alpha(\mathbb{M}) = \{xy : \phi(xy, \mathbb{C}_{1..3}) \geq 2\}$$

SCJ median of canonical genomes - intuition

Let $\mathcal{F}_\star = \mathcal{G}_\star = \{1, 2, 3, ..., n\}$
and start with $\mathbb{M} = [1]\ [2]\ ...\ [n]$

$\alpha(\mathbb{M}) = \emptyset$ and $\mathsf{s}_{\mathrm{SCJ}}(\mathbb{M}) = |\alpha(\mathbb{C}_1)| + |\alpha(\mathbb{C}_2)| + |\alpha(\mathbb{C}_3)|$

Effect of adding an adjacency xy to $\mathbb{M}$:

1. If xy is not present in any genome among $\{\mathbb{C}_1, \mathbb{C}_2, \mathbb{C}_3\}$, then $\Delta\mathsf{s}_{\mathrm{SCJ}} = +3$.
2. If xy is present in exactly one genome among $\{\mathbb{C}_1, \mathbb{C}_2, \mathbb{C}_3\}$, then $\Delta\mathsf{s}_{\mathrm{SCJ}} = +1$.
   ($\Delta\mathsf{d}_{\mathrm{SCJ}}(\mathbb{M}, \mathbb{C}_\mathtt{i}) = -1$, but $2 \times \Delta\mathsf{d}_{\mathrm{SCJ}}(\mathbb{M}, \mathbb{C}_\mathtt{i}) = +1$)
3. If xy is present in exactly two genomes among $\{\mathbb{C}_1, \mathbb{C}_2, \mathbb{C}_3\}$, then $\Delta\mathsf{s}_{\mathrm{SCJ}} = -1$.
   ($2 \times \Delta\mathsf{d}_{\mathrm{SCJ}}(\mathbb{M}, \mathbb{C}_\mathtt{i}) = -1$, but $\Delta\mathsf{d}_{\mathrm{SCJ}}(\mathbb{M}, \mathbb{C}_\mathtt{i}) = +1$)
4. If xy is present in all three genomes $\{\mathbb{C}_1, \mathbb{C}_2, \mathbb{C}_3\}$, then $\Delta\mathsf{s}_{\mathrm{SCJ}} = -3$.

SCJ median of k canonical genomes

Given k canonical genomes $\mathbb{C}_1, \mathbb{C}_2, \ldots \mathbb{C}_k$, find another canonical genome $\mathbb{M}$ that minimizes the sum:

$$\begin{aligned} s_{SCJ}(\mathbb{M}) &= d_{SCJ}(\mathbb{M}, \mathbb{C}_1) + d_{SCJ}(\mathbb{M}, \mathbb{C}_2) + \ldots + d_{SCJ}(\mathbb{M}, \mathbb{C}_k) \\ &= |\alpha(\mathbb{C}_1)| + |\alpha(\mathbb{C}_2)| + \ldots + |\alpha(\mathbb{C}_k)| \; + \; \omega(\mathbb{M}) \end{aligned}$$

Analogously to the median of three genomes, we need to minimize:

$$\omega(\mathbb{M}) = \sum_{xy \in \alpha(\mathbb{M})} \omega(xy)$$

where $\omega(xy) = k - 2 \cdot \phi(xy, \mathbb{C}_{1..k}) \in \{-k, -k+2, \ldots, +k-2, +k\}$.

$k=4$ $\{-4, -2, 0, +2, +4\}$

$k=5$ $\{-5, -3, -1, +1, +3, +5\}$

For minimizing $\omega(\mathbb{M})$:

- Do not add to $\mathbb{M}$ any adjacency xz that have $\omega(xz) > 0$:
  this happens when $\phi(xz, \mathbb{C}_{1..k}) < \frac{k}{2}$ (xz occurs in less than half of the genomes among $\mathbb{C}_1, \mathbb{C}_2, \ldots, \mathbb{C}_k$).
- Add to $\mathbb{M}$ any adjacency xy that have $\omega(xy) < 0$:
  this happens when $\phi(xy, \mathbb{C}_{1..3}) > \frac{k}{2}$ (xy occurs in more than half of the genomes among $\mathbb{C}_1, \mathbb{C}_2, \ldots, \mathbb{C}_k$).
- For $z \neq y$: $\omega(xz) > 0 \Leftrightarrow \omega(xy) < 0$.
- Any adjacency xy with $\omega(xy) = 0$ is optional (can be added to the median or not). If there is no such an adjacency (e.g., if k is odd), the SCJ median problem has a unique solution.

In general, the following set of adjacencies define a SCJ median of k genomes:

$$\alpha(\mathbb{M}) = \left\{ xy : \phi(xy, \mathbb{C}_{1..k}) > \frac{k}{2} \right\}$$

SCJ median of k canonical linear genomes

1. Compute the general SCJ median $\mathbb{M}$ as described above.

2. For each circular chromosome in $\mathbb{M}$, remove one adjacency xy with smallest weight $\omega(xy)$.

SCJ halving of a duplicated genome

Given a duplicated genome $\mathbb{D}$, find a singular genome $\mathbb{H}$ that minimizes the SCJ double distance:

$$d^2_{\mathrm{SCJ}}(\mathbb{H}, \mathbb{D}) = d_{\mathrm{SCJ}}(2\cdot\mathbb{H}, \mathbb{D})$$

Therefore:

$$\begin{aligned}
d_{\mathrm{SCJ}}(2\cdot\mathbb{H}, \mathbb{D}) &= |\alpha(2\cdot\mathbb{H}) \setminus \alpha(\mathbb{D})| + |\alpha(\mathbb{D}) \setminus \alpha(2\cdot\mathbb{H})| \\
&= \sum_{xy\in\alpha(\mathbb{H})}(2-\phi(xy,\mathbb{D})) + \sum_{xy\notin\alpha(\mathbb{H})}\phi(xy,\mathbb{D}) \\
&= \sum_{xy}[\ \phi(xy,\mathbb{H})\cdot(2-\phi(xy,\mathbb{D})) + (1-\phi(xy,\mathbb{H}))\cdot\phi(xy,\mathbb{D})\ ] \\
&= \sum_{xy}[\ 2\cdot\phi(xy,\mathbb{H}) - \phi(xy,\mathbb{H})\cdot\phi(xy,\mathbb{D}) + \phi(xy,\mathbb{D}) - \phi(xy,\mathbb{H})\cdot\phi(xy,\mathbb{D})\ ] \\
&= |\alpha(\mathbb{D})| + \sum_{xy}[\ \phi(xy,\mathbb{H})(2-2\cdot\phi(xy,\mathbb{D}))\ ] \\
&= |\alpha(\mathbb{D})| + \sum_{xy\in\alpha(\mathbb{H})}(2-2\cdot\phi(xy,\mathbb{D}))
\end{aligned}$$

SCJ halving of a duplicated genome

$$\begin{aligned} d^2_{\mathrm{SCJ}}(\mathbb{H},\mathbb{D}) &= |\alpha(\mathbb{D})| + \sum_{xy\in\alpha(\mathbb{H})}(2-2\cdot\phi(xy,\mathbb{D})) \\ &= |\alpha(\mathbb{D})| + \omega(\mathbb{H}) \end{aligned}$$

Since $|\alpha(\mathbb{D})|$ is given (does not depend on $\mathbb{H}$), for minimizing $d^2_{\mathrm{SCJ}}(\mathbb{H},\mathbb{D})$ we need to minimize:

$$\omega(\mathbb{H}) = \sum_{xy\in\alpha(\mathbb{H})}\omega(xy) = \sum_{xy\in\alpha(\mathbb{H})}(2-2\cdot\phi(xy,\mathbb{D}))$$

where $\omega(xy) = 2-2\cdot\phi(xy,\mathbb{D}) \in \{-2,0,+2\}$.

For minimizing $\omega(\mathbb{H})$:

- Do not add to $\mathbb{H}$ any adjacency xz that have $\omega(xz) > 0$:
  this happens when $\phi(xz,\mathbb{D}) = 0$ (xz does not occur in $\mathbb{D}$).
- Add to $\mathbb{H}$ any adjacency xy that have $\omega(xy) < 0$:
  this happens when $\phi(xy,\mathbb{D}) = 2$ (xy occurs twice in $\mathbb{D}$).
- For $z \neq y$: $\omega(xz) > 0 \Leftrightarrow \omega(xy) < 0$.
- Any adjacency xy with $\omega(xy) = 0$ (xy occurs once in $\mathbb{D}$) is optional (can be added to $\mathbb{H}$ or not).

Solution with the minimum number of adjacencies: $\alpha(\mathbb{H}) = \{xy : \phi(xy,\mathbb{D}) = 2\}$

SCJ aliquoting of a k-folded genome

Given a k-folded genome $\mathbb{K}$, find a singular genome $\mathbb{A}$ that minimizes the SCJ k-folded distance:

$$\mathrm{d}^k_{\mathrm{SCJ}}(\mathbb{A}, \mathbb{K}) = \mathrm{d}_{\mathrm{SCJ}}(\mathbf{k}\cdot\mathbb{A}, \mathbb{K})$$

Therefore:

$$\begin{aligned}
\mathrm{d}_{\mathrm{SCJ}}(\mathbf{k}\cdot\mathbb{A}, \mathbb{K}) &= |\alpha(\mathbf{k}\cdot\mathbb{A}) \setminus \alpha(\mathbb{K})| \quad + \quad |\alpha(\mathbb{K}) \setminus \alpha(\mathbf{k}\cdot\mathbb{A})| \\
&= \textstyle\sum_{xy\in\alpha(\mathbb{A})}(k - \phi(xy, \mathbb{K})) \quad + \quad \sum_{xy\notin\alpha(\mathbb{A})} \phi(xy, \mathbb{K}) \\
&= \textstyle\sum_{xy}[\ \phi(xy, \mathbb{A}) \cdot (k - \phi(xy, \mathbb{K})) \quad + \quad (1 - \phi(xy, \mathbb{A})) \cdot \phi(xy, \mathbb{K})\ ] \\
&= \textstyle\sum_{xy}[\ k \cdot \phi(xy, \mathbb{A}) - \phi(xy, \mathbb{A}) \cdot \phi(xy, \mathbb{K}) \quad + \quad \phi(xy, \mathbb{K}) - \phi(xy, \mathbb{A}) \cdot \phi(xy, \mathbb{K})\ ] \\
&= |\alpha(\mathbb{K})| \quad + \quad \textstyle\sum_{xy}[\ \phi(xy, \mathbb{A})(k - 2 \cdot \phi(xy, \mathbb{K}))\ ] \\
&= |\alpha(\mathbb{K})| \quad + \quad \textstyle\sum_{xy\in\alpha(\mathbb{A})}(k - 2 \cdot \phi(xy, \mathbb{K}))
\end{aligned}$$

The solution for the SCJ aliquoting problem of a k-folded genome is:

$$\alpha(\mathbb{A}) = \left\{ xy : \phi(xy, \mathbb{K}) > \frac{k}{2} \right\}$$

SCJ guided halving/aliquoting of a k-folded genome

Given a k-folded genome $\mathbb{K}$ and a canonical genome $\mathbb{C}$ find a canonical genome $\mathbb{A}$ that minimizes the sum:

$$\mathrm{ga}_{\mathrm{SCJ}}(\mathbb{A}) = \mathrm{d}^{k}_{\mathrm{SCJ}}(\mathbb{A},\mathbb{K}) + \mathrm{d}_{\mathrm{SCJ}}(\mathbb{A},\mathbb{C}) = \mathrm{d}_{\mathrm{SCJ}}(\mathtt{k}\cdot\mathbb{A},\mathbb{K}) + \mathrm{d}_{\mathrm{SCJ}}(\mathbb{A},\mathbb{C})$$

Therefore:

$$\begin{aligned}
\mathrm{ga}_{\mathrm{SCJ}}(\mathbb{A})) &= |\alpha(\mathtt{k}\cdot\mathbb{A}) \setminus \alpha(\mathbb{K})| \;+\; |\alpha(\mathbb{K}) \setminus \alpha(\mathtt{k}\cdot\mathbb{A})| \;+\; |\alpha(\mathbb{A}) \setminus \alpha(\mathbb{C})| \;+\; |\alpha(\mathbb{C}) \setminus \alpha(\mathbb{A})| \\
&= \textstyle\sum_{xy\in\alpha(\mathbb{A})}(k-\phi(xy,\mathbb{K})) \;+\; \sum_{xy\notin\alpha(\mathbb{A})}\phi(xy,\mathbb{K}) \;+\; \sum_{xy\in\alpha(\mathbb{A})}(1-\phi(xy,\mathbb{C})) \;+\; \sum_{xy\notin\alpha(\mathbb{A})}\phi(xy,\mathbb{C}) \\
&= \textstyle\sum_{xy\in\alpha(\mathbb{A})}(k+1-\phi(xy,\mathbb{K},\mathbb{C})) \;+\; \sum_{xy\notin\alpha(\mathbb{A})}\phi(xy,\mathbb{K},\mathbb{C}) \\
&= \textstyle\sum_{xy}[\;\phi(xy,\mathbb{A})\cdot(k+1-\phi(xy,\mathbb{K},\mathbb{C})) \;+\; (1-\phi(xy,\mathbb{A}))\cdot\phi(xy,\mathbb{K},\mathbb{C})\;] \\
&= \textstyle\sum_{xy}[\;(k+1)\cdot\phi(xy,\mathbb{A}) - \phi(xy,\mathbb{A})\cdot\phi(xy,\mathbb{K},\mathbb{C}) \;+\; \phi(xy,\mathbb{K},\mathbb{C}) - \phi(xy,\mathbb{A})\cdot\phi(xy,\mathbb{K},\mathbb{C})\;] \\
&= |\alpha(\mathbb{K})| \;+\; |\alpha(\mathbb{C})| \;+\; \textstyle\sum_{xy}[\;\phi(xy,\mathbb{A})(k+1-2\cdot\phi(xy,\mathbb{K},\mathbb{C}))\;] \\
&= |\alpha(\mathbb{C})| + |\alpha(\mathbb{K})| \;+\; \textstyle\sum_{xy\in\alpha(\mathbb{A})}(k+1-2\cdot\phi(xy,\mathbb{K},\mathbb{C}))
\end{aligned}$$

The solution for the guided SCJ aliquoting problem of a k-folded genome is:

$$\alpha(\mathbb{A}) = \left\{ xy : \phi(xy,\mathbb{K},\mathbb{C}) > \frac{k+1}{2} \right\}$$

Quiz 2

1 Which of the following statements are true?

A The SCJ median of four canonical genomes is always unique.

B The SCJ median of four canonical genomes cannot be unique.

C The SCJ median of three canonical genomes is always unique.

D The SCJ linear median of three canonical linear genomes is always unique.

E The SCJ guided halving problem is equivalent to the SCJ aliquoting problem.

F The SCJ aliquoting problem can be constrained to linear genomes only.

$k=4$, $w(xy) \in \{-4, -2, \emptyset, 2, 4\}$

$w(xy) \in \{-3, -1, 1, 3\}$

Perfect matching and circular canonical genomes

For a given set $N = \{1, 2, \ldots, n\}$,

let G be a complete graph with vertices $V(G) = \{g^h : g \in N\} \cup \{g^t : g \in N\}$

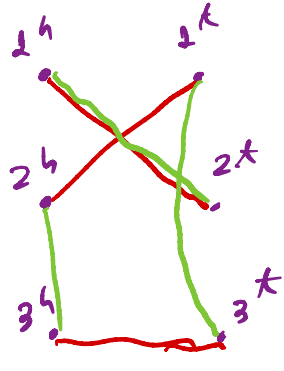
Perfect matching:

set of non-incident edges covering all vertices

Ex : $N = \{1,2,3\}$

$(1\ 2)\ (3)$

$(1\ 2\ \bar{3})$



A perfect matching M in G corresponds to $|M| = n$ adjacencies and, consequently, defines a circular canonical genome $\mathbb{C}$, with $\mathcal{F}(\mathbb{C}) = \mathcal{G}(\mathbb{C}) = N$ and $\alpha(\mathbb{C}) = M$.

SCJ median of k canonical circular genomes

Given k canonical circular genomes $\mathbb{C}_1, \mathbb{C}_2, \ldots \mathbb{C}_k$, find a canonical circular genome $\mathbb{M}$ that minimizes the sum:

$$\begin{aligned} s_{SCJ}(\mathbb{M}) &= d_{SCJ}(\mathbb{M}, \mathbb{C}_1) + d_{SCJ}(\mathbb{M}, \mathbb{C}_2) + \ldots + d_{SCJ}(\mathbb{M}, \mathbb{C}_k) \\ &= |\alpha(\mathbb{C}_1)| + |\alpha(\mathbb{C}_2)| + \ldots + |\alpha(\mathbb{C}_k)| \quad + \quad \omega(\mathbb{M}) \\ &= 3n \quad + \quad \omega(\mathbb{M}) \end{aligned}$$

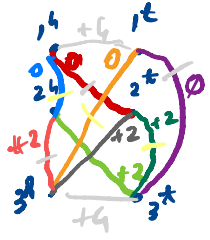
$|\alpha(\mathbb{M})| = n$

Again, we need to minimize $\omega(\mathbb{M}) = \sum_{xy \in \alpha(\mathbb{M})} \omega(xy)$, where $\omega(xy) = k - 2 \cdot \phi(xy, \mathbb{C}_{1..k})$.

(4) (3) (2) (1) (0)
$-4, -2, 0, +2, +4$

1. Build the complete graph G with vertices $V(G) = \{g^h : g \in \mathcal{G}_\star\} \cup \{g^t : g \in \mathcal{G}_\star\}$
2. Assign weights to each edge xy of G: $\omega(xy) = k - 2 \cdot \phi(xy, \mathbb{C}_{1..k})$.

Ex: $C_1 = (1\ 2\ 3)$
$C_2 = (3\ 2\ \bar{1})$
$C_3 = (3\ 1\ \bar{2})$
$C_4 = (3\ \bar{2}\ \bar{1})$



$M_1 = C_3$

$M_2 = C_4$

Perfect matching M in $G \Leftrightarrow$ Circular genome $\mathbb{M}$; with $\omega(M) = \omega(\mathbb{M})$

Minimum weight matching M gives a minimum weight circular SCJ median $\mathbb{M}$

Breakpoint median of canonical circular genomes

Given canonical circular genomes $\mathbb{C}_1$, $\mathbb{C}_2$ and $\mathbb{C}_3$, find a canonical circular genome $\mathbb{M}$ that minimizes the sum:

$$\begin{aligned} s_{BP}(\mathbb{M}) &= d_{BP}(\mathbb{M},\mathbb{C}_1) + d_{BP}(\mathbb{M},\mathbb{C}_2) + d_{BP}(\mathbb{M},\mathbb{C}_k) \\ &= n - \textstyle\sum_{xy\in\alpha(\mathbb{M})}\phi(xy,\mathbb{C}_1) + n - \sum_{xy\in\alpha(\mathbb{M})}\phi(xy,\mathbb{C}_2) + n - \sum_{xy\in\alpha(\mathbb{M})}\phi(xy,\mathbb{C}_3) \\ &= 3n - \textstyle\sum_{xy\in\alpha(\mathbb{M})}\phi(xy,\mathbb{C}_{1..3}) \\ &= 3n - \omega'(\mathbb{M}) \end{aligned}$$

Now we need to maximize $\omega'(\mathbb{M}) = \sum_{xy\in\alpha(\mathbb{M})}\omega'(xy)$, where $\omega'(xy) = \phi(xy,\mathbb{C}_{1..3})$.

1. Build the complete graph G with vertices $V(G) = \{g^h : g \in \mathcal{G}_\star\} \cup \{g^t : g \in \mathcal{G}_\star\}$
2. Assign weights to each edge xy of G: $\omega'(xy) = \phi(xy,\mathbb{C}_{1..k})$.

$w(xy) \in \{0,1,2,3\}$

$C_1 = (1\ 2\ 3\ 4)$

$C_2 = (4\ 1)(\bar{3}\ 2)$

$C_3 = (2\ 4\ 1)(3)$

Perfect matching M in $G \Leftrightarrow$ Circular genome $\mathbb{M}$; with $\omega'(M) = \omega'(\mathbb{M})$

Maximum weight matching M gives a minimum weight circular breakpoint median $\mathbb{M}$

Breakpoint median of canonical genomes

Given canonical genomes $\mathbb{C}_1$, $\mathbb{C}_2$ and $\mathbb{C}_3$, find a canonical genome $\mathbb{M}$ that minimizes the sum:

$$\begin{aligned}
s_{BP}(\mathbb{M}) &= d_{BP}(\mathbb{M},\mathbb{C}_1) + d_{BP}(\mathbb{M},\mathbb{C}_2) + d_{BP}(\mathbb{M},\mathbb{C}_k) \\
&= n - \sum_{xy\in\alpha(\mathbb{M})}\phi(xy,\mathbb{C}_1) - \sum_{x\in\gamma(\mathbb{M})}\frac{\phi(x,\mathbb{C}_1)}{2} + n - \sum_{xy\in\alpha(\mathbb{M})}\phi(xy,\mathbb{C}_2) \\
&\quad - \sum_{x\in\gamma(\mathbb{M})}\frac{\phi(x,\mathbb{C}_2)}{2} + n - \sum_{xy\in\alpha(\mathbb{M})}\phi(xy,\mathbb{C}_3) - \sum_{x\in\gamma(\mathbb{M})}\frac{\phi(x,\mathbb{C}_3)}{2} \\
&= 3n - \sum_{xy\in\alpha(\mathbb{M})}\phi(xy,\mathbb{C}_{1..3}) - \sum_{x\in\gamma(\mathbb{M})}\frac{\phi(x,\mathbb{C}_{1..3})}{2} \\
&= 3n - \omega'(\mathbb{M})
\end{aligned}$$

Now we need to maximize $\omega'(\mathbb{M}) = \sum_{xy\in\alpha(\mathbb{M})}\omega'(xy) + \sum_{x\in\gamma(\mathbb{M})}\omega'(x)$,
where $\omega'(xy) = \phi(xy,\mathbb{C}_{1..3})$ and $\omega'(x) = \frac{\phi(x,\mathbb{C}_{1..3})}{2}$.

1. Build the complete graph G with vertices $V(G) = \{g^h : g \in \mathcal{G}_\star\} \cup \{g^t : g \in \mathcal{G}_\star\}$
2. Assign weights to each edge xy of G: $\omega'(xy) = \phi(xy,\mathbb{C}_{1..k})$.
3. Build the complete graph G_t with vertices $V(G_t) = \{t_{g^h} : g \in \mathcal{G}_\star\} \cup \{t_{g^t} : g \in \mathcal{G}_\star\}$
4. Assign weight 0 to each edge of G_t
5. Add one edge connecting each vertex x in G to the corresponding vertex t_x in G_t, with weight $\omega'(xt_x) = \frac{\phi(x,\mathbb{C}_{1..k})}{2}$

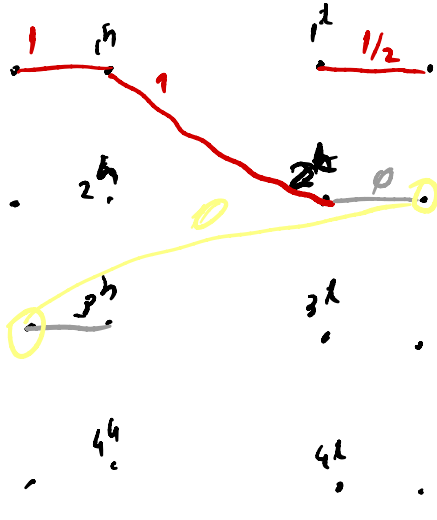
Perfect matching M in $G + G_t \Leftrightarrow$ Genome $\mathbb{M}$; with $\omega'(M) = \omega'(\mathbb{M})$

Maximum weight matching M gives a minimum weight breakpoint median $\mathbb{M}$

$C_1 = [1\ 2\ 3\ 4]$

$C_2 = [3\ 2\ 1]\ [4]$

$C_3 = [\bar{1}\ 2\ \bar{4}\ \bar{3}]$



Breakpoints { halving
guided halving

can be computed

in a similar way

Quiz 3

1 Which of the following statements are true?

A The SCJ aliquoting problem can be constrained to circular genomes only.

B The breakpoint median can only be computed for circular genomes.

C The circular SCJ median is equivalent to the circular breakpoint median of three canonical circular genomes.

D The breakpoint guided halving is NP-hard.

E The problem of computing a circular breakpoint halving of a circular duplicated genome is polynomial.

References

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