Between pop. $r_i r_j$ measure proposal

POP 1 : Frequencies $(p_{00}, p_{01}, p_{10}, p_{11})$

size N

POP 2 : Frequencies $(q_{00}, q_{01}, q_{10}, q_{11})$

size M

H_0 : pop 1, pop 2 are actually 1 population

Formally :

$$\begin{cases} \hat{p}_{00} = \dfrac{N p_{00} + M q_{00}}{N + M} \\ \vdots \\ \hat{p}_{11} = \dfrac{N p_{11} + M q_{11}}{N + M} \end{cases}$$

[Each of the $N+M$ gametes is sampled indep. from Multinomial $(\hat{p}_{00}, \dots, \hat{p}_{11})$]

Test idea: Is it realistic that N samples from this "big population" have '00' frequency equal to p_{00} and not $\hat{p}_{00}$?

Under H_0 : $p_{00} \sim \text{Normal}\left(\hat{p}_{00}, \dfrac{\hat{p}_{00}(1 - \hat{p}_{00})}{n}\right)$ by CLT

$$\text{p-value} = \mathbb{P}\left(|P_{00} - \hat{P}_{00}| > |P_{00} - \hat{P}_{00}| \right)$$

$$= \mathbb{P}\left(\left| \sqrt{\frac{\hat{P}_{00}(1-\hat{P}_{00})}{n}}\, Z \right| > |P_{00} - \hat{P}_{00}| \right)$$

where $Z \sim N(0,1)$

$$= \cancel{2 \min \left[\mathbb{P}\left(\left(\sqrt{\frac{\hat{P}_{00}(1-\hat{P}_{00})}{n}}\, Z \right) > |P_{00} - \hat{P}_{00}| \right), \mathbb{P}\left(- \;'' \; > |P_{00} - \hat{P}_{00}| \right) \right]}$$

$$= 1 - \Phi\left(\sqrt{\frac{n}{\hat{P}_{00}(1-\hat{P}_{00})}}\, |P_{00} - \hat{P}_{00}| \right)$$

Of course you can do 8 of these tests,

then perhaps take the max/min p-value,

or an average of the 8