Electronic Appendix 1

On the derivations of expressions for $Var\left(\frac{N^x}{N^y}\right)$ **and** $RSD\%\left(\frac{N^x}{N^y}\right)$**:**

(i) trivial case of ordinary Poisson distributed signals devoid of excess variance:

$$Var(N^x)=\overline{N}^x;\ Var(N^y)=\overline{N}^y;\ Cov(N^x,N^y)=0$$

$$\Downarrow$$

$$Var\left(\frac{N^x}{N^y}\right)=\left(\frac{1}{\overline{N}^y}\right)^2 Var(N^x)+\frac{(\overline{N}^x)^2}{(\overline{N}^y)^4}Var(N^y)-2\left(\frac{1}{\overline{N}^y}\right)\left(\frac{\overline{N}^x}{(\overline{N}^y)^2}\right)Cov(N^x,N^y)=$$

$$=\left(\frac{1}{\overline{N}^y}\right)^2\overline{N}^x+\frac{(\overline{N}^x)^2}{(\overline{N}^y)^4}\overline{N}^y-0=\frac{\overline{N}^x}{(\overline{N}^y)^2}\left[1+\frac{\overline{N}^x}{\overline{N}^y}\right]=\left(\frac{\overline{N}^x}{\overline{N}^y}\right)^2\left[\frac{1}{\overline{N}^x}+\frac{1}{\overline{N}^y}\right]$$

(ii) general case of doubly stochastic Poisson distributed signals with an excess variance (assuming that the both isotopes have constant transmission efficiencies):

$$Var(N^x)=\overline{\overline{N}}^x+p^2Var(M^x);\ Var(N^y)=\overline{\overline{N}}^y+p^2Var(M^y);\ Cov(N^x,N^y)=p^xp^yCov(M^x,M^y);$$

$$Let\ us\ introduce\ Pearson's\ \rho(M^x,M^y)=\frac{Cov(M^x,M^y)}{\left[Var(M^x)Var(M^y)\right]^{1/2}}\in\left[-1;+1\right]$$

$$\Downarrow$$

$$Var\left(\frac{N^x}{N^y}\right)=\left(\frac{1}{\overline{\overline{N}}^y}\right)^2 Var(N^x)+\frac{(\overline{\overline{N}}^x)^2}{(\overline{\overline{N}}^y)^4}Var(N^y)-2\left(\frac{1}{\overline{\overline{N}}^y}\right)\left(\frac{\overline{\overline{N}}^x}{(\overline{\overline{N}}^y)^2}\right)Cov(N^x,N^y)=$$

$$=\left(\frac{1}{\overline{\overline{N}}^y}\right)^2\left[\overline{\overline{N}}^x+\left(p^x\right)^2Var(M^x)\right]+\frac{(\overline{\overline{N}}^x)^2}{(\overline{\overline{N}}^y)^4}\left[\overline{\overline{N}}^y+\left(p^y\right)^2Var(M^y)\right]-2\left(\frac{1}{\overline{\overline{N}}^y}\right)\left(\frac{\overline{\overline{N}}^x}{(\overline{\overline{N}}^y)^2}\right)p^xp^yCov(M^x,M^y)=$$

$$=\frac{\overline{\overline{N}}^x}{(\overline{\overline{N}}^y)^2}\left[1+\frac{\overline{\overline{N}}^x}{\overline{\overline{N}}^y}\right]+\left[\frac{(p^x)^2}{(\overline{\overline{N}}^y)^2}Var(M^x)-2\frac{\overline{\overline{N}}^x p^xp^y}{(\overline{\overline{N}}^y)^3}\rho(M^x,M^y)\left[Var(M^x)Var(M^y)\right]^{1/2}+\frac{(\overline{\overline{N}}^x)^2(p^y)^2}{(\overline{\overline{N}}^y)^4}Var(M^y)\right]=$$

$$=\frac{\overline{\overline{N}}^x}{(\overline{\overline{N}}^y)^2}\left[1+\frac{\overline{\overline{N}}^x}{\overline{\overline{N}}^y}\right]+\left[\frac{p^xs(M^x)}{\overline{\overline{N}}^y}-\frac{\overline{\overline{N}}^x p^ys(M^y)}{(\overline{\overline{N}}^y)^2}\right]^2+2\frac{\overline{\overline{N}}^x p^xp^y}{(\overline{\overline{N}}^y)^3}\left[1-\rho(M^x,M^y)\right]s(M^x)s(M^y)=$$

$$=\frac{\overline{\overline{N}}^x}{(\overline{\overline{N}}^y)^2}\left[1+\frac{\overline{\overline{N}}^x}{\overline{\overline{N}}^y}\right]+\left[\frac{p^x}{\overline{\overline{N}}^y}\right]^2\left[s(M^x)-\frac{\overline{\overline{N}}^x p^y}{\overline{\overline{N}}^y p^x}s(M^y)\right]^2+2\frac{\overline{\overline{N}}^x p^xp^y}{(\overline{\overline{N}}^y)^3}\left[1-\rho(M^x,M^y)\right]s(M^x)s(M^y)=$$

$$=\frac{\overline{\overline{N}}^x}{(\overline{\overline{N}}^y)^2}\left[1+\frac{\overline{\overline{N}}^x}{\overline{\overline{N}}^y}\right]+\left[\frac{p^x}{\overline{\overline{N}}^y}\right]^2\left[s(M^x)-\frac{\overline{M}^x}{\overline{M}^y}s(M^y)\right]^2+2\frac{\overline{\overline{N}}^x p^xp^y}{(\overline{\overline{N}}^y)^3}\left[1-\rho(M^x,M^y)\right]s(M^x)s(M^y)=$$

$$=\left.\frac{\overline{\overline{N}}^x}{(\overline{\overline{N}}^y)^2}\left[1+\frac{\overline{\overline{N}}^x}{\overline{\overline{N}}^y}\right]+2\frac{\overline{\overline{N}}^x p^xp^y}{(\overline{\overline{N}}^y)^3}\left[1-\rho(M^x,M^y)\right]s(M^x)s(M^y)\ \right|_{s(M)\ is\ proportional\ to\ M}$$

It immediately follows from the derivation above that

$$RSD\%\left(\frac{N^x}{N^y}\right)=\left[\frac{1}{\overline{\overline{N}}^x}+\frac{1}{\overline{\overline{N}}^y}+2\left[1-\rho(M^x,M^y)\right]\frac{s(M^x)}{\overline{M}^x}\frac{s(M^y)}{\overline{M}^y}\right]^{1/2}\times 100$$

For signals where the excess variance is the dominating variance component, we can assume that

$$Var(N) = \overline{\overline{N}} + p^2 Var(M) \approx p^2 Var(M) \;\Big|\; p^2 Var(M) >> \overline{\overline{N}}$$

Accordingly, we obtain:

$$\rho(M^x, M^y) = \frac{Cov(M^x, M^y)}{\left[Var(M^x)Var(M^y)\right]^{1/2}} = \frac{\dfrac{Cov(N^x, N^y)}{p^x p^y}}{\left[\dfrac{Var(N^x)}{(p^x)^2}\dfrac{Var(M^y)}{(p^y)^2}\right]^{1/2}} = \frac{Cov(N^x, N^y)}{\left[Var(N^x)Var(M^y)\right]^{1/2}} = \rho(N^x, N^y)$$

$$s(M^x) = \frac{s(N^x)}{p^x};\; s(M^y) = \frac{s(N^y)}{p^y};\; \overline{M}^x = \frac{\overline{\overline{N}}^x}{p^x};\; \overline{M}^y = \frac{\overline{\overline{N}}^y}{p^y}$$

$$\Downarrow$$

$$RSD\%\left(\frac{N^x}{N^y}\right) \approx \left[\frac{1}{\overline{\overline{N}}^x} + \frac{1}{\overline{\overline{N}}^y} + 2\left[1 - \rho(N^x, N^y)\right]\frac{s(N^x)}{\overline{\overline{N}}^x}\frac{s(N^y)}{\overline{\overline{N}}^y}\right]^{1/2} \times 100$$