Single-cell RNA-sequencing: variance stabilizing transformations

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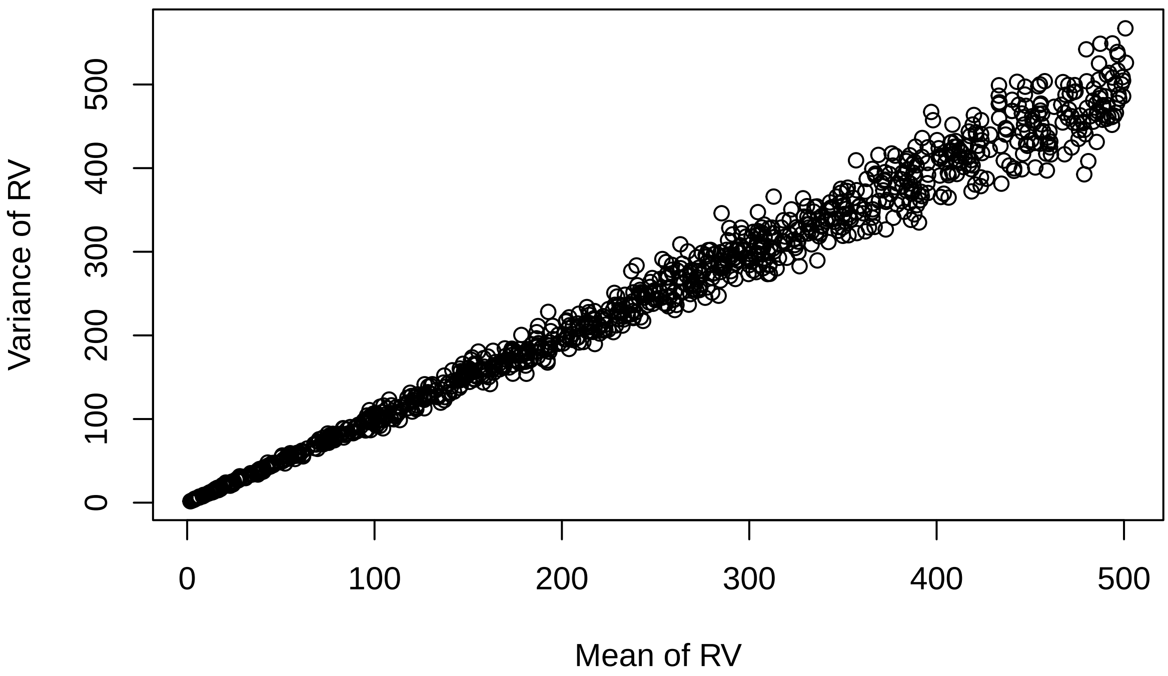
Contents

1 Approximating the variance stabilizing transformation of a Poisson random variable

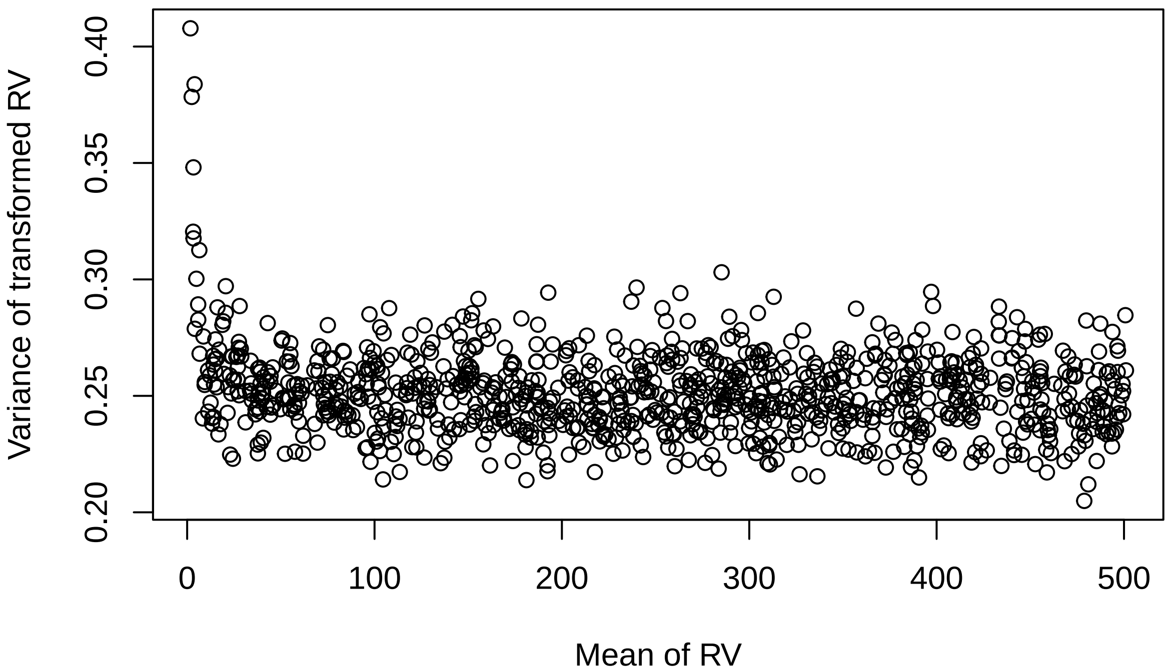
- A random variable $Y \sim Poi(\mu)$ has $Var(Y) = E(Y) = \mu$.
- We are looking for a variance stabilizing transformation (VST) $f(Y)$ such that $Var(f(Y)) = c$, with c any constant. In particular, we need $Var(f(Y))$ to be independent of μ.
- A first-order Taylor series gives us $f(Y) \approx f(\mu) + (Y - \mu)f'(\mu)$.
- Rearranging gives us $\{f(Y) - f(\mu)\}^2 = (Y - \mu)^2 f'(\mu)^2$.
- Which may be written as $Var(f(Y)) = Var(Y)f'(\mu)^2$.
- This shows us that **we want a transformation such that** $f'(\mu)^2 = 1/\mu$ because then $\forall \mu : Var(f(Y)) = 1$! Let's find out.
- The last bullet point can be written as $f'(\mu) = \frac{1}{\sqrt{\mu}}$ and therefore $f(\mu) = \int \frac{1}{\sqrt{\mu}} d\mu = 2\mu^{1/2}$.
- Finally, this shows us that the transformation $f(Y) = 2Y^{1/2}$ ensures $Var(f(Y)) = 1$. Similar, as is often written in the scientific literature, the transformation $f(Y) = Y^{1/2}$ ensures $Var(f(Y)) = 1/4$.
- Note that these derivations all **rely on the first-order Taylor expansion to be a good approximation**. The VST will therefore work better for random variables with a high mean μ as the distribution will be more discrete for random variables with a low mean. We show this using simulation below.

```r
set.seed(871)
N <- 1e3
df <- data.frame(mean=rep(NA, N),
                 var=rep(NA, N),
                 transVar=rep(NA, N))
for(kk in 1:N){
  sampledMu <- runif(n=1, min=1, max=500)
  y <- rpois(n=500, lambda=sampledMu)
  df[kk,] <- c(mean(y), var(y), var(sqrt(y)))
}

plot(x=df$mean, y=df$var,
     xlab = "Mean of RV", ylab="Variance of RV")
```




```
plot(x=df$mean, y=df$transVar,
     xlab = "Mean of RV", ylab="Variance of transformed RV")
```



Question. Why is the first plot heteroscedastic?

Answer.

Remember that $Var(\hat{\mu}) = \frac{\hat{\mu}}{n}$. Since for all random variables in our simulation n is equal, in our case we have that $Var(\hat{\mu}) = c\hat{\mu}$. The variance on estimating the mean thus increases with the mean.