1 Notation

We use the following notation:

1. Reads $=$ (numReads, readLen, Read$_i$). Here Read$_i$ is the sequence of the ith read.
2. Trans $=$ (NumTrans, TranLen$_i$, Tran$_i$). Here Tran$_i$ is the sequence of the ith transcript.
3. Contigs $=$ (NumContigs, ContigLen$_j$, Contig$_j$). Here Contig$_j$ is the sequence of the jth contig.
4. Expr$_i$ = the number of reads truely mapping to transcript i.
5. Coverage$_j$ = the number of reads truely mapping to contig j.
6. ContigsFromTrans $=$ (NumContigsFromTran$_i$, ContigsFromTran$_i$). Here ContigsFromTran$_i$ is the set of indices of the contigs which originate from transcript i, and NumContigsFromTran$_i$ is the cardinality of that set.
7. ws = the overlap window size required to joint two reads into a contig.

All of the above are random variables, except numReads, readLen, and ws.

Unless there is ambiguity, for random variables X and Y, we will write $P(x)$ instead of $P(X = x)$, and $P(x|y)$ instead of $P(X = x|Y = y)$. We write $X =_D Y$ if X equals Y in distribution. All indices within sequences start at 0.

Our score is score(reads, contigs) $= P($reads, contigs$)$. Of course, we are really interested in the normalized version $P($contigs$|$reads$)$. The score is related to the joint distribution of all random variables listed above by marginalization:

$$P(\text{reads}, \text{contigs}, \text{trans}, \text{expr}, \text{coverage}, \text{contigsFromTrans})$$
$$= \int P(\text{reads}, \text{contigs}, \text{trans}, \text{expr}, \text{coverage}, \text{contigsFromTrans})\, d\text{trans}\, d\text{expr}\, d\text{coverage}\, d\text{contigsFromTrans}$$

We want to evaluate the score, and we will do this by a Laplace-like approximation, as follows: (i) specify the joint distribution, (ii) find a mode or near-mode of of this distribution, (iii) perform a mode-based approximation of the integral over hidden variables.

2 The joint distribution

We decompose the joint distribution as follows:

$$P(\text{reads}, \text{trans}, \text{expr}, \text{contigs}, \text{coverage}, \text{contigsFromTrans}) = P(\text{trans}, \text{expr})$$
$$\cdot P(\text{reads}|\text{trans}, \text{expr})$$
$$\cdot P(\text{contigs}, \text{coverage}, \text{contigsFromTrans}|\text{reads}, \text{trans}, \text{expr})$$

In the rest of this section, we stipulate functional forms for each of these distributions.

2.1 Distribution of Trans, Expr

First, for the prior distribution $P($trans, expr$)$, we stipulate, similarly to the current model, that:

1. NumTrans $\sim$ Poisson(μ_0).

2. $\text{TranLen}_i|\{\text{NumTrans} = \text{numTrans}\} \sim \text{NegativeBinomial}(r_0, p_0)$, for $i = 1, \ldots, \text{numTrans}$.

3. $\text{Tran}_i|\{\text{NumTrans} = \text{numTrans}, \text{TranLen}_i = \text{tranLen}_i\} \sim \text{Uniform}(\{\texttt{A}, \texttt{T}, \texttt{G}, \texttt{C}\}^{\text{tranLen}_i})$.

4. $\text{Expr}_i|\{\text{NumTrans} = \text{numTrans}, \text{TranLen}_i = \text{tranLen}_i, \text{Tran}_i = \text{tran}_i\} \sim \text{Uniform}(\{1, 2, \ldots, \text{numReads}\})$.

(A non-uniform distribution for Expr_i might be more reasonable - but also more complicated.) So

$$P(\text{trans}, \text{expr})$$

$$= P(\text{numTrans}) \prod_{i=1}^{\text{numTrans}} P(\text{tranLen}_i|\text{numTrans}) \cdot P(\text{tran}_i|\text{numTrans}, \text{tranLen}_i) \cdot P(\text{expr}_i|\text{numTrans}, \text{tranLen}_i, \text{tran}_i)$$

$$= \text{Poisson}(\text{numTrans}|\mu_0) \prod_{i=1}^{\text{numTrans}} \text{NegativeBinomial}(\text{tranLen}_i|r_0, p_0) \cdot 4^{-\text{tranLen}_i} \cdot \text{numReads}^{-1}$$

$$= \frac{\mu_0^{\text{numTrans}}}{\text{numTrans}!} e^{-\mu_0} \prod_{i=1}^{\text{numTrans}} \binom{\text{tranLen}_i + r_0 - 1}{\text{tranLen}_i} (1 - p_0)^{r_0} p_0^{\text{tranLen}_i} \cdot 4^{-\text{tranLen}_i} \cdot \text{numReads}^{-1}$$

$$= \frac{(\mu_0(1 - p_0)^{r_0}/\text{numReads})^{\text{numTrans}}}{\text{numTrans}!} e^{-\mu_0} \prod_{i=1}^{\text{numTrans}} \binom{\text{tranLen}_i + r_0 - 1}{\text{tranLen}_i} (p_0/4)^{\text{tranLen}_i}$$

where (μ_0, r_0, p_0) are the prior parameters.

2.2 Distribution of $\text{Reads}|\{\text{Trans}, \text{Expr}\}$

For the data's conditional distribution, we use RSEM:

$$P(\text{reads}|\text{trans}, \text{expr}) = P_{RSEM}(\text{reads}|\text{trans}, \text{expr})$$

No correction is needed because we are conditioning on the actual transcripts, not contigs.

2.3 Distribution of $(\text{Contigs}, \text{Coverage}, \text{ContigsFromTrans})|\{\text{Reads}, \text{Trans}, \text{Expr}\}$

For the distribution of contigs (and their coverage and originating transcripts), we use a simple Lander-Waterman–like approach (Lander and Waterman (1988)). (We could also use Bo's approach, which is perhaps in some ways more accurate; the approach here is mainly designed to make maximization easier later on.)

First, like in Bo's current approach, we assume that the contigs (and coverage) are conditionally independent of the reads, given the transcripts (and expression), i.e., in symbols:

$$(\text{Contigs}, \text{Coverage}, \text{ContigsFromTrans})|\{\text{Reads}, \text{Trans}, \text{Expr}\} =_D (\text{Contigs}, \text{Coverage}, \text{ContigsFromTrans})|\{\text{Trans}, \text{Expr}\}$$

Recall that numReads and readLen are not random; these quantities will be very important for the distributions below.

Next, we decompose the conditional distribution of $(\text{Contigs}, \text{Coverage}, \text{ContigsFromTrans})$ as follows:

$$P(\text{contigs}, \text{coverage}, \text{contigsFromTrans}|\text{trans}, \text{expr})$$

$$= P(\text{numContigsFromTran}|\text{trans}, \text{expr})$$

$$\cdot P(\text{contigsFromTran}|\text{numContigsFromTran}, \text{trans}, \text{expr})$$

$$\cdot P(\text{coverage}|\text{contigsFromTran}, \text{numContigsFromTran}, \text{trans}, \text{expr})$$

$$\cdot P(\text{contigLen}|\text{coverage}, \text{contigsFromTrans}, \text{trans}, \text{expr})$$

$$\cdot P(\text{contig}|\text{contigLen}, \text{coverage}, \text{contigsFromTrans}, \text{trans}, \text{expr})$$

2.3.1 Distribution of NumContigsFromTran|{Trans, Expr}

We assume that the number of contigs from transcript i is conditionally independent of the number of contigs from transcript j. So

$$P(\text{numContigsFromTran}|\text{trans}, \text{expr}) = \prod_{i=1}^{\text{numTrans}} P(\text{numContigsFromTran}_i|\text{tran}_i, \text{expr}_i)$$

Next, we find $P(\text{numContigsFromTran}_i|\text{tran}_i, \text{expr}_i)$. According to Lander-Waterman, if a transcript has length l and expression x, then the probability it generates n contigs is $\text{Binomial}(n|l, \alpha(1-\alpha)^{\text{readLen}-\text{ws}})$, where $\alpha = 1 - (1 - l^{-1})^x$ is the probability that at least one of the x reads starts at a particular position.

Reason: First:

1. l^{-1} is the probability that a particular read starts at a particular position, assuming a uniform RSPD, and assuming (falsely) that reads can start even at the end of the transcript (otherwise it would be $(l - \text{readLen} + 1)^{-1}$). (See Figure 1.)

2. So $1 - l^{-1}$ is the probability that a particular read does not start at a particular position.

3. So $(1 - l^{-1})^x$ is the probability that none of the x reads starts at a particular position, assuming that the read start positions are independent.

4. So $\alpha = 1 - (1 - l^{-1})^x$ is the probability that at least one of the x reads starts at a particular position.

Second: The "beginning of the end" of a contig occurs at position k if (i) at least one read starts at position k, and (ii) no read starts at any of the subsequent $\text{readLen} - \text{ws}$ positions. (See Figure 2.) Call this event B_k. The probability of this event is $\alpha(1-\alpha)^{\text{readLen}-\text{ws}}$, assuming (again) independence between read start positions.

Third: The number of contigs that come from a transcript is equal to the number of "beginning of the end" events B_k that occur. If we (i) assume that the B_k are independent (so that, for example, "beginning of the end" events can occur even right next to each other), and (ii) we ignore edge effects (so that "beginning of the end" events have equal probability even at the rightmost end of the transcript), then the probability of getting n contigs is $\text{Binomial}(n|l, \alpha(1-\alpha)^{\text{readLen}-\text{ws}})$. (Note: Assumption (i) is grossly incorrect. Assumption (ii) is perhaps not too bad if there are long poly(A) tails. Alternatively, we could use the more complicated formulas found by Wendl and Barbazuk (2005), or Bo's approach, to take into account the edge effects. But this makes maximization more complicated later on.)

In summary:

$$P(\text{numContigsFromTran}_i|\text{tran}_i, \text{expr}_i) = \text{Binomial}(\text{numContigsFromTran}_i|\text{tranLen}_i, \alpha_i(1-\alpha_i)^{\text{readLen}-\text{ws}})$$

where $\alpha_i = 1 - (1 - \text{tranLen}_i^{-1})^{\text{expr}_i}$ is the probability that at least one of the expr_i reads starts at a particular position in transcript i.

2.3.2 Distribution of ContigsFromTran|{NumContigsFromTran, Trans, Expr}

We assume that the chance of any particular assignment of contigs to transcripts, conditional on the number of contigs from each transcript, is uniform over the relevant set. The relevant set is the assignments of $\text{numContigsFromTran}_i$ contigs to transcript i, for each i, without replacement, where there are $\text{numContigs} = \sum_{i=1}^{\text{numTrans}} \text{numContigsFromTran}_i$ contigs total. (numContigs is a deterministic function of numContigsFromTran.) The size of this set is given by the multinomial coefficient. So:

$$P(\text{contigsFromTran}|\text{numContigsFromTran}, \text{trans}, \text{expr}) = \binom{\text{numContigs}}{\text{numContigsFromTran}_i : i = 1, \ldots, \text{numTrans}}^{-1}$$

```
01234567890123456789
-----
 -----
       [...]
               ----- 15 = 20 - 5
            +++++
             +++++
              +++++
               +++++
                +++++ 19 = 20 - 1
```

Figure 1: What is the probability that a particular read starts from a particular position? Here transcript length is 20 and read length is 5. Reads can start at positions $0, 1, \ldots, 15$, i.e., at $16 = 20 - 5 + 1 = \text{tranLen} - \text{readLen} + 1$ distinct positions. Assuming uniform RSPD, the chance of starting at any of these positions is $1/(\text{tranLen} - \text{readLen} + 1)$. Assuing, as we do for simplicity, that reads can start even at positions $16, 17, \ldots, 19$, i.e., at $20 = \text{tranLen}$ distinct positions, the chance of starting at any of these positions is $1/\text{tranLen}$.

```
01234567890123456789
  -----        Read occurs at position 2.
   .....       Read fails to occur at position 3.
    .....      Read fails to occur at position 4.
     .....     Read fails to occur at position 5.
```

Figure 2: Example of a contig ending. Here transcript length is 20, read length is 5, and window size is 2. The contig ends when there is one read occurrence, followed by $3 = 5 - 2 = \text{readLen} - \text{ws}$ failures to occur.

2.3.3 Distribution of $\text{Coverage}|\{\text{ContigsFromTrans}, \text{Trans}, \text{Expr}\}$

First, we stipulate that the coverage of the contigs from transcript i is conditionally independent of both the other transcripts and of the coverage of the contigs from other transcripts, conditional on the transcript i. Using the notation $X_{(i)} = (X_j : j \in \text{ContigsFromTran}_i)$, this gives

$$P(\text{coverage}|\text{contigsFromTrans}, \text{trans}, \text{expr})$$
$$= \prod_{i=1}^{\text{numTrans}} P(\text{coverage}_{(i)}|\text{contigsFromTran}_i, \text{tran}_i, \text{expr}_i)$$

If we also, for the moment, assume that the coverages of contigs from transcript i are also conditionally independent, letting $\text{Coverage}'_{(i)}$ be the conditionally independent version of the random variable, then

$$P(\text{coverage}'_{(i)}|\text{contigsFromTran}_i, \text{tran}_i, \text{expr}_i)$$
$$= \prod_{j \in \text{contigsFromTran}_i} P(\text{coverage}'_j|\text{contigsFromTran}_i, \text{tran}_i, \text{expr}_i)$$

and we can use Lander-Waterman to find $P(\text{coverage}'_j|\text{contigsFromTran}_i, \text{tran}_i, \text{expr}_i)$.

According to Lander-Waterman,

$$P(\text{coverage}'_j|\text{contigsFromTran}_i, \text{tran}_i, \text{expr}_i) = \text{Geometric}(\text{coverage}'_j|(1 - \alpha_i)^{\text{readLen} - \text{ws}}).$$

Reason: Assume that contig j has already started, so there are currently c reads covering the left prefix of contig j, with rightmost read starting at position k within the transcript. The contig ends, with total coverage c, if $\text{readLen} - \text{ws}$ reads do not occur, starting at position $k + 1$; this happens with probability $\gamma_i = (1 - \alpha_i)^{\text{readLen} - \text{ws}}$ (see previous paragraph). Thus, the chance of getting coverage c, for any c, is the chance that an event with probability γ_i (namely, the absence

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of readLen $-$ ws reads in a row) fails to occur c times. This is the geometric distribution with termination probability γ_i. (We use the variant which includes 0 in the support, because if the termination event occurs in the first trial, then read coverage is 0. It would be more accurate to exclude this possibility - that that would make the formulas slightly more complicated.)

Above, we temporarily assumed that the coverages of contigs from transcript i are conditionally independent, but this is certainly not true, because the sum of the coverages equals the expression, i.e., $\sum_{j\in\text{ContigsFromTran}_i}\text{Coverage}_i = \text{Expr}_i$. Therefore we instead assume that the coverages of contigs from transcript i are conditionally independent, conditional not just on the transcript and its expression but also on the event that the sum of the coverages equals the expression, i.e., the event $B_i := \{\omega : \sum_{j\in\text{ContigsFromTran}_i}\}$:

$$P(\text{coverage}_{(i)}|\text{contigsFromTran}_i,\text{tran}_i,\text{expr}_i)$$
$$= P(\text{coverage}_{(i)}|B_i,\text{contigsFromTran}_i,\text{tran}_i,\text{expr}_i)P(B_i|\text{contigsFromTran}_i,\text{tran}_i,\text{expr}_i)$$
$$+ P(\text{coverage}_{(i)}|B_i^c,\text{contigsFromTran}_i,\text{tran}_i,\text{expr}_i)P(B_i^c|\text{contigsFromTran}_i,\text{tran}_i,\text{expr}_i)$$
$$= P(\text{coverage}_{(i)}|B_i,\text{contigsFromTran}_i,\text{tran}_i,\text{expr}_i)$$

The last equality holds because the conditional probability of B_i is stipulated to be 1.

It remains to specify $P(\text{coverage}_{(i)}|B_i,\text{contigsFromTran}_i,\text{tran}_i,\text{expr}_i)$. We saw above that under the assumption of conditional independence of the coverages, each coverage is conditionally distributed according to Geometric(γ_i). Conditioning on B_i restricts the support of $\text{coverage}_{(i)}$, but does not otherwise change the distribution. Fact: In general, if $X_i \sim$ Geometric(p) iid, then $\sum_{i=1}^n X_i \sim$ NegativeBinomial($n, 1-p$). See the next paragraph for a proof. Applying this to our case,

$$P(\text{coverage}_{(i)}|B_i,\text{contigsFromTran}_i,\text{tran}_i,\text{expr}_i)$$
$$= \frac{\prod_{j\in\text{contigsFromTran}_i}\text{Geometric}(\text{coverage}_j|\gamma_i)}{\text{NegativeBinomial}(\text{expr}_i|\text{numContigsFromTran}_i, 1-\gamma_i)}$$

Reason for the fact mentioned in the previous paragraph, that in general, if $X_i \sim$ Geometric(p) iid, then $\sum_{i=1}^n X_i \sim$ NegativeBinomial($n, 1-p$): If X is a random variable, then let the MGF $M_X(t) = Ee^{tX}$. In general, if $M_X = M_Y$ then $X =_D Y$. If X is Geometric(p) and Y is NegativeBinomial($n, 1-p$), then $M_X(t) = \frac{p}{1-(1-p)e^t}$ and $M_Y(t) = \left(\frac{p}{1-(1-p)e^t}\right)^n$. The MGF of $\sum_{i=1}^n X_i$ is:

$$M_{\sum_{i=1}^n X_i}(t) = Ee^{t\sum_{i=1}^n X_i} = E\prod_{i=1}^n e^{tX_i} = \prod_{i=1}^n Ee^{tX_i} = \prod_{i=1}^n M_X(t) = M_X(t)^n = M_Y(t)$$

so $\sum_{i=1}^n X_i =_D Y$ as claimed.

In summary:

$$P(\text{coverage}|\text{contigsFromTrans},\text{trans},\text{expr})$$
$$= \prod_{i=1}^{\text{numTrans}} P(\text{coverage}_{(i)}|\text{contigsFromTran}_i,\text{tran}_i,\text{expr}_i)$$
$$= \prod_{i=1}^{\text{numTrans}} P(\text{coverage}_{(i)}|B_i,\text{contigsFromTran}_i,\text{tran}_i,\text{expr}_i)$$
$$= \prod_{i=1}^{\text{numTrans}} \frac{\prod_{j\in\text{contigsFromTran}_i}\text{Geometric}(\text{coverage}_j|\gamma_i)}{\text{NegativeBinomial}(\text{expr}_i|\text{numContigsFromTran}_i, 1-\gamma_i)}$$

2.3.4 Distribution of $\text{ContigLen}|\{\text{Coverage}, \text{ContigsFromTrans}, \text{Trans}, \text{Expr}\}$

Just as for the coverage, we assume that the contig lengths for contigs from one transcript are conditionally independent of other transcripts and their contigs:

$$P(\text{contigLen}|\text{coverage}, \text{contigsFromTrans}, \text{trans}, \text{expr})$$

$$= \prod_{i=1}^{\text{numTrans}} P(\text{contigLen}_{(i)}|\text{coverage}_{(i)}, \text{contigsFromTran}_i, \text{trans}_i, \text{expr}_i)$$

Also, just as for the coverage, we (i) find how the contig lengths for a particular transcript would be distributed assuming conditional independence even among contigs from a single transcript, (ii) reinstatement of the dependence, by restricting the domain of the joint distribution and normalizing.

Let A_i be the event $\{\omega : \text{Coverage}_{(i)} = \text{coverage}_{(i)}, \text{ContigsFromTran}_i = \text{contigsFromTran}_i, \text{Trans}_i = \text{trans}_i, \text{Expr}_i = \text{expr}_i\}$.

2.3.4.1 (i) The distribution, assuming conditional independence even among contigs from a single transcript
Let $\text{ContigLen}'_{(i)}$ be the conditionally independent version of $\text{ContigLen}_{(i)}$.

Recall (a) that we are assuming that all reads from a transcript start (i) independently of each other and (ii) uniformly along the length of the transcript, including even at the end of the transcript. I.e., the probability that a particular read r from transcript i starts at position k of transcript i is tranLen_i^{-1}, independently of all other reads. Recall also (b) that, by definition, each contig is a contiguous collection of reads, in the sense that, if one enumerates the reads involved in this contig from left to right, there is always at least ws bases of overlap between each adjacent (in the enumeration) read. See Figure 3 for an example.

Consider a contig j from transcript i. Due to item (b), contig j's length $\text{contigLen}'_j$ must be between readLen and $\text{readLen} \cdot \text{coverage}_j$. Moreover, each possible way to arrange the coverage_j reads involved in contig j consistent with item (b) is equally likely, due to item (a). Therefore, the conditional probability of contig j having length $\text{contigLen}'_j$ is proportional to the number of ways the coverage_j reads can be arranged into a contig of length $\text{contigLen}'_j$. In symbols,

$$P(\text{contigLen}'_j|A_i) = \frac{\text{numArrangements}(\text{coverage}_j, \text{contigLen}'_j, \text{readLen})}{\sum_{l=\text{readLen}}^{\text{readLen} \cdot \text{coverage}_j} \text{numArrangements}(\text{coverage}_j, l, \text{readLen})}$$

Here numArrangements need not be considered to include different permutations of read identities, since doing so would just introduce the same factor $\text{coverage}_j!$ in both the numerator and denominator. (Cf. Figure 3.)

Claim: $\text{numArrangements}(\text{coverage}_j, \text{contigLen}'_j, \text{readLen}) = \binom{\text{coverage}_j - 1}{\text{contigLen}'_j - \text{readLen}}_{\text{readLen}+1}$, where

$$\binom{n}{k}_N = \begin{cases} 0 & \text{if } n < 0 \text{ or } k < 0 \text{ or } k > (N-1) \cdot n \\ 1 & \text{if } n = 0 \text{ and } k = 0 \\ \sum_{j=0}^{N-1} \binom{n-1}{k-j}_N & \text{otherwise} \end{cases}$$

Proof: Fix an enumeration of the coverage_j reads involved in contig j from left to right, as described in item (b) above. Each read can be thought to "newly contribute" a certain number of bases, in the sense that no previous (in the enumeration) read covers these bases, but the read in question does cover them. See Figure 4 for an example. The first (and leftmost) read always contributes readLen bases. Each remaining read can contribute between 0 bases (if it

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completely overlaps the previous read) and readLen bases (if it starts just after the previous read), assuming that we require window size of 0.

For each arrangement a of the reads, let $x = x(a)$ be the corresponding "new-contribution" vector, i.e., x_r is the number of bases newly contributed by read r in the arrangement. Note that there is a 1-1 correspondence between arrangements a and new-contribution vectors x. Thus the number of arrangements of the reads into a contig of length $\text{contigLen}'_j$ is equal to the number of valid new-contribution vectors, i.e., the number of vectors $x \in \{\text{readLen}\} \times \{0,\ldots,\text{readLen}\}^{\text{coverage}_j - 1}$ such that $\sum_{r=1}^{\text{coverage}_j - 1} x_r = \text{contigLen}'_j$.

How many such new-contribution vectors are there? The first read always newly covers readLen bases. Each new-contribution vector says how to allocate the remaining $\text{contigLen}'_j - \text{readLen}$ bases among the remaining $\text{coverage}_j - 1$ reads, allowing at most readLen positions to be allocated to each read. We can think of the bases as being unlabelled, in the sense that the new-contribution vectors do not keep track of *which* specific (identified) bases are newly covered by each read, but rather just *how many* bases are newly covered by each read. We can think of the reads as being labelled, in the sense that each new-contribution vector says how many bases are newly contributed by each read which is labelled by its position within the (fixed) enumeration. Thus, the number of new-contribution vectors is the number of distinct ways in which $k := \text{contigLen}'_j - \text{readLen}$ balls (i.e., bases) can be allocated to $n := \text{coverage}_j - 1$ urns (i.e., reads), allowing at most $N - 1 := \text{readLen}$ balls (i.e., bases) to fall in each urn (i.e., read). It is known that the number of ways to do this is $\binom{n}{k}_N$: see comments by N-E. Fahssi from OEIS entries `http://oeis.org/A008287` and `http://oeis.org/A035343`, and cf. also Fahssi (2012).

For empirical evidence of the claim, see `howManyWaysToCoverAContig.py`. ∎

Claim: $\sum_{l=\text{readLen}}^{\text{readLen}\cdot\text{coverage}_j} \text{numArrangements}(\text{coverage}_j, l, \text{readLen}) = (\text{readLen} + 1)^{\text{coverage}_j - 1}$.

Proof: Note that

$$\sum_{l=\text{readLen}}^{\text{readLen}\cdot\text{coverage}_j} \text{numArrangements}(\text{coverage}_j, l, \text{readLen})$$

$$= \sum_{l=\text{readLen}}^{\text{readLen}\cdot\text{coverage}_j} \binom{\text{coverage}_j - 1}{l - \text{readLen}}_{\text{readLen}+1}$$

$$= \sum_{l=0}^{\text{readLen}\cdot(\text{coverage}_j - 1)} \binom{\text{coverage}_j - 1}{l}_{\text{readLen}+1}$$

the $(\text{coverage}_j - 1)$th row sum of the array with entries $(n, k) = \binom{n}{k}_{\text{readLen}+1}$. It is a fact (see `http://oeis.org/A027907` for the trinomial case) that these row sums are $n \mapsto N^n$, i.e., in our case, the $(\text{coverage}_j - 1)$th row sum is $(\text{readLen} + 1)^{\text{coverage}_j - 1}$.

For empirical evidence, see `howManyWaysToCoverAContig.py`. ∎

Plugging in from the claims,

$$P(\text{contigLen}'_j | A_i) = \frac{\text{numArrangements}(\text{coverage}_j, \text{contigLen}'_j, \text{readLen})}{\sum_{l=\text{readLen}}^{\text{readLen}\cdot\text{coverage}_j} \text{numArrangements}(\text{coverage}_j, l, \text{readLen})}$$

$$= \binom{\text{coverage}_j - 1}{\text{contigLen}'_j - \text{readLen}}_{\text{readLen}+1} (\text{readLen} + 1)^{-(\text{coverage}_j - 1)}$$

(Note: This is essentially Eq. (2.4) in Fahssi (2012), with $k := \text{coverage}_j - 1$, $n := \text{contigLen}'_j - \text{readLen}$, $\mathbf{a} := (1, 1, \ldots, 1) \in \mathbb{N}^{\text{readLen}+1}$, and $N := \text{readLen} + 1$.)

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```
0123456    contig
aaaaa
bbbbb
  ccccc

0123456    contig
aaaaa
 bbbbb
  ccccc

0123456    contig
aaaaa
  bbbbb
  ccccc
```

Figure 3: All the ways to get a contig of length 7 from 3 reads of length 5, when we do not consider read identity. If we consider read identity, then the number of ways is multiplied by 3!.

```
012345678901    contig
-----           contributes 5 new bases
   ..---         contributes 3 new bases
   .....         contributes 0 new bases
   ....-         contributes 1 new bases
     ..---        contributes 3 new bases
```

Figure 4: How many bases does each read contribute to a contig? Here contig length is 12 and read length is 5. Newly contributed bases in each read are marked by $-$, and other bases are marked by $..$. For example, read 1 starts at position 0 and read 2 starts at position 3, so read 2 contributes $3 - 0 = 3$ bases.

(Miscellaneous note: The mean and variance of ContigLen$'_j|A_i$ are

$$E(\text{ContigLen}'_j|A_i) = \text{readLen} \cdot (\text{coverage}_j + 1)/2$$

$$\text{Var}(\text{ContigLen}'_j|A_i) = \text{readLen} \cdot (\text{readLen} + 2) \cdot (\text{coverage}_j - 1)/12$$

See `howManyWaysToCoverAContig.py`.)

2.3.4.2 (ii) The distribution, with the conditional dependence reinstated by restricting the support of the joint distribution and normalizing.

When we reinstate conditional dependence, we need to take into account the fact that $\sum_{j \in \text{contigsFromTran}_i} \text{contigLen}_j \leq \text{tranLen}_i$, i.e., the support is smaller than when we assumed conditional independence. This does not affect the numerator of the pmf given in the last section, i.e., numArrangements$(\text{coverage}_j, \text{contigLen}'_j, \text{readLen})$ [assuming that the transcript is longer than the contig], since the number of arrangements was calculated without reference to the other contigs. In other words,

$$P(\text{contigLen}_{(i)}|A_i) = \frac{\prod_{j \in \text{contigsFromTran}_i} \text{numArrangements}(\text{coverage}_j, \text{contigLen}_j, \text{readLen})}{\text{denom}_i}$$

$$= \frac{\prod_{j \in \text{contigsFromTran}_i} \binom{\text{coverage}_j - 1}{\text{contigLen}_j - \text{readLen}}_{\text{readLen}+1}}{\text{denom}_i}$$

for contigLen$_{(i)}$ such that $\sum_{j \in \text{contigsFromTran}_i} \text{contigLen}_j \leq \text{tranLen}_i$.

However, since the support is smaller, the reinstatement of conditional dependence does affect the denominator.

Specifically, the denominator is

$$\text{denom}_i = \sum_{l:\sum_j l_j \leq \text{tranLen}_i} \prod_{j \in \text{contigsFromTran}_i} \text{numArrangements}(\text{coverage}_j, l_j, \text{readLen})$$

$$= \sum_{l:\sum_j l_j \leq \text{tranLen}_i} \prod_{j \in \text{contigsFromTran}_i} \binom{\text{coverage}_j - 1}{l_j - \text{readLen}}_{\text{readLen}+1}$$

where the $\sum_j$ is short for $\sum_{j \in \text{contigsFromTran}_i}$. This is the total number of ways to arrange coverage_{j_1} reads into a contig of length l_{j_1}, and coverage_{j_2} reads into a contig of length l_{j_2}, etc., for all contigs j_k from transcript i, subject to the total length of all the contigs from transcript i being less than or equal to the length of transcript i.

In order to evaluate denom_i, we use the following "Vandermonde convolution" identity from Fahssi (2012), Table 1:

$$\sum_{i+j=n} \binom{r}{i}_N \binom{s}{j}_N = \binom{r+s}{n}_N$$

Applying this to our case,

$$\sum_{l_{j_1}+l_{j_2}=L} \binom{\text{coverage}_{j_1} - 1}{l_{j_1} - \text{readLen}}_{\text{readLen}+1} \binom{\text{coverage}_{j_2} - 1}{l_{j_2} - \text{readLen}}_{\text{readLen}+1}$$

$$= \sum_{l_{j_1}+l_{j_2}=L-2\cdot\text{readLen}} \binom{\text{coverage}_{j_1} - 1}{l_{j_1}}_{\text{readLen}+1} \binom{\text{coverage}_{j_2} - 1}{l_{j_2}}_{\text{readLen}+1}$$

$$= \binom{\text{coverage}_{j_1} + \text{coverage}_{j_2} - 2}{L - 2\cdot\text{readLen}}_{\text{readLen}+1}$$

and by applying this recursively

$$\sum_{l:\sum_j l_j=L} \prod_{j \in \text{contigsFromTran}_i} \binom{\text{coverage}_j - 1}{l_j - \text{readLen}}_{\text{readLen}+1}$$

$$= \binom{(\sum_j \text{coverage}_j) - \text{numContigsFromTran}_i}{L - \text{numContigsFromTran}_i \cdot \text{readLen}}_{\text{readLen}+1}$$

Thus, plugging in,

$$\text{denom}_i = \sum_{l:\sum_j l_j \leq \text{tranLen}_i} \prod_{j \in \text{contigsFromTran}_i} \binom{\text{coverage}_j - 1}{l_j - \text{readLen}}_{\text{readLen}+1}$$

$$= \sum_{L=0}^{\text{tranLen}_i} \sum_{l:\sum_j l_j=L} \prod_{j \in \text{contigsFromTran}_i} \binom{\text{coverage}_j - 1}{l_j - \text{readLen}}_{\text{readLen}+1}$$

$$= \sum_{L=0}^{\text{tranLen}_i} \binom{(\sum_j \text{coverage}_j) - \text{numContigsFromTran}_i}{L - \text{numContigsFromTran}_i \cdot \text{readLen}}_{\text{readLen}+1}$$

$$= \sum_{L=0}^{\text{tranLen}_i - \text{numContigsFromTran}_i \cdot \text{readLen}} \binom{(\sum_j \text{coverage}_j) - \text{numContigsFromTran}_i}{L}_{\text{readLen}+1}$$

$$= \sum_{L=0}^{\text{tranLen}_i - \text{numContigsFromTran}_i \cdot \text{readLen}} \binom{\text{expr}_i - \text{numContigsFromTran}_i}{L}_{\text{readLen}+1}$$

a partial row sum. (See `howManyWaysToCoverAContig.py` for empirical verification of this formula.)

Recall from the definition of the polynomial coefficients $\binom{n}{k}_N$ that if $k > (N-1) \cdot n$, then the coefficient is 0. Thus, in the sum above, if $L > \text{readLen} \cdot (\text{expr}_i - \text{numContigsFromTran}_i)$, then the Lth term is 0. Therefore, if $\text{tranLen}_i > \text{readLen} \cdot \text{expr}_i$, then the partial row sum will be a full row sum, and $\text{denom}_i = (\text{readLen} + 1)^{\text{expr}_i - \text{numContigsFromTran}_i}$.

Thus

$$P(\text{contigLen}_{(i)}|A_i) = \frac{\prod_{j \in \text{contigsFromTran}_i} \text{numArrangements}(\text{coverage}_j, \text{contigLen}_j, \text{readLen})}{\text{denom}_i}$$

$$= \frac{\prod_{j \in \text{contigsFromTran}_i} \binom{\text{coverage}_j - 1}{\text{contigLen}_j - \text{readLen}}_{\text{readLen}+1}}{\sum_{L=0}^{\text{tranLen}_i - \text{numContigsFromTran}_i \cdot \text{readLen}} \binom{\text{expr}_i - \text{numContigsFromTran}_i}{L}_{\text{readLen}+1}}$$

for $\text{contigLen}_{(i)}$ such that $\sum_{j \in \text{contigsFromTran}_i} \text{contigLen}_j \leq \text{tranLen}_i$.

In summary,

$$P(\text{contigLen}|\text{coverage}, \text{contigsFromTrans}, \text{trans}, \text{expr})$$

$$= \prod_{i=1}^{\text{numTrans}} P(\text{contigLen}_{(i)}|\text{coverage}_{(i)}, \text{contigsFromTran}_i, \text{trans}_i, \text{expr}_i)$$

$$= \prod_{i=1}^{\text{numTrans}} \frac{\prod_{j \in \text{contigsFromTran}_i} \binom{\text{coverage}_j - 1}{\text{contigLen}_j - \text{readLen}}_{\text{readLen}+1}}{\sum_{L=0}^{\text{tranLen}_i - \text{numContigsFromTran}_i \cdot \text{readLen}} \binom{\text{expr}_i - \text{numContigsFromTran}_i}{L}_{\text{readLen}+1}}$$

2.3.5 Distribution of $\text{Contig}|\{\text{ContigLen}, \text{Coverage}, \text{NumContigsFromTran}_i, \text{Tran}_i, \text{Expr}_i)\}$

Again, we assume that the contigs from one transcript are conditionally independent of other transcripts and their contigs:

$$P(\text{contig}|\text{contigLen}, \text{coverage}, \text{contigsFromTrans}, \text{trans}, \text{expr})$$

$$= \prod_{i=1}^{\text{numTrans}} P(\text{contig}_{(i)}|\text{contigLen}_{(i)}, \text{coverage}_{(i)}, \text{contigsFromTran}_i, \text{trans}_i, \text{expr}_i)$$

We stipulate that $P(\text{contig}_{(i)}|\text{contigLen}_{(i)}, \text{coverage}_{(i)}, \text{numContigsFromTran}_i, \text{tran}_i, \text{expr}_i)$ is uniform over the relevant set. The relevant set is defined by two constraints on the contigs: (i) each contig is a contiguous subsequence of its transcript, and (ii) all the contigs are disjoint subsequences. Note that we do not admit the possibility that contigs might be erroneous wrt the transcripts. So the relevant set is the set of possible contig placements subject to these constraints.

In each contig placement, there are $k = (\text{tranLen}_i - \sum_{j=1}^{\text{numContigsFromTran}_i} \text{contigLen}_j)$ uncovered bases. For now, fix one ordering of the contigs. Each uncovered base can be placed before contig 1, after contig 1, after contig 2, ..., after contig $\text{numContigsFromTran}_i$, i.e., at any of $n = (\text{numContigsFromTran}_i + 1)$ relative positions. The number of ways of placing uncovered bases in such relative positions, where the different uncovered bases are treated as equivalent (so order doesn't matter), is equal to the number of multisets of k elements, each chosen with replacement from n choices, namely, $\binom{n+k-1}{k}$. See `numPositions.R` and Figure 5.

Therefore the conditional probability of the contig placements, and hence of the contigs, is

$$P(\text{contig}_{(i)}|\text{contigLen}_{(i)}, \text{coverage}_{(i)}, \text{numContigsFromTran}_i, \text{tran}_i, \text{expr}_i)$$

$$= \binom{n+k-1}{k}^{-1} = \binom{n+k-1}{n-1}^{-1}$$

$$= \binom{\text{numContigsFromTran}_i + \text{tranLen}_i - \sum_{j=1}^{\text{numContigsFromTran}_i} \text{contigLen}_j}{\text{numContigsFromTran}_i}^{-1}$$

```
            Column 0                     Column 1                     Column 2
            --------                     --------                     --------
transcript: 01234567890123456789         01234567890123456789         0123456789012345678
contigs:       xxxxxxxyyyyyzzzzzz 000        
             xxxxxxx yyyyyzzzzzz 001
             xxxxxxxyyyyy zzzzzz 002
             xxxxxxxyyyyyzzzzzz   003         xxxxxxxyyyyyzzzzzz 00
            xxxxxxx  yyyyyzzzzzz 011
            xxxxxxx yyyyy zzzzzz 012
            xxxxxxx yyyyyzzzzzz  013         xxxxxxx yyyyyzzzzzz 01
            xxxxxxxyyyyy  zzzzzz 022
            xxxxxxxyyyyy zzzzzz  023         xxxxxxxyyyyy zzzzzz 02
            xxxxxxxyyyyyzzzzzz    033         xxxxxxxyyyyyzzzzzz  03         xxxxxxxyyyyyzzzzzz 0
            xxxxxxx   yyyyyzzzzzz 111
            xxxxxxx  yyyyy zzzzzz 112        xxxxxxx  yyyyyzzzzzz 11
            xxxxxxx  yyyyyzzzzzz  113
            xxxxxxx yyyyy  zzzzzz 122
            xxxxxxx yyyyy zzzzzz  123        xxxxxxx yyyyy zzzzzz 12
            xxxxxxx yyyyyzzzzzz   133        xxxxxxx yyyyyzzzzzz  13         xxxxxxx yyyyyzzzzzz 1
            xxxxxxxyyyyy   zzzzzz 222        xxxxxxxyyyyy  zzzzzz 22
            xxxxxxxyyyyy  zzzzzz  223
            xxxxxxxyyyyy zzzzzz   233        xxxxxxxyyyyy zzzzzz  23         xxxxxxxyyyyy zzzzzz 2
            xxxxxxxyyyyyzzzzzz    333        xxxxxxxyyyyyzzzzzz   33         xxxxxxxyyyyyzzzzzz  3
            [same, with order xzy]          [same, with order xzy]          [same, with order xzy]
            [same, with order yxz]          [same, with order yxz]          [same, with order yxz]
            [same, with order yzx]          [same, with order yzx]          [same, with order yzx]
            [same, with order zxy]          [same, with order zxy]          [same, with order zxy]
            [same, with order zyx]          [same, with order zyx]          [same, with order zyx]

            Column 3                     Column 4                     Column 5
            --------                     --------                     --------
transcript: 01234567890123456789         01234567890123456789         0123456789012345678
contigs:       xxxxxxxyyyyyyyyyy 000
             xxxxxxx yyyyyyyyyy 001
             xxxxxxxyyyyyyyyyy   002         xxxxxxxyyyyyyyyyy 00
            xxxxxxx  yyyyyyyyyy 011
            xxxxxxx yyyyyyyyyy  012         xxxxxxx yyyyyyyyyy 01
            xxxxxxxyyyyyyyyyy    022         xxxxxxxyyyyyyyyyy  02         xxxxxxxyyyyyyyyyy 0
            xxxxxxx   yyyyyyyyyy 111
            xxxxxxx  yyyyyyyyyy  112        xxxxxxx  yyyyyyyyyy 11
            xxxxxxx yyyyyyyyyy   122        xxxxxxx yyyyyyyyyy  12         xxxxxxx yyyyyyyyyy 1
            xxxxxxxyyyyyyyyyy    222        xxxxxxxyyyyyyyyyy   22         xxxxxxxyyyyyyyyyy  2
            [same, with order yx]           [same, with order yx]          [same, with order yx]
```

Figure 5: Each column shows a transcript, in the first line, and all possible contig placements, in the remaining line. Each contig placement is shown both (i) according to which bases of the transcript each contig covers, with contig 1 = xxxxxxx, contig 2 = yyyyy, and contig 3 = zzzzzz, and also (ii) according to its vector of relative positions of uncovered bases, where 0 = "before contig 1" and i = "after contig i. For example, " xxxxxxxyyyyy zzzzzz" and "002" represent the same contig placement. We get the following number of contig placements:

- In column 0, where $n = 4, k = 3$, there are $20 = \binom{4+3-1}{3}$ placements.
- In column 1, where $n = 4, k = 2$, there are $10 = \binom{4+2-1}{2}$ placements.
- In column 2, where $n = 4, k = 1$, there are $4 = \binom{4+1-1}{1}$ placements.
- In column 3, where $n = 3, k = 3$, there are $10 = \binom{3+3-1}{3}$ placements.
- In column 4, where $n = 3, k = 2$, there are $6 = \binom{3+2-1}{2}$ placements.
- In column 5, where $n = 3, k = 1$, there are $3 = \binom{3+1-1}{1}$ placements.

2.3.6   Summary of the distribution of $(\text{Contigs}, \text{Coverage}, \text{ContigsFromTrans}) | \{\text{Reads}, \text{Trans}, \text{Expr}\}$

In summary,

$$
P(\text{contigs}, \text{coverage}, \text{contigsFromTrans} | \text{reads}, \text{trans}, \text{expr})
$$
$$
= P(\text{contigs}, \text{coverage}, \text{contigsFromTrans} | \text{trans}, \text{expr})
$$
$$
= P(\text{numContigsFromTran} | \text{trans}, \text{expr})
$$
$$
\cdot P(\text{contigsFromTran} | \text{numContigsFromTran}, \text{trans}, \text{expr})
$$
$$
\cdot P(\text{coverage} | \text{contigsFromTran}, \text{numContigsFromTran}, \text{trans}, \text{expr})
$$
$$
\cdot P(\text{contigLen} | \text{coverage}, \text{contigsFromTrans}, \text{trans}, \text{expr})
$$
$$
\cdot P(\text{contig} | \text{contigLen}, \text{coverage}, \text{contigsFromTrans}, \text{trans}, \text{expr})
$$
$$
= \left[\prod_{i=1}^{\text{numTrans}} \text{Binomial}(\text{numContigsFromTran}_i | \text{tranLen}_i, \alpha_i (1-\alpha_i)^{\text{readLen}-\text{ws}}) \right]
$$
$$
\cdot \left[\binom{\text{numContigs}}{\text{numContigsFromTran}_i : i = 1, \dots, \text{numTrans}}^{-1} \right]
$$
$$
\cdot \left[\prod_{i=1}^{\text{numTrans}} \frac{\prod_{j \in \text{contigsFromTran}_i} \text{Geometric}(\text{coverage}_j | \gamma_i)}{\text{NegativeBinomial}(\text{expr}_i | \text{numContigsFromTran}_i, 1-\gamma_i)} \right]
$$
$$
\cdot \left[\prod_{i=1}^{\text{numTrans}} \frac{\prod_{j \in \text{contigsFromTran}_i} \binom{\text{coverage}_j - 1}{\text{contigLen}_j - \text{readLen}}_{\text{readLen}+1}}{\sum_{L=0}^{\text{tranLen}_i - \text{numContigsFromTran}_i \cdot \text{readLen}} \binom{\text{expr}_i - \text{numContigsFromTran}_i}{L}_{\text{readLen}+1}} \right]
$$
$$
\cdot \left[\prod_{i=1}^{\text{numTrans}} \binom{\text{numContigsFromTran}_i + \text{tranLen}_i - \sum_{j=1}^{\text{numContigsFromTran}_i} \text{contigLen}_j}{\text{numContigsFromTran}_i}^{-1} \right]
$$

2.4   Distribution of $(\text{Contigs}, \text{Coverage}, \text{ContigsFromTrans}) | \{\text{Reads}, \text{Trans}, \text{Expr}\}$, Try 2

First, like in Bo's current approach, we assume that the contigs (and coverage) are conditionally independent of the reads, given the transcripts (and expression), i.e., in symbols:

$$(\text{Contigs}, \text{Coverage}, \text{ContigsFromTrans}) | \{\text{Reads}, \text{Trans}, \text{Expr}\} =_D (\text{Contigs}, \text{Coverage}, \text{ContigsFromTrans}) | \{\text{Trans}, \text{Expr}\}$$

Recall that numReads and readLen are not random; these quantities will be very important for the distributions below.

A key thing is how to represent the contigs? The answer is that:

1. There are transcripts Tran_i, $i \in \{1, 2, \dots, \text{NumTrans}\}$.
2. For each transcript i, there are contigs $\text{Contig}_{i,j}$, $j \in \{1, 2, \dots, \text{NumContigsFromTran}_i\}$.

Thus:

$$
P(\text{contigs}, \text{coverage} | \text{trans}, \text{expr})
$$
$$
= \prod_{i=1}^{\text{numTrans}} P(\text{contigs}_i, \text{coverage}_i | \text{tran}_i, \text{expr}_i)
$$

Note that we do not know the assignment of contigs to transcripts. So we also use the representation:

1. There are transcripts Tran_i, $i \in \{1, 2, \dots, \text{NumTrans}\}$.
2. There are contigs Contig_j, $j \in \{1, 2, \dots, \text{NumContigs}\}$.

3. There is a transcript-to-contigs map $\text{ContigsFromTran}_i \subset \{1, 2, \dots, \text{NumContigs}\}$, with $\text{ContigsFromTran}_i \cap \text{ContigsFromTran}_{i'} = \varnothing$ and $\cup_i \text{ContigsFromTran}_i = \{1, 2, \dots, \text{NumContigs}\}$.

In this representation, one needs to account for the different ways to assign contig indices to transcripts. However, we consider all of these to be equivalent so there is no need to do further normalization. Thus

$$
\begin{aligned}
&P(\text{contigs}, \text{coverage}, \text{contigsFromTrans}|\text{trans}, \text{expr}) \\
&= P(\text{contigs}, \text{coverage}|\text{trans}, \text{expr}) \\
&= \prod_{i=1}^{\text{numTrans}} P(\text{contigs}_i, \text{coverage}_i|\text{tran}_i, \text{expr}_i)
\end{aligned}
$$

2.4.1 The distribution of $\text{Contigs}_i, \text{Coverage}_i|\text{Tran}_i, \text{Expr}_i$

In this section, all statements are understood to be asserted to hold, conditionally on $\{\omega : \text{Tran}_i = \text{tran}_i, \text{Expr}_i = \text{expr}_i\}$.

We use the following shorthand notation:

1. $n = \text{numContigsFromTran}_i$
2. $\mathscr{J} = \text{contigsFromTran}_i$.
3. $n_{c,l} = |\{j \in \mathscr{J} : \text{coverage}_j = c, \text{contigLen}_j = l\}|$.
4. $\mathbf{n} = (n_{c,l})$, thought of as a vector or matrix as appropriate.

Note that $\sum_c \sum_l n_{c,l} = n = |\mathscr{J}|$.

What is $P(\text{contigs}_i, \text{coverage}_i|\text{tran}_i, \text{expr}_i)$? We find the exact distribution under the following stipulations:

1. Stipulation 1: The start positions of the expr_i reads are distributed uniformly among the possible start positions.
2. Stipulation 2: The start positions of the expr_i reads are independent.
3. Stipulation 3: All reads share a common read length readLen.
4. Stipulation 4: A contig is defined to be a maximal contiguous subsequence of the transcript such that every base is covered by at least one read.

Lemma 1. *Under Stipulations 3 and 4 given above, the number of read placements such that there are (i) n contigs and (ii) $n_{c,l}$ contigs with length l and coverage c is:*

$$
\text{numPlacements}(\mathbf{n}; \text{readLen}, \text{tranLen}) = \binom{n}{\mathbf{n}} \binom{\text{tranLen}_i + 1 - \sum_{j \in \mathscr{J}} \text{contigLen}_j}{n} \prod_{j \in \mathscr{J}} \binom{\text{coverage}_j - 1}{\text{contigLen}_j - \text{readLen}}_{\text{readLen}+1}
$$

Lemma 2. *Under Stipulations 3 and 4 given above, the total number of possible read placements is*

$$
\text{numPlacements}(\text{readLen}, \text{tranLen}) = \binom{\text{expr}_i + \text{tranLen}_i - \text{readLen}}{\text{expr}_i}
$$

Theorem 3. *Under the stipulations given above, the*

$$
P(\text{contigs}_i, \text{coverage}_i|\text{tran}_i, \text{expr}_i) = \frac{\text{numPlacements}(\mathbf{n}; \text{readLen}, \text{tranLen})}{\text{numPlacements}(\text{readLen}, \text{tranLen})}
$$

$$
= \frac{\binom{n}{\mathbf{n}} \binom{\text{tranLen}_i + 1 - \sum_{j \in \mathscr{J}} \text{contigLen}_j}{n} \prod_{j \in \mathscr{J}} \binom{\text{coverage}_j - 1}{\text{contigLen}_j - \text{readLen}}_{\text{readLen}+1}}{\binom{\text{expr}_i + \text{tranLen}_i - \text{readLen}}{\text{expr}_i}}
$$

```
transscript:    01234567890123456789
arrangement 1: aaaaaaaaabbbbbb
arrangement 2: aaaaaaaaa bbbbbb
arrangement 3:    bbbbbb aaaaaaaaa
etc
```

Figure 6: Illustration of our assumption that J is constant with respect to contig ordering and start positions within a transcript. In this case, regardless of how we arrange the two contigs `aaaaaaaaa` and `bbbbbb` within the transcript, we assume that J is constant.

3   Mode of the joint distribution

We want to maximize (or at least approximately maximize) the function

$$J(\text{trans}, \text{expr}, \text{coverage}, \text{contigsFromTrans}) = P(\text{reads}, \text{trans}, \text{expr}, \text{contigs}, \text{coverage}, \text{contigsFromTrans})$$

with (reads, contigs) held fixed.

We will assume that the contigs are "correct", i.e., are error-free contiguous subsequences of the transcripts. We will also assume that J is constant with respect to contig ordering and start positions within a transcript; this is exactly true for everything except for the data likelihood, and for the RSEM-based likelihood it is almost true (or is it exactly true?); for an example, see Figure 6.

Due to these assumptions, we do not need to explicitly write down the sequences of the transcripts that maximize the objective. Rather, we just need to answer the questions: (i) Which contigs should be said to come from the same transcripts as each other, and (ii) how long should these transcripts be? so as to maximize the objective J.

We also need to find the optimal coverage of the contigs. This, together with the assignment of contigs to transcripts, will automatically give us the optimal expression of the transcripts.

We will use the following approach based on greedy coordinate ascent.

Step 1: Run RSEM, using the contigs as the reference. This will give us τ_j, the MLE of the fraction of reads that come from each contig.

Find the optimal coverage coverage*.

1. Start with an RSEM-based estimate coverage* of the coverage, based on the contigs and the reads. (coverage* $= \lfloor \tau \cdot \text{numReads} \rfloor$ where τ is the "transcript-level expression" (based on contigs) produced by RSEM.)

2. Figure out analytically which contigs should be joined into transcripts, based on the coverage and length of the contigs. This gives trans* and contigsFromTrans*. (We never need to know explicitly the sequence of the transcripts outside of the contigs.)

3. Sum appropriate entries of coverage* to get expr*.

The tricky part is item 2. In the following two subsections, we will (i) determine how the data likelihood $P(\text{reads}|\text{trans}, \text{expr})$ changes when we join contigs into a transcript, and (ii) determine how the overall joint probability changes when we join contigs into a transcript. After that, we will (iii) formulate a simple algorithm to make high-probability transcripts from contigs.

should be "joined together" into transcripts, and (ii) how long should the transcripts be? so as to maximize the objective J.

Due to these assumptions, maximization of J requires us to answer the following question: Which contigs should be "joined together" into transcripts so as to maximize the objective J?

```
trans:  1:  AAAAAAAAAA
        2:  GGGGGGG
        ... [other transcripts]
trans': 12: TTTAAAAAAAAAAAATTTTTTTTGGGGGGGTTTT
        ... [other transcripts]
```

Figure 7: Here we join transcripts 1 and 2 into transcript 12, with extra bases (all "T"s in this case) in between and on the ends.

Due to these assumptions, maximization of J involves answering two (linked) questions:

1. Which contigs should be "joined together" into transcripts so as to maximize the objective J?

   Order doesn't matter here. A transcript could be longer than the corresponding contigs.

2. What are the expression and coverage? A transcript's expression is the sum of the coverage of its contigs.

We want an approximation of the mode that can be found as easily as possible. Our strategy is:

1. Start with an RSEM-based estimate coverage* of the coverage, based on the contigs and the reads. (coverage$^* = \lfloor \tau \cdot \text{numReads} \rfloor$ where τ is the "transcript-level expression" (based on contigs) produced by RSEM.)

2. Figure out analytically which contigs should be joined into transcripts, based on the coverage and length of the contigs. This gives trans* and contigsFromTrans*. (We never need to know explicitly the sequence of the transcripts outside of the contigs.)

3. Sum appropriate entries of coverage* to get expr*.

The tricky part is item 2. In the following two subsections, we will (i) determine how the data likelihood $P(\text{reads}|\text{trans}, \text{expr})$ changes when we join contigs into a transcript, and (ii) determine how the overall joint probability changes when we join contigs into a transcript. After that, we will (iii) formulate a simple algorithm to make high-probability transcripts from contigs.

3.1 How does the joint distribution change when we join two transcripts together?

Throughout this subsection, we consider two transcript sets:

1. trans, which contains transcripts with indices $\mathscr{I} \cup \{1,2\}$, and

2. trans$'$, which contains transcripts with indices $\mathscr{I} \cup \{12\}$.

Here, transcript 12 contains transcript 1 and transcript 2 as disjoint subsequences, with possibly some extra bases added in between 1's and 2's sequences or on the ends, but not within 1's or 2's sequences. See Figure 7. The set $\mathscr{I}$ contains the indices of transcripts common to both trans and trans$'$. Obviously, numTrans$'$ = numTrans -1. Also, expr$'_{12}$ = expr$_1$ + expr$_2$. Also, numContigsFromTran$'_{12}$ = numContigsFromTran$_1$ + numContigsFromTran$_2$ and contigsFromTran$'_{12}$ = contigsFromTran$_1$ $\cup$ contigsFromTran$_2$.

The idea, of course, is that trans is the "original transcripts" and trans$'$ is the "hopefully higher-probability transcripts". Initially, trans will be the contigs.

3.1.1 How does the data likelihood $P(\text{reads}|\text{trans}, \text{expr})$ change when we join two transcripts together?

Recall that $P(\text{reads}|\text{trans}, \text{expr}) = P_{RSEM}(\text{reads}|\text{trans}, \text{expr})$. We use the notation $\mathbb{P}(\dots) = P_{RSEM}(\dots|\text{trans}, \text{expr})$ and $\mathbb{P}'(\dots) = P_{RSEM}(\dots|\text{trans}', \text{expr}')$. We want to figure out how $\mathbb{P}$ differs from $\mathbb{P}'$.

According to RSEM's model, the joint distribution decomposes as

$$\prod_{n=1}^{N} \mathbb{P}(g_n, f_n, s_n, o_n, l_n, q_n, r_n) = \prod_{n=1}^{N} \mathbb{P}(g_n)\mathbb{P}(f_n|g_n)\mathbb{P}(s_n|g_n, f_n)\mathbb{P}(l_n|f_n)\mathbb{P}(o_n|g_n)\mathbb{P}(q_n)\mathbb{P}(r_n|g_n, f_n, s_n, l_n, o_n, q_n)$$

where (assuming single-end data)

1. $N =$ numReads, indexed by n,
2. G_n is the parent transcript's index,
3. F_n is the fragment length,
4. S_n is the start position,
5. O_n is the orientation,
6. L_n is the read length,
7. Q_n is the quality score sequence, and
8. R_n is the read sequence.

When the parent transcript $G_n = g_n \in \mathscr{I}$, the shared transcript index set, then $\mathbb{P}(g_n, f_n, s_n, o_n, l_n, q_n, r_n) = \mathbb{P}'(g_n, f_n, s_n, o_n, l_n, q_n, r_n)$, since $\mathbb{P}(g_n) = \mathbb{P}'(g_n)$ and all the other parts of the decomposition are also the same.

What about when G_n is 1 or 2? In that case, $G'_n = 12$. So:

1. G_n: $\mathbb{P}'(G_n = 12) = \mathbb{P}(G_n = 1) + \mathbb{P}(G_n = 2)$, since every read that came from 1 or 2 under $\mathbb{P}$ comes from 12 under $\mathbb{P}'$, and no other reads come from $\mathbb{P}'$. Specifically, $\mathbb{P}(G_n = j) = \text{expr}_j/\text{numReads}$, and $\mathbb{P}'(G_n = j) = \text{expr}'_j/\text{numReads}$.

2. F_n: It is difficult to say how the fragment length distribution $F_n|G_n$ changes, since it is modelled nonparametrically. However, it seems perhaps reasonable to assume, in our present analysis, that $\mathbb{P}(f_n|g_n) = 1(f_n = \text{tranLen}_{g_n})$, i.e., to pretend that every fragment consists of the entire transcript (and hence to ignore the fact that reads come from fragments, not transcripts). This is similar to the first RSEM paper.

3. S_n: For the start position S_n, we will assume a uniform RSPD along the whole feasible length of the fragment, i.e., the transcript. So:

$$\mathbb{P}(s_n|g_n, f_n) = (\text{tranLen}_{g_n} - \text{readLen} + 1)^{-1}$$
$$\mathbb{P}'(s_n|g_n, f_n) = (\text{tranLen}'_{g_n} - \text{readLen} + 1)^{-1}$$

4. O_n: The orientation's conditional distribution is the same under $\mathbb{P}$ and $\mathbb{P}'$.

5. L_n: The read length's conditional distribution is the same under $\mathbb{P}$ and $\mathbb{P}'$. We will assume that the read length is fixed at readLen.

6. Q_n: The quality score's conditional distribution is the same under $\mathbb{P}$ and $\mathbb{P}'$.

7. R_n: The read sequence's conditional distribution is the same under $\mathbb{P}$ and $\mathbb{P}'$.

Putting this all together, the odds ratio of the RSEM joint distributions is

$$\frac{\prod_{n=1}^{N} \mathbb{P}(g_n, f_n, s_n, o_n, l_n, q_n, r_n)}{\prod_{n=1}^{N} \mathbb{P}'(g_n', f_n, s_n, o_n, l_n, q_n, r_n)} = \frac{\prod_{n:g_n \in \{1,2\}} \mathbb{P}(g_n)(\text{tranLen}_{g_n} - \text{readLen} + 1)^{-1}}{\prod_{n:g_n'=12} \mathbb{P}'(g_n')(\text{tranLen}_{g_n'}' - \text{readLen} + 1)^{-1}}$$

$$= \frac{\prod_{j \in \{1,2\}} \left[(\text{expr}_j/\text{numReads})(\text{tranLen}_j - \text{readLen} + 1)^{-1}\right]^{|\{n:g_n=j\}|}}{\left[(\text{expr}_{12}'/\text{numReads})(\text{tranLen}_{12}' - \text{readLen} + 1)^{-1}\right]^{|\{n:g_n'=12\}|}}$$

$$= \frac{\prod_{j \in \{1,2\}} \left[\text{expr}_j \cdot (\text{tranLen}_j - \text{readLen} + 1)^{-1}\right]^{|\{n:g_n=j\}|}}{\left[\text{expr}_{12}' \cdot (\text{tranLen}_{12}' - \text{readLen} + 1)^{-1}\right]^{|\{n:g_n'=12\}|}}$$

$$= \frac{\prod_{j \in \{1,2\}} \left[\text{expr}_j \cdot (\text{tranLen}_j - \text{readLen} + 1)^{-1}\right]^{\text{expr}_j}}{\left[\text{expr}_{12}' \cdot (\text{tranLen}_{12}' - \text{readLen} + 1)^{-1}\right]^{\text{expr}_{12}'}}$$

where $g_n' = 12$ if $g_n \in \{1,2\}$, and $g_n' = g_n$ otherwise. The penultimate identity holds because numReads does not depend on g_n. The last identity holds because $|\{n : g_n = j\}| = \text{expr}_j$ and $|\{n : g_n' = 12\}| = \text{expr}_{12}$.

Of course, we are really interested in the log ratio of the marginal (wrt RSEM) distributions $P(\text{reads}|\text{trans}, \text{expr})$ and $P(\text{reads}|\text{trans}', \text{expr}')$. We will approximate the integrals via BIC:

$$\log P(\text{reads}|\text{trans}, \text{expr}) = \log \mathbb{P}(l, r, q)$$

$$= \log \int \prod_{n=1}^{N} \mathbb{P}(g_n, f_n, s_n, o_n, l_n, q_n, r_n) \, dg \, df \, ds \, do$$

$$= \left(\sum_{n=1}^{N} \log \mathbb{P}(g_n^*, f_n^*, s_n^*, o_n^*, l_n, q_n, r_n)\right) - \frac{1}{2} \text{numTrans} \log \text{numReads}$$

So the log odds is:

$$\log P(\text{reads}|\text{trans}, \text{expr}) - \log P(\text{reads}|\text{trans}', \text{expr}')$$

$$= \log \mathbb{P}(l, r, q) - \log \mathbb{P}'(l, r, q)$$

$$= \left(\sum_{n=1}^{N} \log \mathbb{P}(g_n^*, f_n^*, s_n^*, o_n^*, l_n, q_n, r_n)\right) - \frac{1}{2} \text{numTrans} \log \text{numReads}$$

$$\quad - \left(\sum_{n=1}^{N} \log \mathbb{P}(g_n'^*, f_n^*, s_n^*, o_n^*, l_n, q_n, r_n)\right) + \frac{1}{2} \text{numTrans}' \log \text{numReads}$$

$$= \log \left(\frac{\prod_{n=1}^{N} \mathbb{P}(g_n^*, f_n^*, s_n^*, o_n^*, l_n, q_n, r_n)}{\prod_{n=1}^{N} \mathbb{P}(g_n'^*, f_n^*, s_n^*, o_n^*, l_n, q_n, r_n)}\right) - \frac{1}{2} \log \text{numReads}$$

We have used that $\text{numTrans} - \text{numTrans}' = 1$. Substituting from the joint log odds above,

$$\log P(\text{reads}|\text{trans}, \text{expr}) - \log P(\text{reads}|\text{trans}', \text{expr}')$$

$$= \log \left(\frac{\prod_{j \in \{1,2\}} \left[\text{expr}_j \cdot (\text{tranLen}_j - \text{readLen} + 1)^{-1}\right]^{\text{expr}_j}}{\left[\text{expr}_{12}' \cdot (\text{tranLen}_{12}' - \text{readLen} + 1)^{-1}\right]^{\text{expr}_{12}'}}\right) - \frac{1}{2} \log \text{numReads}$$

$$= -\left(\text{expr}_{12}' \log \text{expr}_{12}' - \sum_{j \in \{1,2\}} \text{expr}_j \log \text{expr}_j\right)$$

$$\quad + \left(\text{expr}_{12}' \log(\text{tranLen}_{12}' - \text{readLen} + 1) - \sum_{j \in \{1,2\}} \text{expr}_j \log(\text{tranLen}_j - \text{readLen} + 1)\right)$$

$$\quad - \frac{1}{2} \log \text{numReads}$$

3.1.2 How does the prior $P(\text{trans}, \text{expr})$ change when we join two transcripts together?

Recall that

$$P(\text{trans}, \text{expr}) = \frac{(\mu_0(1-p_0)^{r_0}/\text{numReads})^{\text{numTrans}}}{\text{numTrans}!} e^{-\mu_0} \prod_{i=1}^{\text{numTrans}} \binom{\text{tranLen}_i + r_0 - 1}{\text{tranLen}_i} (p_0/4)^{\text{tranLen}_i}$$

so the log odds

$$\log P(\text{trans}, \text{expr}) - \log P(\text{trans}', \text{expr}')$$

$$= \log \frac{\frac{(\mu_0(1-p_0)^{r_0}/\text{numReads})^{\text{numTrans}}}{\text{numTrans}!} e^{-\mu_0} \prod_{i=1}^{\text{numTrans}} \binom{\text{tranLen}_i + r_0 - 1}{\text{tranLen}_i} (p_0/4)^{\text{tranLen}_i}}{\frac{(\mu_0(1-p_0)^{r_0}/\text{numReads})^{\text{numTrans}'}}{\text{numTrans}'!} e^{-\mu_0} \prod_{i=1}^{\text{numTrans}'} \binom{\text{tranLen}_i' + r_0 - 1}{\text{tranLen}_i'} (p_0/4)^{\text{tranLen}_i'}}$$

Note that $\text{tranLen}_i = \text{tranLen}_i'$ for all $i \notin \{1, 2, 12\}$, so there is a lot of cancellation:

$$\cdots = \log \left(\frac{\frac{(\mu_0(1-p_0)^{r_0}/\text{numReads})^{\text{numTrans}}}{\text{numTrans}!}}{\frac{(\mu_0(1-p_0)^{r_0}/\text{numReads})^{\text{numTrans}'}}{\text{numTrans}'!}} \cdot \frac{\prod_{i \in \{1,2\}} \binom{\text{tranLen}_i + r_0 - 1}{\text{tranLen}_i} (p_0/4)^{\text{tranLen}_i}}{\binom{\text{tranLen}_{12}' + r_0 - 1}{\text{tranLen}_{12}'} (p_0/4)^{\text{tranLen}_{12}'}} \right)$$

Note that $\text{numTrans} - \text{numTrans}' = 1$ and $\text{numTrans}!/\text{numTrans}'! = \text{numTrans}$. So

$$\cdots = \log \left(\frac{(\mu_0(1-p_0)^{r_0}/\text{numReads})^{\text{numTrans}-\text{numTrans}'}}{\text{numTrans}!/\text{numTrans}'!} \cdot \frac{\prod_{i \in \{1,2\}} \binom{\text{tranLen}_i + r_0 - 1}{\text{tranLen}_i} (p_0/4)^{\text{tranLen}_i}}{\binom{\text{tranLen}_{12}' + r_0 - 1}{\text{tranLen}_{12}'} (p_0/4)^{\text{tranLen}_{12}'}} \right)$$

$$= \log \left(\frac{\mu_0(1-p_0)^{r_0}}{\text{numReads} \cdot \text{numTrans}} \cdot \frac{\prod_{i \in \{1,2\}} \binom{\text{tranLen}_i + r_0 - 1}{\text{tranLen}_i} (p_0/4)^{\text{tranLen}_i}}{\binom{\text{tranLen}_{12}' + r_0 - 1}{\text{tranLen}_{12}'} (p_0/4)^{\text{tranLen}_{12}'}} \right)$$

Applying the log,

$$\log P(\text{trans}, \text{expr}) - \log P(\text{trans}', \text{expr}') = \log \left(\frac{\mu_0(1-p_0)^{r_0}}{\text{numReads} \cdot \text{numTrans}} \right)$$

$$+ \left(-\log \binom{\text{tranLen}_{12}' + r_0 - 1}{\text{tranLen}_{12}'} + \sum_{i \in \{1,2\}} \log \binom{\text{tranLen}_i + r_0 - 1}{\text{tranLen}_i} \right)$$

$$+ \left(-\text{tranLen}_{12}' + \sum_{i \in \{1,2\}} \text{tranLen}_i \right) \log(p_0/4)$$

3.1.3 How does $P(\text{contig}, \text{coverage}, \text{contigsFromTrans}|\text{trans}, \text{expr})$ change when we join two transcripts together? Try 2

Note that

$$\frac{P(\text{contig}, \text{coverage}, \text{contigsFromTrans}'|\text{trans}', \text{expr}')}{P(\text{contig}, \text{coverage}, \text{contigsFromTrans}|\text{trans}, \text{expr})}$$

$$= \frac{P(\text{contig}'_{(12)}, \text{coverage}'_{(12)}|\text{trans}'_{12}, \text{expr}'_{12})}{P(\text{contig}_{(1)}, \text{coverage}_{(1)}|\text{trans}_1, \text{expr}_1)P(\text{contig}_{(2)}, \text{coverage}_{(2)}|\text{trans}_2, \text{expr}_2)}$$

$$= \frac{\dfrac{\binom{\text{numContigsFromTran}'_{12}}{\text{numContigsWithStats}'_{12}}\binom{\text{tranLen}_i+1-\sum_{j\in\text{contigsFromTran}'_{12}}\text{contigLen}_j}{\text{numContigsFromTran}'_{12}}\prod_{j\in\text{contigsFromTran}'_{12}}\binom{\text{coverage}_j-1}{\text{contigLen}_j-\text{readLen}}_{\text{readLen}+1}}{\binom{\text{expr}'_{12}+\text{tranLen}'_{12}-\text{readLen}}{\text{expr}'_{12}}}}{\prod_{i\in\{1,2\}}\dfrac{\binom{\text{numContigsFromTran}_i}{\text{numContigsWithStats}_i}\binom{\text{tranLen}_i+1-\sum_{j\in\text{contigsFromTran}_i}\text{contigLen}_j}{\text{numContigsFromTran}_i}\prod_{j\in\text{contigsFromTran}_i}\binom{\text{coverage}_j-1}{\text{contigLen}_j-\text{readLen}}_{\text{readLen}+1}}{\binom{\text{expr}_i+\text{tranLen}_i-\text{readLen}}{\text{expr}_i}}}$$

where $\text{numContigsWithStats}_i = (\text{numContigsWithStats}_{i,c,l})$, $\text{numContigsWithStats}_{i,c,l} = |\{j\in\text{contigsFromTran}_i : \text{coverage}_j = c, \text{contigLen}_j = l\}|$. Note that $\text{contigsFromTran}'_{12} = \text{contigsFromTran}_1 \,\dot\cup\, \text{contigsFromTran}_2$ so the rightmost products of factors cancel and we get:

$$= \frac{\dfrac{\binom{\text{numContigsFromTran}'_{12}}{\text{numContigsWithStats}'_{12}}\binom{\text{tranLen}'_{12}+1-\sum_{j\in\text{contigsFromTran}'_{12}}\text{contigLen}_j}{\text{numContigsFromTran}'_{12}}}{\binom{\text{expr}'_{12}+\text{tranLen}'_{12}-\text{readLen}}{\text{expr}'_{12}}}}{\prod_{i\in\{1,2\}}\dfrac{\binom{\text{numContigsFromTran}_i}{\text{numContigsWithStats}_i}\binom{\text{tranLen}_i+1-\sum_{j\in\text{contigsFromTran}_i}\text{contigLen}_j}{\text{numContigsFromTran}_i}}{\binom{\text{expr}_i+\text{tranLen}_i-\text{readLen}}{\text{expr}_i}}}$$

$$= \rho_1\rho_2\rho_3$$

We consider each of the three factors separately.

First,

$$\rho_1 = \frac{\binom{\text{numContigsFromTran}'_{12}}{\text{numContigsWithStats}'_{12}}}{\prod_{i\in\{1,2\}}\binom{\text{numContigsFromTran}_i}{\text{numContigsWithStats}_i}}$$

$$= \frac{\dfrac{\text{numContigsFromTran}'_{12}!}{\prod_c\prod_l\text{numContigsWithStats}'_{12,c,l}!}}{\dfrac{\text{numContigsFromTran}_1!\,\text{numContigsFromTran}_2!}{\prod_c\prod_l\text{numContigsWithStats}_{1,c,l}!\,\text{numContigsWithStats}_{2,c,l}!}}$$

Note that $\text{numContigsFromTran}'_{12} = \text{numContigsFromTran}_1 + \text{numContigsFromTran}_2$ and $\text{numContigsWithStats}'_{12,c,l} = \text{numContigsWithStats}_{1,c,l} + \text{numContigsWithStats}_{2,c,l}$, so we can rearrange:

$$\rho_1 = \frac{\dfrac{\text{numContigsFromTran}'_{12}!}{\text{numContigsFromTran}_1!\,\text{numContigsFromTran}_2!}}{\prod_c\prod_l\dfrac{\text{numContigsWithStats}'_{12,c,l}!}{\text{numContigsWithStats}_{1,c,l}!\,\text{numContigsWithStats}_{2,c,l}!}}$$

$$= \frac{\binom{\text{numContigsFromTran}'_{12}}{\text{numContigsFromTran}_1}}{\prod_c\prod_l\binom{\text{numContigsWithStats}'_{12,c,l}}{\text{numContigsWithStats}_{1,c,l}}}$$

Second,

$$\rho_2 = \frac{\binom{\text{tranLen}'_{12}+1-\sum_{j\in\text{contigsFromTran}'_{12}}\text{contigLen}_j}{\text{numContigsFromTran}'_{12}}}{\prod_{i\in\{1,2\}}\binom{\text{tranLen}_i+1-\sum_{j\in\text{contigsFromTran}_i}\text{contigLen}_j}{\text{numContigsFromTran}_i}}$$

$$= \frac{\frac{(\text{tranLen}'_{12}+1-\sum_{j\in\text{contigsFromTran}'_{12}}\text{contigLen}_j)!}{\text{numContigsFromTran}'_{12}!(\text{tranLen}'_{12}+1-\sum_{j\in\text{contigsFromTran}'_{12}}\text{contigLen}_j-\text{numContigsFromTran}'_{12})!}}{\prod_{i\in\{1,2\}}\frac{(\text{tranLen}_i+1-\sum_{j\in\text{contigsFromTran}_i}\text{contigLen}_j)!}{\text{numContigsFromTran}_i!(\text{tranLen}_i+1-\sum_{j\in\text{contigsFromTran}_i}\text{contigLen}_j-\text{numContigsFromTran}_i)!}}$$

$$= \frac{1}{\binom{\text{numContigsFromTran}'_{12}}{\text{numContigsFromTran}_1}}\frac{\frac{(\text{tranLen}'_{12}+1-\sum_{j\in\text{contigsFromTran}'_{12}}\text{contigLen}_j)!}{(\text{tranLen}'_{12}+1-\sum_{j\in\text{contigsFromTran}'_{12}}\text{contigLen}_j-\text{numContigsFromTran}'_{12})!}}{\prod_{i\in\{1,2\}}\frac{(\text{tranLen}_i+1-\sum_{j\in\text{contigsFromTran}_i}\text{contigLen}_j)!}{(\text{tranLen}_i+1-\sum_{j\in\text{contigsFromTran}_i}\text{contigLen}_j-\text{numContigsFromTran}_i)!}}$$

$$= \frac{\frac{(\text{tranLen}'_{12}+1-\sum_{j\in\text{contigsFromTran}'_{12}}\text{contigLen}_j)_{(\text{numContigsFromTran}'_{12})}}{\prod_{i\in\{1,2\}}(\text{tranLen}_i+1-\sum_{j\in\text{contigsFromTran}_i}\text{contigLen}_j)_{(\text{numContigsFromTran}_i)}}}{\binom{\text{numContigsFromTran}'_{12}}{\text{numContigsFromTran}_1}}$$

where $(n)_{(k)} = n!/(n-k)!$.

Third,

$$\rho_3 = \frac{\frac{1}{\binom{\text{expr}'_{12}+\text{tranLen}'_{12}-\text{readLen}}{\text{expr}'_{12}}}}{\prod_{i\in\{1,2\}}\frac{1}{\binom{\text{expr}_i+\text{tranLen}_i-\text{readLen}}{\text{expr}_i}}}$$

$$= \frac{\prod_{i\in\{1,2\}}\binom{\text{expr}_i+\text{tranLen}_i-\text{readLen}}{\text{expr}_i}}{\binom{\text{expr}'_{12}+\text{tranLen}'_{12}-\text{readLen}}{\text{expr}'_{12}}}$$

$$= \frac{\prod_{i\in\{1,2\}}\frac{(\text{expr}_i+\text{tranLen}_i-\text{readLen})!}{\text{expr}_i!(\text{tranLen}_i-\text{readLen})!}}{\frac{(\text{expr}'_{12}+\text{tranLen}'_{12}-\text{readLen})!}{\text{expr}'_{12}!(\text{tranLen}'_{12}-\text{readLen})!}}$$

$$= \binom{\text{expr}'_{12}}{\text{expr}_1}\frac{\prod_{i\in\{1,2\}}\frac{(\text{expr}_i+\text{tranLen}_i-\text{readLen})!}{(\text{tranLen}_i-\text{readLen})!}}{\frac{(\text{expr}'_{12}+\text{tranLen}'_{12}-\text{readLen})!}{(\text{tranLen}'_{12}-\text{readLen})!}}$$

$$= \binom{\text{expr}'_{12}}{\text{expr}_1}\frac{\prod_{i\in\{1,2\}}(\text{tranLen}_i-\text{readLen}+1)^{\overline{(\text{expr}_i)}}}{(\text{tranLen}'_{12}-\text{readLen}+1)^{\overline{(\text{expr}'_{12})}}}$$

since $\text{expr}'_{12} = \text{expr}_1 + \text{expr}_2$. Here $(n)^{\overline{(k)}} = n\cdot(n+1)\cdots(n+k-1) = (n+k-1)!/(n-1)!$, so that

$$\frac{(\text{expr}_i+\text{tranLen}_i-\text{readLen})!}{(\text{tranLen}_i-\text{readLen})!}$$
$$= \frac{((\text{tranLen}_i-\text{readLen}+1)+(\text{expr}_i)-1)!}{((\text{tranLen}_i-\text{readLen}+1)-1)!}$$
$$= (\text{tranLen}_i-\text{readLen}+1)^{\overline{(\text{expr}_i)}}$$

Thus, in summary:

$$\frac{P(\text{contig}, \text{coverage}, \text{contigsFromTrans}'|\text{trans}', \text{expr}')}{P(\text{contig}, \text{coverage}, \text{contigsFromTrans}|\text{trans}, \text{expr})}$$

$$= \frac{\binom{\text{numContigsFromTran}'_{12}}{\text{numContigsFromTran}_1}}{\prod_c \prod_l \binom{\text{numContigsWithStats}'_{12,c,l}}{\text{numContigsWithStats}_{1,c,l}}} \frac{\frac{(\text{tranLen}'_{12}+1-\sum_{j\in\text{contigsFromTran}'_{12}} \text{contigLen}_j)^{\overline{(\text{numContigsFromTran}'_{12})}}}{\prod_{i\in\{1,2\}}(\text{tranLen}_i+1-\sum_{j\in\text{contigsFromTran}_i} \text{contigLen}_j)^{\overline{(\text{numContigsFromTran}_i)}}}}{\binom{\text{numContigsFromTran}'_{12}}{\text{numContigsFromTran}_1}}$$

$$\cdot \binom{\text{expr}'_{12}}{\text{expr}_1} \frac{\prod_{i\in\{1,2\}}(\text{tranLen}_i - \text{readLen}+1)^{\overline{(\text{expr}_i)}}}{(\text{tranLen}'_{12} - \text{readLen}+1)^{\overline{(\text{expr}'_{12})}}}$$

$$= \frac{\frac{(\text{tranLen}'_{12}+1-\sum_{j\in\text{contigsFromTran}'_{12}} \text{contigLen}_j)^{\overline{(\text{numContigsFromTran}'_{12})}}}{\prod_{i\in\{1,2\}}(\text{tranLen}_i+1-\sum_{j\in\text{contigsFromTran}_i} \text{contigLen}_j)^{\overline{(\text{numContigsFromTran}_i)}}}}{\prod_c \prod_l \binom{\text{numContigsWithStats}'_{12,c,l}}{\text{numContigsWithStats}_{1,c,l}}} \binom{\text{expr}'_{12}}{\text{expr}_1} \frac{\prod_{i\in\{1,2\}}(\text{tranLen}_i - \text{readLen}+1)^{\overline{(\text{expr}_i)}}}{(\text{tranLen}'_{12} - \text{readLen}+1)^{\overline{(\text{expr}'_{12})}}}$$

The log odds is:

$$\log P(\text{contig}, \text{coverage}, \text{contigsFromTrans}'|\text{trans}', \text{expr}') - \log P(\text{contig}, \text{coverage}, \text{contigsFromTrans}|\text{trans}, \text{expr})$$

$$= \log \left((\text{tranLen}'_{12}+1 - \sum_{j\in\text{contigsFromTran}'_{12}} \text{contigLen}_j)_{\underline{(\text{numContigsFromTran}'_{12})}} \right.$$

$$- \left(\sum_{i\in\{1,2\}} \log \left((\text{tranLen}_i+1 - \sum_{j\in\text{contigsFromTran}_i} \text{contigLen}_j)_{\underline{(\text{numContigsFromTran}_i)}} \right) \right) \right)$$

$$- \left(\sum_c \sum_l \log \binom{\text{numContigsWithStats}'_{12,c,l}}{\text{numContigsWithStats}_{1,c,l}} \right)$$

$$+ \log \binom{\text{expr}'_{12}}{\text{expr}_1}$$

$$+ \left(\sum_{i\in\{1,2\}} \log \left((\text{tranLen}_i - \text{readLen}+1)^{\overline{(\text{expr}_i)}} \right) \right)$$

$$- \log \left((\text{tranLen}'_{12} - \text{readLen}+1)^{\overline{(\text{expr}'_{12})}} \right)$$

3.1.4 Summary of the log odds

In summary,

$$\log P(\text{contig},\text{coverage},\text{contigsFromTrans},\text{trans},\text{expr},\text{reads}) - \log P(\text{contig},\text{coverage},\text{contigsFromTrans}',\text{trans}',\text{expr}',\text{reads})$$

$$= \left(\text{expr}'_{12} \log \text{expr}'_{12} - \sum_{j \in \{1,2\}} \text{expr}_j \log \text{expr}_j \right)$$

$$- \left(\text{expr}'_{12} \log(\text{tranLen}'_{12} - \text{readLen} + 1) - \sum_{j \in \{1,2\}} \text{expr}_j \log(\text{tranLen}_j - \text{readLen} + 1) \right)$$

$$+ \frac{1}{2} \log \text{numReads}$$

$$- \log \left(\frac{\mu_0 (1 - p_0)^{r_0}}{\text{numReads} \cdot \text{numTrans}} \right)$$

$$+ \left(\log \binom{\text{tranLen}'_{12} + r_0 - 1}{\text{tranLen}'_{12}} - \sum_{i \in \{1,2\}} \log \binom{\text{tranLen}_i + r_0 - 1}{\text{tranLen}_i} \right)$$

$$+ \left(\text{tranLen}'_{12} - \sum_{i \in \{1,2\}} \text{tranLen}_i \right) \log(p_0/4)$$

$$+ \log \left((\text{tranLen}'_{12} + 1 - \sum_{j \in \text{contigsFromTran}'_{12}} \text{contigLen}_j) \underline{_{(\text{numContigsFromTran}'_{12})}} \right)$$

$$- \left(\sum_{i \in \{1,2\}} \log \left((\text{tranLen}_i + 1 - \sum_{j \in \text{contigsFromTran}_i} \text{contigLen}_j) \underline{_{(\text{numContigsFromTran}_i)}} \right) \right)$$

$$- \left(\sum_c \sum_l \log \left(\frac{\text{numContigsWithStats}'_{12,c,l}}{\text{numContigsWithStats}_{1,c,l}} \right) \right)$$

$$+ \log \left(\frac{\text{expr}'_{12}}{\text{expr}_1} \right)$$

$$+ \left(\sum_{i \in \{1,2\}} \log \left((\text{tranLen}_i - \text{readLen} + 1)^{\overline{(\text{expr}_i)}} \right) \right)$$

$$- \log \left((\text{tranLen}'_{12} - \text{readLen} + 1)^{\overline{(\text{expr}'_{12})}} \right)$$

3.2 How should one choose tranLen'?

We use the same notation from the previous subsection.

Claim: If one joins transcripts 1 and 2 into a single transcript 12, then J is maximized by setting $\text{tranLen}'_{12} = \text{tranLen}_1 + \text{tranLen}_2$, i.e., by setting $\text{tranLen}'_{12}$ as small as possible.

Proof: We look at all the terms of the log odds $\log P(\text{contig},\text{coverage},\text{contigsFromTrans}',\text{trans}',\text{expr}',\text{reads}) - \log P(\text{contig},\text{coverage},\text{co}$ that include $\text{tranLen}'_{12}$. The terms that include $\text{tranLen}'_{12}$ are:

1. First, the term $-\text{expr}'_{12} \log(\text{tranLen}'_{12} - \text{readLen} + 1)$ is contributed by $\log P(\text{reads}|\text{trans}',\text{expr}') - \log P(\text{reads}|\text{trans},\text{expr})$.
2. Second, the terms

(i) $\log \binom{\text{tranLen}'_{12}+r_0-1}{\text{tranLen}'_{12}} + \log((r_0-1)!)$ and

(ii) $\text{tranLen}'_{12} \log(p_0/4)$

are contributed by $\log P(\text{trans}',\text{expr}') - \log P(\text{trans},\text{expr})$. (We added the $\log((r_0-1)!)$ term because part of the log binomial coefficient this is constant wrt $\text{tranLen}'_{12}$.)

3. Third, the terms

(i) $\log \left(\text{tranLen}'_{12} + 1 - \sum_{j\in\text{contigsFromTran}'_{12}} \text{contigLen}_j\right)_{\underline{(\text{numContigsFromTran}'_{12})}}$ and

(ii) $-\log \left(\text{tranLen}'_{12} - \text{readLen} + 1\right)^{\overline{(\text{expr}'_{12})}}$

are contributed by $\log P(\text{contig},\text{coverage},\text{contigsFromTrans}'|\text{trans}',\text{expr}') - \log P(\text{contig},\text{coverage},\text{contigsFromTrans}|\text{trans},\text{expr})$

We want to find the $\text{tranLen}'_{12}$ that maximizes the sum of these terms. To make this easier, we will treat the $\text{tranLen}'_{12}$ as a real number and take derivatives. We will also use the following shorthand:

1. $t = \text{tranLen}'_{12}$.

2. $x = \text{expr}'_{12}$.

3. $a = \text{readLen} - 1$.

4. $b = r_0 - 1$.

5. $c = \log(p_0/4)$.

6. $d = 1 - \sum_{j\in\text{contigsFromTran}'_{12}} \text{contigLen}_j$.

7. $h = \text{numContigsFromTran}'_{12}$.

(Note: t,x,a,b,h are positive, while c and d are negative. Also we require that $t > (1-d)+1 = d$.) The objective is:

$$J(\text{tranLen}'_{12}) = -\text{expr}'_{12} \log(\text{tranLen}'_{12} - \text{readLen} + 1) + \log \left(\frac{\text{tranLen}'_{12}+r_0-1}{\text{tranLen}'_{12}}\right) + \log((r_0-1)!) + \text{tranLen}'_{12} \log(p_0/4)$$

$$+ \log \left(\text{tranLen}'_{12} + 1 - \sum_{j\in\text{contigsFromTran}'_{12}} \text{contigLen}_j\right)_{\underline{(\text{numContigsFromTran}'_{12})}} - \log \left(\text{tranLen}'_{12} - \text{readLen} + 1\right)^{\overline{(\text{expr}'_{12})}}$$

i.e.,

$$J(t) = -x\log(t-a) + \log\binom{t+b}{t} + \log(b!) + tc + \log(t+d)_{\underline{(h)}} - \log(t-a)^{\overline{(x)}}$$

Note:

1. $\log\binom{t+b}{t} + \log(b!) = \log((t+b)!) - \log(t!) - \log(b!) + \log(b!) = \log((t+b)!) - \log(t!) = \log[1\cdot 2\cdots(t+b)] - \log[1\cdot 2\cdots t] = \sum_{i=1}^{t+b}\log(i) - \sum_{i=1}^{t}\log(i) = \sum_{i=t+1}^{t+b}\log(i) = \sum_{i=1}^{b}\log(t+i)$.

2. $\log(t+d)_{\underline{(h)}} = \log[(t+d)!/(t+d-h)!] = \log[(t+d-h+1)\cdot(t+d-h+2)\cdots(t+d)] = \sum_{i=1}^{h}\log(t+d-h+i)$.

3. $\log(t-a)^{\overline{(x)}} = \log[(t-a)\cdot(t-a+1)\cdots(t-a+x-1)] = \sum_{i=0}^{x-1}\log(t-a+i) = \sum_{i=1}^{x}\log(t-a+1+i)$.

So:

$$J(t) = -x\log(t-a) + \left(\sum_{i=1}^{b}\log(t+i)\right) + tc + \left(\sum_{i=1}^{h}\log(t+d-h+i)\right) - \left(\sum_{i=1}^{x}\log(t-a+1+i)\right)$$

And the derivative:

$$J'(t) = -\frac{x}{t-a} + \left(\sum_{i=1}^{b}\frac{1}{t+i}\right) + c + \left(\sum_{i=1}^{h}\frac{1}{t+d-h+i}\right) - \left(\sum_{i=1}^{x}\frac{1}{t-a+1+i}\right)$$

3.3   How to choose which transcripts to merge?

For the default Trinity assembly on the real Trinity mouse data, there are about 50000 contigs. There are about $50000^2/2 = 1,250,000,000$ pairs of contigs. Thus any approach that requires us to compute something for all pairs is a nonstarter. This rules out looking at all pairs of contigs and deciding which ones to merge based on some pairwise criterion.

Instead, we will (i) build an ordered list of contigs and (ii) decide which ones to merge based on the list. This requires us to find some bounds. I.e., we want to be able to say that if two contigs differ more than a certain amount according to the list's ordering criterion, then combining them will be a bad idea.

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EXTRA STUFF

3.3.1 How does $(\text{Contigs}, \text{Coverage}, \text{ContigsFromTrans}) | \{\text{Reads}, \text{Trans}, \text{Expr}\}$ change when we join two transcripts together?

Recall that

$$
\begin{aligned}
&P(\text{contigs}, \text{coverage}, \text{contigsFromTrans} | \text{reads}, \text{trans}, \text{expr}) \\
&= P(\text{numContigsFromTran} | \text{trans}, \text{expr}) \\
&\quad \cdot P(\text{contigsFromTran} | \text{numContigsFromTran}, \text{trans}, \text{expr}) \\
&\quad \cdot P(\text{coverage} | \text{contigsFromTran}, \text{numContigsFromTran}, \text{trans}, \text{expr}) \\
&\quad \cdot P(\text{contigLen} | \text{coverage}, \text{contigsFromTrans}, \text{trans}, \text{expr}) \\
&\quad \cdot P(\text{contig} | \text{contigLen}, \text{coverage}, \text{contigsFromTrans}, \text{trans}, \text{expr})
\end{aligned}
$$

We will address each of these separately.

3.3.1.1 How does $P(\text{numContigsFromTran} | \text{trans}, \text{expr})$ change when we join two transcripts together? Note

$$
\begin{aligned}
&\log P(\text{numContigsFromTran} | \text{trans}, \text{expr}) - \log P(\text{numContigsFromTran}' | \text{trans}', \text{expr}') \\
&= \left[\sum_{i=1}^{\text{numTrans}} \log \text{Binomial}(\text{numContigsFromTran}_i | \text{tranLen}_i, \alpha_i (1 - \alpha_i)^{\text{readLen} - \text{ws}}) \right] \\
&\quad - \left[\sum_{i=1}^{\text{numTrans}'} \log \text{Binomial}(\text{numContigsFromTran}_i' | \text{tranLen}_i', \alpha_i' (1 - \alpha_i')^{\text{readLen} - \text{ws}}) \right] \\
&= \log \text{Binomial}(\text{numContigsFromTran}_1 | \text{tranLen}_1, \alpha_1 (1 - \alpha_1)^{\text{readLen} - \text{ws}}) \\
&\quad + \log \text{Binomial}(\text{numContigsFromTran}_2 | \text{tranLen}_2, \alpha_2 (1 - \alpha_2)^{\text{readLen} - \text{ws}}) \\
&\quad - \log \text{Binomial}(\text{numContigsFromTran}_{12}' | \text{tranLen}_{12}', \alpha_{12}' (1 - \alpha_{12}')^{\text{readLen} - \text{ws}})
\end{aligned}
$$

where $\alpha_i = 1 - (1 - \text{tranLen}_i^{-1})^{\text{expr}_i}$.

3.3.1.2 How does $P(\text{contigsFromTran}|\text{numContigsFromTran}, \text{trans}, \text{expr})$ **change when we join two transcripts together?** Note

$\log P(\text{contigsFromTran}|\text{numContigsFromTran}, \text{trans}, \text{expr})$

$- \log P(\text{contigsFromTran}'|\text{numContigsFromTran}', \text{trans}', \text{expr}')$

$= -\log \binom{\text{numContigs}}{\text{numContigsFromTran}_i : i = 1, \ldots, \text{numTrans}}$

$\quad + \log \binom{\text{numContigs}}{\text{numContigsFromTran}_i' : i = 1, \ldots, \text{numTrans}'}$

$= -\log(\text{numContigs}!) + \sum_{i=1}^{\text{numTrans}} \log(\text{numContigsFromTran}_i!)$

$\quad + \log(\text{numContigs}!) - \sum_{i=1}^{\text{numTrans}'} \log(\text{numContigsFromTran}_i'!)$

$= \log(\text{numContigsFromTran}_1!) + \log(\text{numContigsFromTran}_2!) - \log(\text{numContigsFromTran}_{12}'!)$

$= \log(\text{numContigsFromTran}_1!) + \log(\text{numContigsFromTran}_2!) - \log((\text{numContigsFromTran}_1 + \text{numContigsFromTran}_2)!)$

$= -\log \binom{\text{numContigsFromTran}_1 + \text{numContigsFromTran}_2}{\text{numContigsFromTran}_1}$

3.3.1.3 How does $P(\text{coverage}|\text{contigsFromTran}, \text{numContigsFromTran}, \text{trans}, \text{expr})$ **change when we join two transcripts together?** Note

$\log P(\text{coverage}|\text{contigsFromTran}, \text{numContigsFromTran}, \text{trans}, \text{expr})$

$\quad - \log P(\text{coverage}|\text{contigsFromTran}', \text{numContigsFromTran}', \text{trans}', \text{expr}')$

$= \log \left(\prod_{i=1}^{\text{numTrans}} \frac{\prod_{j \in \text{contigsFromTran}_i} \text{Geometric}(\text{coverage}_j | \gamma_i)}{\text{NegativeBinomial}(\text{expr}_i | \text{numContigsFromTran}_i, 1 - \gamma_i)} \right)$

$\quad - \log \left(\prod_{i=1}^{\text{numTrans}'} \frac{\prod_{j \in \text{contigsFromTran}_i'} \text{Geometric}(\text{coverage}_j' | \gamma_i')}{\text{NegativeBinomial}(\text{expr}_i' | \text{numContigsFromTran}_i', 1 - \gamma_i')} \right)$

$= \left[\sum_{i=1}^{\text{numTrans}} \left(\sum_{j \in \text{contigsFromTran}_i} \log \text{Geometric}(\text{coverage}_j | \gamma_i) \right) - \log \text{NegativeBinomial}(\text{expr}_i | \text{numContigsFromTran}_i, 1 - \gamma_i) \right]$

$\quad - \left[\sum_{i=1}^{\text{numTrans}'} \left(\sum_{j \in \text{contigsFromTran}_i'} \log \text{Geometric}(\text{coverage}_j | \gamma_i') \right) - \log \text{NegativeBinomial}(\text{expr}_i' | \text{numContigsFromTran}_i', 1 - \gamma_i') \right]$

$= \left(\sum_{j \in \text{contigsFromTran}_1} \log \text{Geometric}(\text{coverage}_j | \gamma_1) \right) - \log \text{NegativeBinomial}(\text{expr}_1 | \text{numContigsFromTran}_1, 1 - \gamma_1)$

$\quad + \left(\sum_{j \in \text{contigsFromTran}_2} \log \text{Geometric}(\text{coverage}_j | \gamma_2) \right) - \log \text{NegativeBinomial}(\text{expr}_2 | \text{numContigsFromTran}_2, 1 - \gamma_2)$

$\quad - \left(\sum_{j \in \text{contigsFromTran}_{12}'} \log \text{Geometric}(\text{coverage}_j | \gamma_{12}') \right) + \log \text{NegativeBinomial}(\text{expr}_{12}' | \text{numContigsFromTran}_{12}', 1 - \gamma_{12}')$

$= -\log \text{NegativeBinomial}(\text{expr}_1 | \text{numContigsFromTran}_1, 1 - \gamma_1)$

$\quad - \log \text{NegativeBinomial}(\text{expr}_2 | \text{numContigsFromTran}_2, 1 - \gamma_2)$

$\quad + \log \text{NegativeBinomial}(\text{expr}_{12}' | \text{numContigsFromTran}_{12}', 1 - \gamma_{12}')$

where $\gamma_i = (1 - \alpha_i)^{\text{readLen}-\text{ws}}$. The last equality holds because $\text{contigsFromTran}_{12}' = \text{contigsFromTran}_1 \cup \text{contigsFromTran}_2$.

3.3.1.4 How does $P(\text{contigLen}|\text{coverage}, \text{contigsFromTrans}, \text{trans}, \text{expr})$ change when we join two transcripts together? Note

$$\log P(\text{contigLen}|\text{coverage}, \text{contigsFromTrans}, \text{trans}, \text{expr})$$
$$- \log P(\text{contigLen}|\text{coverage}, \text{contigsFromTrans}', \text{trans}', \text{expr}')$$

$$= \log\left(\prod_{i=1}^{\text{numTrans}} \frac{\prod_{j\in\text{contigsFromTran}_i}\binom{\text{coverage}_j-1}{\text{contigLen}_j-\text{readLen}}_{\text{readLen}+1}}{\sum_{L=0}^{\text{tranLen}_i-\text{numContigsFromTran}_i\cdot\text{readLen}}\binom{\text{expr}_i-\text{numContigsFromTran}_i}{L}_{\text{readLen}+1}}\right)$$

$$- \log\left(\prod_{i=1}^{\text{numTrans}'} \frac{\prod_{j\in\text{contigsFromTran}'_i}\binom{\text{coverage}_j-1}{\text{contigLen}_j-\text{readLen}}_{\text{readLen}+1}}{\sum_{L=0}^{\text{tranLen}'_i-\text{numContigsFromTran}'_i\cdot\text{readLen}}\binom{\text{expr}'_i-\text{numContigsFromTran}'_i}{L}_{\text{readLen}+1}}\right)$$

$$= \log\left(\frac{\prod_{j\in\text{contigsFromTran}_1}\binom{\text{coverage}_j-1}{\text{contigLen}_j-\text{readLen}}_{\text{readLen}+1}}{\sum_{L=0}^{\text{tranLen}_1-\text{numContigsFromTran}_1\cdot\text{readLen}}\binom{\text{expr}_1-\text{numContigsFromTran}_1}{L}_{\text{readLen}+1}}\right)$$

$$+ \log\left(\frac{\prod_{j\in\text{contigsFromTran}_2}\binom{\text{coverage}_j-1}{\text{contigLen}_j-\text{readLen}}_{\text{readLen}+1}}{\sum_{L=0}^{\text{tranLen}_2-\text{numContigsFromTran}_2\cdot\text{readLen}}\binom{\text{expr}_2-\text{numContigsFromTran}_2}{L}_{\text{readLen}+1}}\right)$$

$$- \log\left(\frac{\prod_{j\in\text{contigsFromTran}'_{12}}\binom{\text{coverage}_j-1}{\text{contigLen}_j-\text{readLen}}_{\text{readLen}+1}}{\sum_{L=0}^{\text{tranLen}'_{12}-\text{numContigsFromTran}'_{12}\cdot\text{readLen}}\binom{\text{expr}'_{12}-\text{numContigsFromTran}'_{12}}{L}_{\text{readLen}+1}}\right)$$

$$= -\log\left(\sum_{L=0}^{\text{tranLen}_1-\text{numContigsFromTran}_1\cdot\text{readLen}}\binom{\text{expr}_1-\text{numContigsFromTran}_1}{L}_{\text{readLen}+1}\right)$$

$$- \log\left(\sum_{L=0}^{\text{tranLen}_2-\text{numContigsFromTran}_2\cdot\text{readLen}}\binom{\text{expr}_2-\text{numContigsFromTran}_2}{L}_{\text{readLen}+1}\right)$$

$$+ \log\left(\sum_{L=0}^{\text{tranLen}'_{12}-\text{numContigsFromTran}'_{12}\cdot\text{readLen}}\binom{\text{expr}'_{12}-\text{numContigsFromTran}'_{12}}{L}_{\text{readLen}+1}\right)$$

If $\text{tranLen}_i > \text{readLen}\cdot\text{expr}_i$, then the denominators above are $(\text{readLen}+1)^{\text{expr}_i-\text{numContigsFromTran}_i}$, in which case,

$$\log P(\text{contigLen}|\text{coverage}, \text{contigsFromTrans}, \text{trans}, \text{expr})$$
$$- \log P(\text{contigLen}|\text{coverage}, \text{contigsFromTrans}', \text{trans}', \text{expr}')$$
$$= -\log\left((\text{readLen}+1)^{\text{expr}_1-\text{numContigsFromTran}_1}\right)$$
$$- \log\left((\text{readLen}+1)^{\text{expr}_2-\text{numContigsFromTran}_2}\right)$$
$$+ \log\left((\text{readLen}+1)^{\text{expr}'_{12}-\text{numContigsFromTran}'_{12}}\right)$$
$$= -(\text{expr}_1-\text{numContigsFromTran}_1)\log(\text{readLen}+1)$$
$$- (\text{expr}_2-\text{numContigsFromTran}_2)\log(\text{readLen}+1)$$
$$+ (\text{expr}'_{12}-\text{numContigsFromTran}'_{12})\log(\text{readLen}+1)$$
$$= 0$$

3.3.1.5 How does $P(\text{contig}|\text{contigLen}, \text{coverage}, \text{contigsFromTrans}, \text{trans}, \text{expr})$ **change when we join two transcripts together?** Note

$$\log P(\text{contig}|\text{contigLen}, \text{coverage}, \text{contigsFromTrans}, \text{trans}, \text{expr})$$

$$- \log P(\text{contig}|\text{contigLen}, \text{coverage}, \text{contigsFromTrans}', \text{trans}', \text{expr}')$$

$$= \log \left(\prod_{i=1}^{\text{numTrans}} \left(\frac{\text{numContigsFromTran}_i + \text{tranLen}_i - \sum_{j=1}^{\text{numContigsFromTran}_i} \text{contigLen}_j}{\text{numContigsFromTran}_i} \right)^{-1} \right)$$

$$- \log \left(\prod_{i=1}^{\text{numTrans}'} \left(\frac{\text{numContigsFromTran}_i' + \text{tranLen}_i' - \sum_{j=1}^{\text{numContigsFromTran}_i'} \text{contigLen}_j}{\text{numContigsFromTran}_i'} \right)^{-1} \right)$$

$$= - \log \left(\frac{\text{numContigsFromTran}_1 + \text{tranLen}_1 - \sum_{j=1}^{\text{numContigsFromTran}_1} \text{contigLen}_j}{\text{numContigsFromTran}_1} \right)$$

$$- \log \left(\frac{\text{numContigsFromTran}_2 + \text{tranLen}_2 - \sum_{j=1}^{\text{numContigsFromTran}_2} \text{contigLen}_j}{\text{numContigsFromTran}_2} \right)$$

$$+ \log \left(\frac{\text{numContigsFromTran}_{12}' + \text{tranLen}_{12}' - \sum_{j=1}^{\text{numContigsFromTran}_{12}'} \text{contigLen}_j}{\text{numContigsFromTran}_{12}'} \right)$$