

## OSIRIS V2.4 Release Notes

12/05/2014

### New Kits

1. Added PowerPlex Fusion 6C kit.
2. Added ABI Minifiler kit.
3. Added kit for NIDDK's study of tri-nucleotide repeat instability diseases, particularly, fragile X. This is still in development.

### New Features

#### User Interface

1. User interface improvements, especially for Macintosh, because of updated WxWidgets.
2. Lab Settings Sample Thresholds tab has been reformatted to group, highlight and indent settings and thresholds on the Sample Thresholds tab.

#### Improved artifact and allele calling

1. Improved allele and artifact recognition. Improved the signature selection in case the basic double Gaussian curve fit is marginal. Now OSIRIS chooses the best of three alternatives, or reverts to original. Whichever signature is ultimately selected, the resulting fitted curve is now added to the list of curves to contribute to further peak analysis.
2. Improved pull-up analysis accuracy. Created and incorporated a formula that estimates accuracy of peak sizing in terms of the ambient noise level for channel, and peak height, width and fit.
3. Improved allele and locus assignment of peaks occurring between loci. The new logic flow compares number of unambiguous peaks only because ambiguous peaks in a locus have uncertain status. Also, the new MessageBook logic incorporates the differential and potential assessments of the fractional filter, excessive residual displacement, and whether a peak is an accepted off-grid allele. This involved rewriting the MessageBook logic pertaining to this analysis and supplementing the changes by modifying software.
4. Improved homozygous peak detection to account for Y-STR loci. Formerly, a Y-STR locus could not be called for a single allele falling below the homozygous threshold. In the new version, the test for adequate homozygous height is based solely on the maximum expected number of alleles in the locus versus the number of alleles present in the locus.
5. Alleles appearing in negative controls are now called rather than simply flagged as artifacts. This will allow users to identify sources of contamination, as needed.
6. Improved adenylation algorithm to call as an allele any –A peak below the adenylation threshold if it is on-ladder. Now, any –A peak that is either on-ladder or that is an accepted off-ladder allele and would be called as adenylation, will be recognized as an allele and adenylation is not reported. This allows OSIRIS to call microvariant alleles that are the minor component of a mixture, such as TH01 9.3/10, where 9.3 is the minor component.

### Improved ladder-to-sample fit metric and notification

1. Ladder-to-sample fit metric option. Added capability for user to select sample-to-ladder fit criterion between most linear time transform (based on max second derivative of transform) and least time transform approximation error (in terms of preserving ILS base pair correspondence between sample and ladder).
2. Ladder-to-sample fit threshold. Added capability for user to specify an approximation error threshold (in percent base pairs) to trigger the poor sample-to-ladder fit error message. Based on the criterion selection in (1), above, Osiris uses the “most linear” fit metric already in V2.3 Lab Settings if the “most linear” selection has been made. If the least error selection is made in (1), then this new approximation error threshold is used.
3. Improved ladder analysis. Optimized the search region and allele base pairs for PowerPlex 21, D18 locus. Previous search region definition could cause infrequently occurring ladders to fail to analyze.

### Improved baselining

1. Improved baselining. Improved normalization process by forcing denser selection of baseline samples and shaping points. This helps to control the cubic spline fit to the baseline, especially in areas where the fit peak density is higher. Also, the same higher density is now used whether or not prefiltering is selected. Previously, prefiltered data used a higher density automatically.
2. Improved baseline curve estimation. Normalization curves are now created with Hermite cubic splines as opposed to natural cubic splines. The new splines have better error characteristics. Derivatives at knots are estimated from knot values using chordal approximation.
3. Improved baseline estimation - prefiltering option added. A new method of prefiltering for normalization has been added as an option. Instead of the previous single pass window averaging, the new method uses three passes, with window widths computed from the specified window by multiplying successively by 1.4303 (and rounding). This is a well-known technique that corrects the tendency for the single pass filter to artificially create high frequency artifacts. MessageBook and Lab Settings options have been added for the new selections.

### Bugs

1. Fixed minor bugs that did not affect accuracy.