

Affymetrix Chromosome Analysis Suite 1.2 Release Notes

(For research use only. Not for use in diagnostic procedures.)

Chromosome Analysis 1.2 includes the following changes/updates:

New Analysis Files and Upgrading from Previous Versions

1. ChAS 1.2 supports NetAffx version NA30.2, NA31, and NA32 analysis files for generation of CYCHP files for the 2.7M Cytogenetics Array, and NA32 for generation of CYCHP files for the CytoScanHD_Array.
2. Some previous NetAffx versions of 2.7M Cytogenetics Array analysis files which may be stored in the ChAS Library folder, such as NA30.1 and earlier, are outdated and will be safely archived upon ChAS 1.2 installation when upgrading from ChAS version 1.0.1 or 1.0.0. Upgrading from ChAS1.1 to ChAS1.2 requires no archiving of files, since the ChAS1.1 Installer did similar archiving of any outdated files used by previously installed earlier ChAS versions (see 3. below for details).
3. ChAS 1.2 will upgrade from any previously installed ChAS versions. The ChAS 1.2 installer will remove the previous version as well as installs the latest version.
4. If you have installed a version of ChAS older than 1.1, the installation of ChAS 1.2 will archive outdated ChAS analysis files into an archive folder in your ChAS library. The user has to click the "Yes" button in order to archive. Choosing "No" will exit the installation. None of the files will be deleted. The following are the outdated files that will be archived during the upgrading to ChAS1.1 from earlier versions of ChAS:
 - Archive ALL "*.chasparams" from ChAS Library
 - Archive ALL "*.chasparams" from User Profiles
 - Archive "Cytogenetics_Array.*.annot.db" from ChAS Library
 - Archive ALL "*.REF_MODEL" files from ChAS Library
 - Archive all *.snpref.a5" files from ChAS Library

After the installation/upgrade you need to download the latest library files from NetAffx from within ChAS, or copy the contents of the Cytogenetics Analysis Files or CytoScanHD Analysis Files folder file from the respective zip package

New Features/Improvements

1. Affymetrix® CytoScan™ HD Array support, including CEL>CYCHP "Single Sample Analysis", viewing of CYCHP results, and creation of custom Reference Model Files.
2. Genotype call data for Affymetrix® CytoScan™ HD Array CYCHP files.
3. Status bar displays the NetAffx database build loaded in the ChAS Browser.
4. Load a different NetAffx Genomic Annotations Browser database into the ChAS Browser without restarting the software
5. View sample and results information in the Sample Information window
6. New Named Settings.(see ChAS 1.2 User Manual/Help Chapter 13 for details)
7. Easily identify User Profiles available for import.
8. Apply user-selected colors to reference annotations (except DGV annotations, which contain a pre-defined set of differential color codes) in the Detail View.

9. Segments table updates:
 - a. When multiple annotations in any of the Reference Annotation tracks overlap a segment, the annotations in the Segments table row are listed in the order that they appear from left to right in the Detail View
 - b. Gene names redundancy has been eliminated in the Segments table. Genes names which overlap a segment are now listed only once in the Segments table, rather than once per splice variant of the same gene.
 - c. The "Types" column sorts segments in the same order that they appear in the Data Types windowpane
10. ChAS verifies the hg version of AED or BED files and will not load files with hg version different from that currently loaded in the ChAS Browser. If the hg version information is not found in the AED or BED file, ChAS warns you before loading the file.
11. AED files created in ChAS 1.2 include the hg version
12. All AED or BED files that are loaded during a session are automatically reloaded in a subsequent session with the same user profile.
13. Reports include CytoRegion and Overlap Map file names.
14. ChAS remembers the destination folder for exported reports for a user profile during a session and in subsequent sessions.
15. Automatic archiving of old library files when new library files are downloaded.
16. ChAS makes use of Java technology. Starting with ChAS version 1.2, ChAS will install a copy of the Java JRE 1.6_24 into the program installation directory for its own use. It does not matter whether you currently do or do not have other versions of the Java JRE or Java SDK installed on your system, and it does not matter if you add or remove other Java instances.

Issues addressed/Bugs fixed

1. A bug was fixed in the Cytogenetics Array (2.7M) analysis pipeline involving the correct computation of median values. All pre-existing ChAS Cytogenetics Array NA30.2 and NA31 Analysis files and Reference Model files are still appropriate to use in ChAS1.2. Data compared from before and after the bug fix was very highly correlated. Comparing data before and after the fix using samples with thousands of gain/loss segments showed no change in these segments. The before and after log2ratio values in these samples had correlation values greater than 0.9999. The rare changes in LOH segmentation and in segment confidence scores had negligible biological impact: >98% of LOH segments had no change in confidence score, and the maximum LOH segment confidence score change ever seen was <4%
2. Fixed The OMIM ID is not listed in the Selection details of Property and Annotation column after a OMIM is added to AED file
3. Fixed when displaying the confidence and MeanMarkerDistance values from CYCHP file or re-calculated confidence values for smoothed/joined segments in the segments table, the values are rounded down instead of up after two decimal points. The values are rounded up after two decimal points

Installation/Upgrade Requirements for Chromosome Analysis Suite 1.2:

1. Chromosome Analysis Suite 1.2 supports the following operating systems:

Operating system on 32-bit

- Windows XP Professional SP3
- Windows 7 Professional

Operating system on 64-bit

- Windows XP Professional SP2
- Windows 7 Professional

Minimum Memory requirement:

- 3 GB RAM (32-bit machine)
- 8 GB RAM (64-bit machine)
- 5 GB free space on C: drive

Recommended Requirements

- 32-bit systems: Quad Core System, 3 GHz with 4 GB RAM
- 64-bit systems: Quad Core System, 3 GHz with 16GB RAM

The following are known issues in Chromosome Analysis Suite 1.2:

1. When you Double click on the color cell to bring up the "pick a color" sub-dialog, it disappears and hides behind the application and it looks like the application has frozen. If it happens the workaround is , use ALT+TAB to find the color-picker dialog and when you close that dialog you can get the other windows to un-freeze
2. When Marker Count = 1 for Cytogenetics CYCHP and SNP6 CNCHP, The Mean Marker Distance (MMD) displays the value "0" for CYCHP and blank for CNCHP.
3. Do not use Excel to edit BED files. ChAS may display non-ASCII characters from your BED file correctly, but the BED format was not designed with such characters in mind and thus you may have problems if you try to share such files with others. The workaround is to use a text editor, but be certain to separate the columns with TAB characters and avoid non-ASCII characters.

The following are known issues that existed in Chromosome Analysis Suite previous version and were not addressed in Chromosome Analysis Suite 1.2:

4. On Windows XP Chinese operating system, sometimes you may see two install window displays at the end of the installation. Click Cancel at the configuration window and OK on the checkbox window. ChAS will be installed and run properly.
5. LOH segment marker count and SNPs in Details View and Graphs table: a small percentage of LOH segments may contain a marker count value which is slightly smaller than the number of SNPs displayed as LOH=1 making up the segment. This is because while the region has been determined by the algorithm to be in the state of LOH, there are a small number (less than 1000 SNPs on the Cytogenetics 2.7M Array) which are not used in the LOH algorithm, but which are used for other allelic and/or copy number data determinations. This is by design, so that only the highest quality SNPs are used to determine a region's zygosity status.

6. ChAS 1.1 and the accompanying NA30.2 annotation files allow independent specification of probesets for Copy Number and for LOH/LCSH analyses. The primary result of this is that a small subset (less than 15%, ~55K) of SNPs on the Cytogenetics Array that are suitable for LOH/LCSH computation but which do not meet Affymetrix's strict standards for accurate Copy Number estimation, are used only for LOH/LCSH calculations and not for Copy Number ascertainment. These SNP markers (with flag = 2 in array-specific annotation files) don't display log2 ratios or CN states. Improvements in Copy Number data are most likely to be seen when Single Sample Analysis is run with ChAS 1.1 using NA30.2 versioned library files, compared to previous versions of ChAS using previous NA version analysis files.
7. Smooth Signal algorithm: The minimum and default values of the median-smooth-marker-count algorithm have changed. Previously where no minimum was set, now the minimum allowed value is the smooth over 3 markers, while the default value in the Single Sample Analysis .chasparam file has been changed from 3 markers (using ChAS1.0.1 and NA30.1 Analysis files) to 5 markers in NA30.2 Single Sample Analysis .chasparam files which accompany ChAS 1.1.
8. The chromosomal location for a particular OMIM gene or disease given on the OMIM site is, in rare cases, different than the location in the ChAS browser that brought the user to that page.

This is because a small number of these discrepancies (~3%) are the result of two bioinformatics issues. First, OMIM provides a gene name field that is used to identify the RefSeq gene for the disease. In doing so, OMIM also provides alternative names and symbols in the same field. Unfortunately these alternative symbols often now refer to a different RefSeq gene than the primary symbol. As a result instead of mapping just the correct gene, the additional genes are mapped to other locations, producing links in the incorrect location in the ChAS browser. Second, OMIM does not provide mapping of the gene or region at the level of chromosomal coordinates. To get this information for use in the ChAS browser the RefSeq genes are aligned to the genome as part of the NetAffx process. Due to different parameter settings, filters, and builds of the genome some differences in locations are observed (Note, less than 1% of the genes map to a different cytoband than is provided by OMIM). All OMIM data should be verified by linking out to the OMIM site, which is the original curated source of the data.
9. In very rare cases an OMIM gene or disease is not present in the OMIM track of the ChAS browser.
10. This is because the gene or region of interest maps to a special region of the genome that is not able to be displayed in the ChAS browser. These special regions come in two different types: 1) There are several genomic segments that are known to be a part of a particular chromosome, but they have not been assigned to a position on the genome; therefore they cannot be displayed in the browser. 2). There are four alternate haplotypes for regions on Chromosome 5, 6, and 22 that are not part of the reference build of the genome and therefore cannot be displayed in the ChAS browser.
11. If you run single sample analysis without having added a CYCHP file suffix during Analysis setup, and then run an analysis using the same CEL file(s) again, writing the results files to the same output folder and without having added a CYCHP file suffix the second time, there is no warning message that the data will be overwritten. This can also occur if the exact same suffix is used and a second set of identically named and suffixed CYCHP files are written to the exact same output folder. STILL EXISTS in 1.2

12. When you sort the Type column in tables by clicking on the column header, the Type column is not sorted alphabetically (the Types are grouped together, but not alphabetically sorted).
13. Very rarely, the order of items in the Files list and the order of tracks in the Detail View in the ChAS Browser may fall out of synch with each other.
When it occurs, the work-around is:
 - Close the program
 - Go to the user profile's folder (listed as the "Preferences" folder in the ChAS About Box) and delete the two files **annotationGenomodelOrder.xml** and **annotationTypeOrder.xml**
 - Re-start the program. The default sort-order will have been restored and the user can once again make synchronous changes to that order in the ChAS software.