

Affymetrix Genotyping Console 4.2 Release Notes

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

Genotyping Console 4.2 includes the following changes and enhancements:

1. Edit Calls within the Cluster Graph.
2. Add or remove SNPs from SNP lists from within the cluster graph.
3. Saturation_GC and Saturation_AT metrics are now displayed after an Intensity QC is performed.
4. Added Axiom CNV Tool and Viewer applications to the Tools menu.

Installation/Upgrade Requirements for Genotyping Console 4.2

1. Genotyping Console 4.2 supports the following operating systems:
 - a. Windows 7 Professional SP1 (64-bit)
 - b. Windows 8.1 Pro (64-bit)
2. Genotyping Console 4.2 will upgrade from previous versions 4.1, 4.1.1, 4.1.2, 4.1.3 and 4.1.4. The GTC 4.2 installer will remove the previous version as well as install the latest version. If Matlab is installed, the installer will ask you if you would like to remove it. Testing has not been performed to upgrade from GTC 1.0, 2.x, 3.x.
3. Genotyping Console 4.2 will also install the Axiom CNV Summary Tool and the Axiom CNV Viewer software. If they have been previously installed, they will be uninstalled and reinstalled in "C:\Program Files\Affymetrix\Tools\Axiom CNV Tools" to enable these tools to be called directly from within Genotyping Console.
4. For Axiom™ myDesign™ Genotyping Arrays and Axiom™ Genome-Wide CHB Array, the call rate metrics will be calculated using the probe sets in the SNP list plus the 3000 SNPQC probe sets. The posterior models file generated during genotyping will include the probe sets in the SNP list plus the 3000 SNPQC probe sets. The contents of the resultant CHP files will only contain analysis results for those probe sets included in the SNP List.
5. Occasionally, customers might see an error if they are performing genotyping for a group of Axiom CEL files that are all the same gender (either all males or all females) and trying to use the generated posterior models file with a gender file including the other gender (female or male) for further genotyping. This error is due to the lack of presence of both genders and the subsequent incomplete content in the generated posterior models file. To avoid this issue, customers shall include both male and female samples during genotyping. Another workaround is to add two lines to the generated posterior models file to handle the incomplete content.

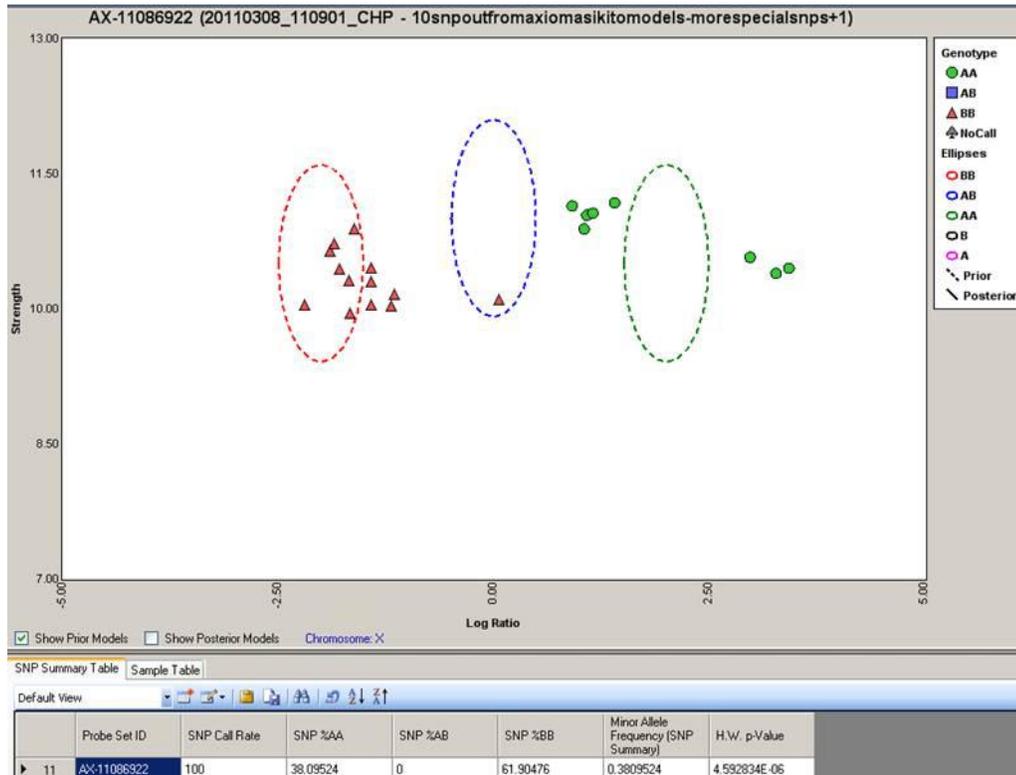
```

GENERIC      -2,0.06,0.2,1,10.5,0.3,0  0,0.06,0.3,10,11.0,0.3,0  2,0.06,0.2,1,10.5,0.3,0  -
0.1,-0.1,-0.1,-0.05,-0.1,-0.05,0,0,0,0,0
GENERIC:1    -2,0.06,0.2,1,10.5,0.3,0  0,0.06,0.3,10,11.0,0.3,0  2,0.06,0.2,1,10.5,0.3,0
-0.1,-0.1,-0.1,-0.05,-0.1,-0.05,0,0,0,0,0
  
```

The following are known issues in Genotyping Console 4.2:

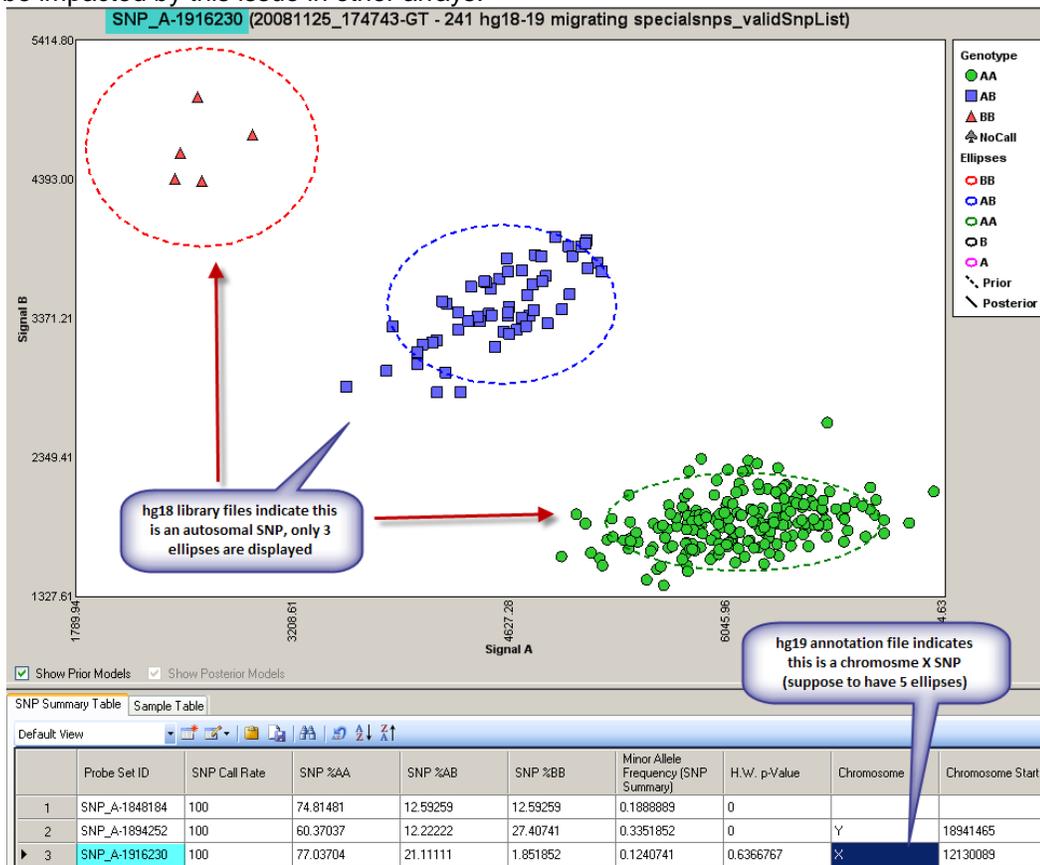
1. When exporting genotype result to root C:\, you may get an error "The logged-on user does not have access to the C:\. Please select a different folder." The work around is to create a subfolder in root C:\ and export to this folder.
2. GTC expects a single SNP Summary db file in an analysis results folder. If more than one exists in the same folder GTC will try and use the first one even if it is not the correct one for an analysis. If users maintain a separate folder for the CHP files from an analysis run (default GTC behavior), this issue will not arise.
3. During the change calls in Cluster Graph, if the sample file is locked, the call won't be changed in the physical sample file but the Cluster Graph still shows that the call is changed.

4. Windows 7 and above now require Administrator level security to access the events log. Non-administrator users running the Support Tool will not be able to collect the events log.
5. If a SNP list contains unconverted chromosome X SNPs (unconverted SNP: there are no SNP specific priors in the models file for that SNP), customers will only see 3 priors ellipses in the cluster graph when that SNP is displayed. The reason is that B and A ellipses are super-imposed with BB and AA ellipses. Posterior ellipses will display the 5 ellipses with information from study samples.



6. Currently, GTC does not prevent users from manually loading models files when the chip-type is unknown and none of the probe set ids in the snp list is found in the models file.
7. When loading cluster graph for Mapping100K array, and if the SNP list filename contains special characters, an unhandled exception is thrown. This error only occurs on Mapping100K Xba and not the Mapping100K Hind.
8. Currently, the cluster graph does not check chp type compatibility. Thus, users can load mix-match versions of model file. Verify that the chp types are the same when creating a cluster graph.
9. If the SNP list selected for genotyping does not use "probeset_id" as the column header the following error message will be displayed in the status window: "FATAL ERROR:ProbesetGenotypeEngine::loadPSFile(): Didnt find probeset_id column in:'D:\GTC4.1.4Lib\00Axiom_TMRiceGT.r1.step1 - Copy.txt'".
10. If you run the Genotyping Axiom Hu array or any other array with a snp list that has no probe set, it will cause the application to throw an exception. Ensure that there is a probe set in the snp list to prevent the error.

11. There is no error displayed when genotyping with duplicate and extra CEL files in the inbred file. User must verify manually that there are no duplicate and extra CEL files in the inbred file.
12. There is no error displayed when genotyping with an invalid hint file (e.g. invalid snp or cel file).
13. Model files edited in MS Excel with added "" will not be accepted by cluster graph. Ensure that edited models file doesn't contain additional "".
14. GTC 4.1 does not automatically upgrade GTC 1.0/2.0 on Spanish operating system. When the installer prompts for a restart to continue, it does not automatically start. Rather the user will need to relaunch the installer to continue with the GTC install. This is only on the Spanish operating system.
15. GTC will crash when loading corrupt models files. If user loads the model file Affymetrix provided or generated by GTC the application will be able to open the files successfully.
16. All the current genotyping analysis library files are generated based on Hg18 genome build. NetAffx annotation version NA 31 and above are from Hg19 genome build. When users view certain SNPs in cluster graph, the information indicated in the graphic area might be different than the annotation information available in the SNP Summary Table. Less than 250 SNPs will be impacted by this issue in SNP6 array. And fewer SNPs will be impacted by this issue in other arrays.



17. SNP 6.0 copy number / LOH analysis has memory leak issue.
 - 1) When users finish copy number analysis for 450 files, GTC needs to be closed before another copy number analysis is initiated.
 - 2) If GTC has been using over 100MB memory before copy number analysis begins, GTC will fail with out of memory error. The workaround is to close other windows within

GTC before copy number analysis starts.

3) When users run segment reporting tool (SRT) right after copy number analysis for 450 files, GTC will fail with out of memory error. The workaround is to close GTC after copy number analysis and re-open GTC to start the SRT.

18. Cancel may take long time when running copy number analysis GC batch mode for na27 or na28 annotation files. The progress bar grays out but analysis continues until it finishes.
19. When the user exports Genotype results for Plink using the transposed option, in the exported tped file the dbSNP rs12635398 is duplicated for two probe sets (SNP_A-2144818 and SNP_A-8548122). If there are multiple probesets associated with the same dbSNP RS ids, GTC will pick probeset that is higher\later when sorted on a descending alphabetical order for the exported file.
20. When a SNP list is opened and sorted by dbSNP RS ID column, the ID is sorted by the first 6 digits, not by the absolute value.
21. In the Segment Report Tool, if the user changes Overlap with known CNV regions value to "zero", the browser will display segments overlapping with the 'genomic variants'. However, the generated segment report file the %CNV_Overlap column will show it as zero.
22. On Vista Aero and Vista Basic settings, the 'Select All' button in Segment Report Tool does not select all the files after unselecting a few files.

The workaround is to click the OK button and then the Segment Report Tool starts to run.

23. After upgrading from GTC 3.0.2 to GTC 4.0, the user cannot open GTC 3.0.2 workspace in GTC 4.0. This only happens if the GTC 3.0.2 workspace is created without any data.

The workaround is to create some data in GTC 3.0.2 and then upgrade it to GTC 4.0.

24. When a user exports genotype results for PLINK using the Standard option contents in the exported ped file are sometimes displayed with as square boxes in Notepad. However, the PLINK export file is compatible with the PLINK tool.
25. Optimizing the annotations when there is not enough free disk space will result in the error "SQLite error cannot rollback – no transactive is active".

The workaround is to free up some disk space and re-download or copy the annotation files again. Disk space usage will depend on the number of annotation files selected to optimize.

26. When you open the annotation file within GTC software, the application will be very slow or hang if you click on the Find button to search for information. This also happens when scrolling or sorting through the annotation table.

Do NOT click the Cancel button once the "find" function has initiated. Instead, please use the task manager to kill the GenotypingConsole.exe process.

27. If the pedigree template does not have the attribute for Sex as Male, Female or Unknown and Affection Status as Unaffected, Affected or Unknown, there is no warning about the missing information while exporting in PLINK format. The application will assign the value 0 to these attributes.
28. In the SNP list, SNP Summary table, and SNP cluster table, the order of SNPs in the Probe Set ID column is not the same between GTC 3.0.2 and GTC 4.0.

However, when the CHP file is exported using this SNP list, SNP Summary table of the SNP cluster table below the cluster graph, the SNPs in the exported file are listed in the same order as that in GTC 3.0.2.

29. SNP5 data generated from GTC 1.0 will not display the attributes in the cluster graph. However, SNP6 data generated from GTC 1.0 works fine. There is no workaround for the SNP5 data generated from GTC 1.0.
30. When adding a large amount of files (ARR/CEL), use the “Select Directory” option instead of the “Select Files” option. If you use the “Select Files” option, an error will occur “... CEL file from x:\directory does not exist...”
31. There are some rounding differences between GTC 3.0.2 and GTC 4.0. The differences are:
 - There are rounding differences in Contrast QC (Random), Contrast QC (Nsp), Contrast QC (Sty), Contrast QC (Nsp/Sty Overlap). However, the Contrast QC and Call Rate are the same in both versions.
 - There are rounding differences in CNV Signal. However, the Call and Confidence call are the same in both versions.
 - There are rounding differences in the call_rate and hom_rate columns for the SNP6 CHP Summary Table.
32. There are rounding differences between GTC 4.0 32-bit and GTC 4.0 64-bit. The differences are:
 - Copy Number for 100K/500K has differences in Log2Ratio, HmmMedianLog2Ratio, and NegLog10PValue. The CNState is the same.
 - Genotyping for SNP6 has rounding differences in Signal B.
33. During SNP list creation, when SNP Call Rate threshold is set as “.9” as search criteria, no SNPs will be returned. The workaround will be to use “0.9 instead of “.9” as criteria.
34. Users cannot unzip a Workspace > 4GB.
Users can zip a Workspace larger than 4GB, but will be unable to unzip the Workspace. To avoid this issue, create and zip a Workspace that is not larger than 4GB in size.
35. If a user opens a “.bed” file in Microsoft Word or Excel and concurrently opens the CNVCHP file in GTC, the GTC application only shows 1 column. This is because the .bed file is in use. To see all columns in GTC, a user can open the .bed file in Notepad at the same time. Alternatively, close the .bed file in Microsoft Word or Excel and the columns will be displayed in GTC.
36. QC thresholds are updated for only one library path for each user profile.
If users have more than one library path for a user profile, the QC metric will only be updated for the default library file folder. You will need to change the library file path to ensure that the other library paths are updated
37. If you select the CHP vs. CHP Concordance Check, the selected batch node is not listed in the pull down box.
38. In the application, there may be inconsistencies in the display of numbers, e.g.05 vs. 0.05.
39. If you select an invalid annotation file, the error message “Failed to open the annotations” appears. Select the correct annotation file and the error will not appear.
40. If file names are too long, you will not be able to view all the region information in the Heat map window.

41. In very rare occasions, when samples have abnormal karyotypes XXYY or XXY where XX is a normal diploid heterozygous, GTC reports the total LOH in the non-PAR regions of chromosome X. This is because the BRLMM-P-Plus algorithm defaults to calling all SNPs in the non-PAR region of the Chr X as a homozygous if a chromosome Y presents. If you see gender calls as unknown in the Karyoview Legend after you run segment reporting tool for these abnormal samples, the LOH calls on chromosome X shall be taken with low expectations.
42. If a user uses SNP 6.0 CNCHP files from GTC 3.x and runs the SRT in GTC 4.0 and above, the following error will occur.

“Annotation file <location>\GenomeWideSNP_6.na<version of the annotation file when CNCHP files were generated>.annot.db not found. This error occurred because the same version of SQLite annotation files are not installed.

Please go to Affymetrix.com and download the earlier versions of annot.db files to the library folder. Then use the “File->Optimize Annotation Files...” menu option to create the indexed annotation file.

The earlier versions of annotation files are located on the Product & Services page> Arrays > Genome-Wide Human SNP 6.0 > Tools & Data under the “Archived NetAffx Annotation Files” heading.
Same rules apply to 100K/500K SRT analysis. GTC 4.0 and above will need NA24 version of the 100K/500K annot.db files for 100K/500K SRT analysis. The NA24 version of the annot.db files are located on the Product & Services page> Arrays > Human Mapping 100K Set (or Human Mapping 500K Array Set) > Tools & Data under the “Archived NetAffx Annotation Files” heading.
43. When you add CNCHP files to a batch, the error “No CNCHP files added or 0 files imported” appears if one or more CNCHP files are of size 0kb. Check the size of the CNCHP files you are attempting to add. After removing the bad CNCHP file(s), you should be able to add the CNCHP files to the batch.
44. This issue affects the 100K/500K mapping arrays with respect to updating the workspace with results files following unpaired CN + LOH runs. An unhandled exception error will appear if you run an unpaired CN + LOH analysis for a data set which contains more “sample files” than the “reference files”
45. SNP 6.0 Intensity files which have previously QC'd with Birdseed V2 must be added together with their accompanying GQC files to a data set. Otherwise, the application will display the error message “QC metrics cannot be displayed until the CEL files have been QC'd”. The same message will be displayed when double clicking on the “All” Intensity data group icon. A message “Intensity Data results are not available” will be displayed when double clicking on the “In Bounds” and “Out of Bounds” Intensity data group icons.

If you receive these error messages, please follow one of these procedures:

For files generated in GTC v2.1 or later:

- Locate the GQC files and copy them into the same directory as the intensity files.
- Add intensity and GQC files simultaneously, making sure the checkbox “Auto-QC Intensity files” is selected.

For files generated in GTC v2.0 or earlier:

- Locate the GQC files and copy them into the same directory as the intensity files.
- Add intensity and GQC files simultaneously, making sure the checkbox “Auto-QC Intensity files” is selected.

- Perform QC again to incorporate the Contrast QC metric. Otherwise, the warning message “QC metrics will be displayed. Since GTC 2.0 and earlier did not have the algorithm to generate Contrast QC data, re-invoking the QC step completes the QC process.

46. In the very rare case of encountering a corrupt or “bad” CEL file, QC may fail.

- If a corrupt CEL file is part of a group of CELs being QC'd, the corrupt CEL may halt the QC process with an “Unhandled Exception” error message, and neither the bad CEL nor the subsequent files to be QC'd will have GQC files successfully generated for them.



- The bad CEL file will be identifiable in the last line of the status messages list at failure, which will say: “Calculating the QC metrics for:” and the name and file path of the bad CEL file.
- Corrupt CEL files which cause QC step to fail must be removed from the system, as GTC software will attempt to QC them again if new data is imported into the Data set. This will fail the process again even though the new CEL files might be fine.
- You must also delete the XML/ARR file and the GQC file of the bad CEL if you need to remove a bad CEL file. This is because the "Auto-Add" automation feature will re-add bad CEL files if the XML/ARR file or GQC file is still in the data set.
- In the very limited number of examples identified, corruption of the files has been seen after a transfer of the original files

47. In GTC 4.1 and above, there is an option to use a proxy server. A proxy server requires authorization to access the internet, you may be unable to download files from NetAffx. You can either disable or enable the proxy server setting.

48. Renaming Results Groups level batch folders only renames groups in the GTC workspace. The Windows file system folder does not get renamed as part of this action.

49. PDF exports of the cluster plot of large SNP lists are limited to a workstation's disk drive capacity. Each SNP's cluster plot is temporarily stored in a PNG file in the user's system temporary directory prior to the PDF file being created, thus there must be enough disk space for the storage of all of these files.

50. The cluster graph feature is designed to function with relatively small SNP lists of up to 200,000 SNPs. The data for each cluster plot is loaded into memory. Too many SNPs in a SNP list will exceed the workstation's memory capacity.

51. When exporting Genotype Results or CN/LOH results, be sure to use a unique name to avoid overwriting previously exported files.

52. When the Browser is started from within GTC, the Browser Help file will fail to open the first time it is used after creating a new profile. Close both GTC and the Browser. Start the Browser from the Start > Programs > Affymetrix > 'GTCBrowser' icon. Open the Browser's Help file.

53. The CNCHP and LOHCHP files for the 100K or 500K arrays do not indicate if the results were derived using Normal or Median normalization.
54. If you load two different CNCHP files with the same name (loaded from different folders), they will display on top of each other in the Browser. Always give results files unique names, even if separate folders are used.
55. On some workstations it is possible for the copy number analysis to fail the very first time it is performed. Restart the analysis a second time.
56. The GTC browser and Toronto/UCSC browsers have a difference in one vs. zero based coordinates.
57. The shading used for denoting the centromeric and acrocentric regions in the cytobands are not exported to a PDF file.
58. Older versions of GTC are allowed to install over newer versions. For example, 2.1 will install over 4.0.