Axiom[™] Batch SSP Tool

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Introduction

The Axiom Batch SSP Tool (BatchSSP) is a standalone software tool used for generating SNP Specific Priors (SSPs) for Axiom AgBio and Human arrays. The tool generates SSPs for biallelic probesets for analysis in Axiom Analysis Suite (AxAS) software.

Use and purpose SNP-specific priors can help improve genotyping results with both accuracy and consistency. During genotyping, prior models for a probeset help inform the genotyping algorithm as to the expected position and size of clusters for that probeset. These models can be generic, or they can be specific for a given probeset (SNP-specific). These prior models in conjunction with the positions and sizes of the clusters from the samples in the dataset create the final models of cluster positions and sizes for the probeset (posteriors).

Priors

The genotyping algorithm uses pre-positioned genotype cluster locations (priors) to calculate the three cluster positions for the sample data, as shown in Figure 1.





Generic priors

Generic priors (developed by Thermo Fisher) work with any probeset, yet are not based on previous data. SNP-specific priors are created from genotyping samples across a batch or multiple batches. These samples in the dataset utilize the algorithm as to what the expected cluster positions and size of clusters for a given probeset will be, as shown in Figure 2. For more information see, the **Axiom Genotyping Data Analysis Solutions Guide**.



System and software requirements

System and software Requirement	
Processor	2.83 GHz (or higher) Pentium Dual Core Processor
Operating System	Windows 7 (64 bit) or 10 (64 bit) Professional with Service Pack 1
Installed software	Axiom Analysis Suite v5.1.1 (or higher)

Sample requirements

The minimum sample size for creating priors is a batch of 96 samples, though it is preferred to use at least 384 samples. The samples should have passed plate QC (average call rate for passing samples \geq 98.5 and percent of passing samples \geq 95). There should be a minimum of 40 male and 40 female samples.

Priors can be made for human and for other species. They can also be made using blood, buccal, saliva or other sample types. If sample types are routinely processed separately, then priors should be designed separately for each type, using at least the stated minimum number of samples required.

Installing the tool

IMPORTANT! Axiom Analysis Suite v5.1.1 (or higher) must be installed BEFORE installing the Axiom Batch SSP Tool.

- 1. Unzip the **Axiom Batch SSP Tool** package file, then double-click on **AxiomBatchSSPSetup**.
- 2. Follow the prompts to install the tool.

Launching the tool

From AxAS

- 1. Launch the AxAS software.
- 2. Open a batch with a Best Practices Workflow.
- 3. Click on the External Tools tab, then click the Axiom Batch SSP Tool button. (Figure 3)

Figure 3	External Tools tab		
applied biosystem	s		
Summary	Sample Table ProbeSet Summary Table External Tools		
Extern	al Tools		
The tools listed below are designed to further analyze the genotype results. These tools may reaccess to the result file.			
Axiom Batch SSP Tool			
Long Format Export Tool			

All batch information is displayed in the Tool's main window after launching it from AxAS, as shown in Figure 5 on page 4.

Note: You cannot use the tool if the displayed batch is open in AxAS. If it is, you will be prompted to close it.

From the Start menu

 After installing the tool, click Start → All Programs → Thermo Fisher Scientific → Axiom Batch SSP Tool.

The tool opens with its fields blank, as shown in Figure 4.

Figure 4 Main window					
applied biosystems	Axiom Batch SSP Tool	? () – ¤ ×			
Select Batch Folder		Browse			
Array Name					
Library File Package					
Format		~			
V Input Options					
Export (Optional)					
		Change Name Generate			

Using the tool

If you launched the tool from the **Start** menu, do the following:

- 1. Click the Browse button.
 - A Select Batch Folder window appears.
- 2. Click to highlight a batch folder, then click **Select Folder**.

The main window populates. (Figure 5)

Figure 5 Main window - populated					
applied biosystems	Axiom Batch SSP Tool ①	(i)	-		×
Select Batch Folder	C:\Users\Public\Documents\AxiomAnalysisSuite\Output\Test		Bro	wse	
Array Name	Axiom_PMDA				
Library File Package	Axiom_PMDA.r7				
Format Human				~	
Input Options					
Export (Optional)					
C:\Users\Public\Docume	ents\AxiomAnalysisSuite\Axiom_PMDA.r7\Axiom_PMDA.r7.20210127.models	ame	Ge	nerate	•

Select batch folder This pane (Figure 6) displays the following information: pane

Figure 6 Select batch folder pane				
Select Batch Folder	C:\Users\Public\Documents\AxiomAnalysisSuite\Output\Test	Browse		
Array Name	Axiom_PMDA			
Library File Package	Axiom_PMDA.r7			
	Figure 6 Sele Select Batch Folder Array Name Library File Package	Figure 6 Select batch folder pane Select Batch Folder C:\Users\Public\Documents\AxiomAnalysisSuite\Output\Test Array Name Axiom_PMDA Library File Package Axiom_PMDA.r7		

- Select Batch Folder: Displays the path of the batch folder you have loaded into the tool. Note: The tool requires a Best Practices Workflow batch, because it utilizes this workflow's output files; Ps.performance.txt and AxiomGT1.snp-posteriors.txt.
- Array Name: The Array Name is displayed here. This field auto-populates after selecting the AxAS batch folder.
- Library File Package: This field is auto-populated with the library package that was used to create your selected AxAS batch.

Format pane

Format is automatically assigned, as it is specific to the array type.

Figure 7 Format pane				
Format	Human	~		

The tool's two default formats are **Human** and **AgBio**. Use the Human format for all human arrays. Use the AgBio format for non-human arrays.

1. Click the Format drop-down button to select a different format (if available).

Input files and threshold pane

The Input Files and Thresholds pane (Figure 8) enables you to use a Probeset ID and/or a Priors file. Thresholds can also be edited here. **Note:** The default Input Threshold values are based on the format.

Figure 8 Input Files pane					
 Input Files (Optional) 		Thresholds			
Probeset ID File:	🗙	Name	Setti	ngs	
		Probesets	Rec	ommended v	5
Priors File:	🔨	Recommended Conversion Types	Chec	klist PolyHighReso	5
		Max nObsMean	=	20.0	5
		Min nObsMean	=	0.2	5
		Min nObsVar	=	1.0	5
		Max nObsVar	=	20.0	5
		Do not include low frequency het probesets			5

Probeset ID File

This is a single column text file with a **probeset_id** header followed by a list of probesets. (Figure 9) The tool uses these probesets to create SSPs.

Figure 9 Example: probeset_id file	
File Edit Format	Vie
probeset_id	
AFFX-SP-000061	
AFFX-SP-000062	
AFFX-SP-000068	
AY_100003653	

Note: This option restricts prior file generation to only the probesets in your selected file. It also disables the **Recommended Conversion Type** (in Thresholds).

If Probesets is set to **Recommended**, then priors will only be generated for probesets with recommended conversion types in the input batch.

Adding a probeset_id file

1. Click the ____ button.

A Select PID File window appears.

2. Navigate to the file, click to highlight it, then click **Open**.

The file is added to the tool.

Priors File

When used, the tool will not generate SSPs using the probesets listed in your selected file. Instead, the priors in your selected Priors File will stay intact and be used in the newly generated priors file.

Note: Your Priors File must be in the biallelic models file format, as shown in Figure 10.

Figure 10 Biallelic models file format example

Priors_Keep.txt - N	tepad		
File Edit Format	View Help		
id BB	AB AA CV		
AFFX-SP-000021	-2.521825,0.037621,20,20,10.548,0.042822,0.007888	-0.293937,0.037621,20,20,10.876508,0.042822,-0.003845	2.273032,0.037621,20,20,10.277561,0.042822
AFFX-SP-000063	-3.168612,0.069705,20,20,10.267238,0.078863,0.003533	0.319048,0.069705,20,20,10.834818,0.078863,0.021787	3.485702,0.069705,20,20,10.357796,0.078863
AFFX-SP-000078	-1.427792,0.037103,20,20,9.734716,0.031398,0.009255	0.445554,0.037103,20,20,10.101529,0.031398,-0.005445	2.32222,0.037103,20,20,9.687257,0.031398,-
AX-100003506	-1.057106,0.031194,20,20,9.841413,0.02592,0.004096	0.433889,0.031194,20,20,10.097299,0.02592,-0.000138	1.827189,0.031194,20,20,9.824717,0.02592,0
AX-100007695	-1.282766,0.031715,20,20,10.207366,0.034261,0.011717	0.717234,0.031715,1,10,10.923661,0.034261,0 2.717234	4,0.031715,1,1,10.334598,0.034261,0 -0
AX-100007701	-2.040798,0.023502,20,20,10.84174,0.027887,-0.011043	-0.266042,0.023502,20,20,10.865474,0.027887,-0.003072	1.610982,0.023502,20,20,10.581757,0.027887
AX-100007708	-1.398571,0.057146,20,20,8.961933,0.070155,0.020962	0.200134,0.057146,20,20,9.250923,0.070155,0.007166	2.53949,0.057146,3.2,4,9.173852,0.070155,-
AX-105110513	-2.562568,0.08997,20,20,10.009466,0.066968,0.005464	0.145741,0.08997,1,10,10.509466,0.066968,0 2.145741	.0.08997,1,1,10.009466,0.066968,0 -0
AY-1051105/13	-1 881716 A A53867 DA DA Q 136871 A A1Q671 A AD315Q	1 257416 @ 053867 2 300237 12 000237 10 024402 @ 040674	_A AA7138 3 257/16 A A53867 A 2 1 Q

Adding a priors file

1. Click the ____ button.

A Select Priors File window appears.

2. Navigate to the file, click to highlight it, then click Open.

The file is added to the tool.

Thresholds

Use the drop-downs, text fields, and check box to change settings and values, as shown in Figure 11.

Figure 11 Thresholds pane					
Thresholds					
Name	Settir	igs			
Probesets	Reco	ommended ~	5		
Recommended Conversion Types	Chec	klist PolyHighReso	5		
Max nObsMean	=	20.0	5		
Min nObsMean	=	0.2	\$		
Min nObsVar		1.0	\$		
Max nObsVar	=	20.0	\$		
Do not include low frequency het probesets			5		

- 1. [Probesets] Click the Recommended drop-down button to change the setting to "All".
- 2. [Recommended Conversion Types] To change the conversion types, click Checklist .

A Recommended Conversion Types window appears. (Figure 12) **Note:** This window is not available if a Probeset ID file has been added to the tool.

(Figure 12 Recommended Conversion Types window				
F	Recommended Conversion Types	*			
	✓ PolyHighResolution				
	☑ NoMinorHom				
	Ο ΟΤΥ				
	MonoHighResolution				
	CallRateBelowThreshold				
	UnexpectedGenotypeFreq				
	Other				
	OK Cancel				

- 3. Click to check or uncheck the appropriate check boxes, then click OK.
- 4. [Max and Min Settings] Use the text field to enter a different weight value.

IMPORTANT! Maximum and minimum weight values should only be changed under the guidance of your Field Support Specialist.

Click **n** to return a changed value back to its factory default.

- [Max nObsMean] The maximum weight allowed for the nObsMean value in the generated priors file.
- [Min nObsMean] The minimum weight allowed for the nObsMean value in the generated priors file.
- [Min nObsVar] The minimum weight allowed for the nObsVar value in the generated priors file.
- [Max nObsVar] The maximum weight allowed for the nObsVar value in the generated priors file.

Additional information about weights and threshold definitions

The nObsMean value is the number of observations for the position of a cluster. nObsVar is the number of observations for the size of a cluster. These are termed weights. Posterior weights are the addition of prior weights and the number of samples in the data. Generic priors have very low weights, allowing clusters to shift and scale with the data. Since SNP-specific priors are generated from a previous run, cluster information is informed by the samples in that previous dataset. Thus, the recommendation is that the weight that was observed in the dataset for a well performing probeset should be kept intact up to a maximum of 20. This cap prevents the priors from having too much influence on the position and size of the clusters in future genotyping runs. In general, the minimum value of weights is set to be equivalent to the generic weights unless the priors are for an agbio array. In these situations, the recommended minimum nObsMean is set to 5. A higher weight on the position of a cluster in the prior helps stabilize the position of the cluster during future genotyping runs, which helps ensure more consistent genotyping.

Threshold	Definition
Format	Default format is based on the batch imported into the tool. Human for human batches with more than 24 samples, and AgBio for all non-human batches. Each format has default values for weights, as listed in Thresholds.
Recommended probesets	Priors will be generated for probesets that are assigned to Recommended conversion types.
Recommended Conversion Types	Prior generation is limited to probesets in selected categories. The categories selected by default are based on the threshold settings that were used in the Axiom Analysis Suite Best Practices Workflow batch.
nObsMean	The number of observations for the position of a cluster in the data.
Max nObsMean	The maximum weight allowed for the nObsMean value in the generated priors file.
Min nObsMean	The minimum weight allowed for the nObsMean value in the generated priors file.
nObsVar	The number of observations for the variation (or size) of the cluster in the data.
Min NoObsVar	The minimum weight allowed for the nObsVar value in the generated priors file.
Max NoObsVar	The maximum weight allowed for the nObsVar value in the generated priors file.
Do not include low frequency het probesets (check box)	When checked, priors will not be assigned to probesets with low het frequency in the Input batch (detection of one to two hets).

5. **[Do not include low frequency het probesets]** If this check box is checked, priors will not be generated for any low frequency probesets you may have uploaded into the tool.

Export options The Best Probeset file resides in your batch folder. Use the **Export** pane (Figure 13) to add it to your export.

- 1. Click the **Export** \bigcirc button.
- 2. Click to check the **Best Probeset File** check box.

Figure 13	Export pane	
Export (Optional)		
Best Prob	eset File	

Priors filename

By default, the priors filename is auto-generated using the array name, date, and models located in the Array package, as shown in Figure 14.

Figure 14 Priors filename pane				
C:\Users\Public\Documents\AxiomAnalysisSuite\Axiom_PMDA.r7\Axiom_PMDA.r7.20210126.models	Change Name Generate			

Changing the filename

1. If you want to change the auto-generated filename, click the Change Name button. A dialog box appears. (Figure 15)

Figure 15 Dialog box				
Output File	Name	×		
Output File Name				
	OK	Cancel		

2. Enter a name, then click OK.

Your new filename is displayed.

Generating your output file 1. Click the Generate button.

A Please Wait window appears. After the priors are successfully generated, the word **Complete** appears in the lower left corner.

Loading a new priors file into AxAS

- 1. Launch the AxAS software.
- 2. Click on the New Analysis tab. (Figure 16)

Note: The array name is displayed in the Array Type field.

Figure 16 AxAS New Analysis tab		
appliedbiosystems		
New Analysis Dashboard Preferences		
Array Type: Axiom_PMDA.r7 ~		
CEL Files: 7		
File Name		
HG00111_mPCR121_Plt3_PMDA_3hrpcp_A01		
HG00126_mPCR121_Plt3_PMDA_3hrpcp_B01		
HG00138_mPCR121_Plt3_PMDA_3hrpcp_C01		
HG00174_mPCR121_Plt3_PMDA_3hrpcp_D01		
HG00243_mPCR121_Plt3_PMDA_3hrpcp_E01		
HG00260_mPCR121_Plt3_PMDA_3hrpcp_F01		

- 3. Click the **Workflow** drop-down to select the workflow you want to use.
- 4. From the Analysis Settings pane (Figure 17), click the **Sample QC** button to reveal the Sample QC file options.

Figure 17 AxAS Analysis Settings pane			
Analysis Settings			
Select Analysis Configurations			
Axiom_PMRA_96orMore.r3 (Default) V Restore Save As			
🔗 General Analysis			
Inbred File Value (optional):			
Use value for all samples 0			
Hints File (optional):			
Gender File (optional):			
Sample OC			
Aviom PMRA 96orMore Sten1 r3 ant-genotype-aviom AviomGT1 ant2			
Prior Model File			
Axiom PMRA.r3.generic prior			
SNP List File (recommended):			
Axiom_PMRA.r3.step1 🗙			
Axiom_PMRA_96orMore_rvc_Step2.r3.apt-genotype-axiom.AxiomGT1.apt2			
Prior Model File:			
SNP List File (recommended):			
Axiom_PMRA.r3.step2			
Posterior File Name (optional):			
···· 🗙			
ps2snp File (recommended):			
Axiom_PMRA.r3.ps2snp_map			

- 5. Confirm the Generic Priors file is displayed in the Prior Model File field.
- 6. Click the **Genotyping** 🕑 button to reveal the Genotyping file options.
- 7. Click the **Prior Model File** button.

The Prior Model File window appears.

8. Click to highlight the newly generated priors file, then click Open.

The new priors model file is displayed.

9. Click the Analysis Setting pane's Save As button.

An Explorer window appears.

10. Enter a name, then click OK.

The Analysis Configuration drop-down menu now contains your saved name.

11. Enter a name for your analysis, then click **Run**.

After your analysis has successfully completed, it will reside in the Dashboard tab window where it can be opened for viewing.

IMPORTANT! For more feature and workflow information, see the **Axiom Analysis Suite User Guide** and the **Axiom Data Analysis Solution Guide**.



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Revision	Date	Description
1	February 2021	Initial release

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