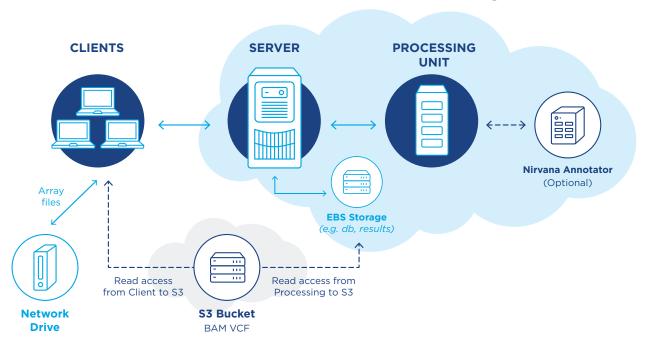


N_xClinical Architecture - AWS

The N_x Clinical system is designed as a truly scalable system that is easy to deploy and maintain by labs of any size, from a single user to a large enterprise. The key to this scalability is the modular design of the system. The core system is composed of three components: Clients, Server, and Processing Unit. Depending on the types of samples processed in N_x Clinical, additional utility software may need to be installed (see below).

N_xClinical on AWS EC2 with storage on EBS





CLIENTS

The Client software is the Graphical User Interface (GUI) utilized by all users to access N_x Clinical. The Client software is installed on multiple computers, allowing multiple users to access N_x Clinical at the same time from within an institution's network as well as remotely. After the initial installation, the system will be able to automatically update the client when the system administrator updates the software. This avoids manually updating each client.



SERVER

The server is the heart of the system; it manages the data in the repository as well as all the resources. (e.g. tracks, users, configurations, etc.). The database storage component of the N_x Clinical server is placed in the EBS Storage with some exceptions for "raw" NGS data (see NGS section). The server component is installed on Amazon AWS EC2 and all clients communicate with the server through a secure http connection. The server should be up and running all the time to service incoming requests from the clients and include a back-up policy to back up the content of the repository on regular basis.





PROCESSING SERVER(S)

The processing server is used to convert raw sample datapoints into variants. It will be hosted on the same EC2 instance. For large scale deployments, the system can utilize multiple Processing Servers in cases where there is demand for processing many samples simultaneously. The Processing Server communicates with the server via a secure protocol. The N_xClinical Admin can specify different processing servers for different types of samples for efficient processing; smaller files (e.g. panels/arrays) can be run on a less powerful processing server while WGS samples can be assigned to a much more powerful processing server. This unit does not require backups

N_xClinical Data File Types

MICROARRAYS

All data including raw array data is stored on the server. Hardware requirements vary based on the type and size of data being processed and managed.

NGS

 N_x Clinical can store and process different types of NGS data. BAM files are processed to derive copy number and BAF. They are also used to process and display read depth and individual reads in the genome browser. VCF files are used for sequence variants.

Processed data from VCF and BAM files is stored in the repository, but the original files are not copied to the server and are kept in their original location. The server keeps track of where these files are located by storing the file path to the files and updating this if the files move. In the case of an AWS setup, these files should be stored in a S3 bucket which is accessible to the EC2 instance running the Processing unit and to the clients on-prem.

NGS data comes in many flavors (VCF files, BAM files from targeted panels, BAM from WES, BAM from WGS) and the size of these files varies. Hardware requirements vary based on the type and size of data being processed and managed. For example, if you are processing deep WGS data, you will need more RAM and faster processing.



N_xClinical Additional Utility Software

NIRVANA ANNOTATOR

 N_x Clinical uses the Illumina Nirvana annotation tool to annotate VCF files in a single seamless workflow beginning with loading of files into N_x Clinical. The Nirvana tool is installed separately from the N_x Clinical system. It is recommended that Nirvana be installed on the same machine as the Processing Server. The installation files are rather large and require at least 60GB of space (including supplementary databases).

BAM MULTISCALE REFERENCE BUILDER

The BAM MultiScale Reference Builder is a separately installed application that is used to generate reference files to be used with the NxClinical software when processing BAM files to derive copy number from NGS platforms. Building a reference file with this utility may only need to be done once if the same reference file will be used for all the experimental NGS samples. This utility should be installed on a user machine that has access to BAM files. Hardware requirements vary based on the size of BAM files that will be used for creating the reference file. For a small NGS panel, 8GB RAM is minimum, but more RAM (up to 32GB) will be needed for deep WGS. The required space for this utility is 6GB.

N_xCLINICAL SAMPLE IMPORTER

The N_x Clinical Sample Importer is an optional command line utility that streamlines and automates sample loading and processing for NxClinical software. It requires as input the sample descriptor file that specifies samples, location, and processing settings. The installation space required for this utility is ~500MB in size.

See hardware recommendation on the next page.



Hardware Recommendation

Below are minimum hardware recommendations. You will need to adjust the RAM and CPU based on your expected volume and type of data being processed and will need to expand disk space as your database grows.

	CLIENT
OPERATING SYSTEMS	64bit Windows Mac OS X (Java 1.8)
RAM	8GB recommended (minimum 4GB) solely for Client application
DISK SPACE	500MB

	AWS SERVER AND PROCESSING UNIT NIRVANA (OPTIONAL)
OPERATING SYSTEMS	CentOS 7 or 8 (Java 1.8)
PLATFORM	EC2 type m4.xlarge (Includes RAM 16GB, Quad core)
EBS STORAGE	Primary: N _x Clinical database storage. Size varies, recommended 100GB minimum Secondary: 500GB depending on throughput & sample data size
ADDITIONAL STORAGE	S3

File sizes can vary widely but here are some examples to help with estimating the amount of disk space you may need: N_x Clinical database storage — 10-170MB per sample, S3 Bucket — Low-pass BAM file: 100MB, Targeted Panel BAM file: 2GB, WES BAM file: 5GB, 30x WGS BAM file: 30GB

REQUEST ADDITIONAL SUPPORT