N$_x$Clinical™ System Requirement
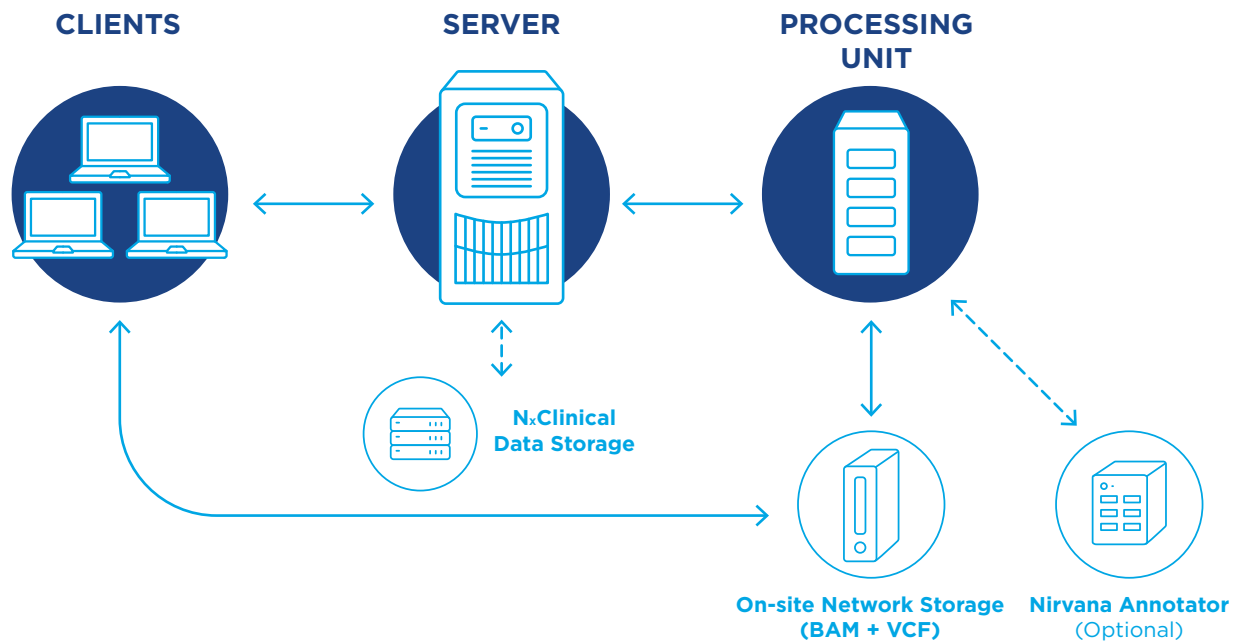
N$_x$Clinical Architecture

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).

CLIENTS   **SERVER**   **PROCESSING UNIT**

N$_x$Clinical Data Storage

On-site Network Storage (BAM + VCF)   **Nirvana Annotator** (Optional)

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 the 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.). All data is stored on the server with some exceptions for "raw" NGS data (see NGS section). The database storage component of the N$_x$Clinical server can be in the same directory as the server installation directory or hosted on a mounted drive. The server component can be installed on a physical server on premises or on a cloud (e.g. Amazon AWS) 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 bases.

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PROCESSING SERVER(S)

The processing server is used to convert raw sample datapoints into variants. It can be hosted on the same machine as the Server, depending on the number and size of samples being processed (recommendation: separate servers). 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$_x$Clinical 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$_x$Clinical 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 on-site network storage 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. It is recommended to store these files on the same network as the server for best performance. If the files are located on a different network, then performance could be impacted greatly. As NGS data can be quite large and take up a lot of space, the use of external drives connected to the server is a good solution for storage of these files.

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.

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N$_x$Clinical 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$_x$CLINICAL 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.

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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.

	OPERATING SYSTEMS	RAM	CPU	DISK SPACE
Client	64bit Windows, Mac OS X (Java 1.8)	8GB recommended (minimum 4GB) solely for Client application		500MB
Processing Unit	64bit Windows; Ubuntu LTS, CentOS 7 or 8 (Java 1.8)	8GB (16GB if using WGS) recommended (4GB minimum) solely for Processing Server *Higher amount of RAM and disk space might be needed depending on throughput and data types.*	Dual core	500MB
Server	64bit Windows; Ubuntu LTS, CentOS 7 or 8 (Java 1.8)	32GB recommended (16GB minimum) *Higher amount of RAM and disk space might be needed depending on throughput and data types.*	Quad core	Varies (recommended 500Gb minimum)
Nirvana (optional)	64bit Windows; CentOS 7 or 8 *Needs to be installed on same machine as Processing*	32GB recommended (16GB minimum) *Higher amount of RAM and disk space might be needed depending on throughput and data types.*	CPU with AVX support. AVX was introduced on Intel with the Sandy Bridge architecture, so Xeons after around 2011 should support it. If using VMWare and if VMWare vMotion is at EVC level L3 (Westmere) or below, increase to at least L4 (Sandybridge).	60GB minimum
BAM MultiScale Reference Builder (optional)	64bit Windows, Mac OS X, Ubuntu LTS, CentOS 7 or 8 (Java 1.8)	16GB (32GB if using WGS) recommended (8GB minimum)		6 GB
NₓClinical Sample Importer (optional)	64bit Windows; Ubuntu LTS, CentOS 7 or 8			500MB

*File sizes can vary widely. Use the following to estimate the amount of disk space needed: 10-170MB per sample, for NₓClinical database storage.

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