




GenoCAD
 Introduction


GenoCAD
 Virginia Tech
 Virginia Bioinformatics Institute

Computer-Assisted Design Software
 for Synthetic Biology


 National Science Foundation
 WHERE DISCOVERIES BEGIN

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www.openhelix.com/genocad

Version 1

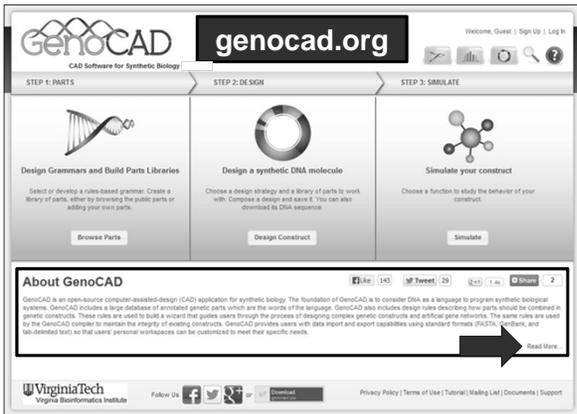



GenoCAD Introduction Agenda

- Introduction and Credits
- Register and Log In
- Step 1: Parts
 - Parts
 - Grammar
 - Import the Training Set
- Step 2: Design
- Step 3: Simulate
- Summary
- Exercises

GenoCAD: <http://www.genocad.org/>


Introduction to GenoCAD



The screenshot shows the GenoCAD website interface. At the top, it says "GenoCAD" and "genocad.org". Below that, there are three main steps:

- STEP 1: PARTS**: Design Grammars and Build Parts Libraries. Select or develop a rules-based grammar. Create a library of parts, either by browsing the public parts or adding your own parts. Button: Browse Parts.
- STEP 2: DESIGN**: Design a synthetic DNA molecule. Choose a design strategy and a library of parts to work with. Complete a design and save it. You can also download its DNA sequence. Button: Design Construct.
- STEP 3: SIMULATE**: Simulate your construct. Choose a function to study the behavior of your construct. Button: Simulate.

Below the steps is an "About GenoCAD" section with a "Read More" link. At the bottom, there are social media links for Virginia Tech and the Virginia Bioinformatics Institute.

- Computer-assisted design software for synthetic biology
- Visit GenoCAD.org

Support for GenoCAD

What is GenoCAD™?
GenoCAD is an open-source computer-assisted-design (CAD) application for synthetic biology. The foundation of GenoCAD is to consider DNA as a language to program synthetic systems. GenoCAD includes a large database of annotated genetic parts which are the words of the language. GenoCAD also includes design rules describing how parts should be combined. These rules are used to build a scaffold that guides users through the process of designing complex genetic constructs and artificial gene networks. The same GenoCAD compiler to maintain the integrity of existing constructs. GenoCAD provides users with data import and export capabilities using standard formats (FASTA, GenBank, etc.) so that users' personal workspaces can be customized to meet their specific needs.

Getting started
Step by step tutorial Documents
Technical support, Support

Who develops GenoCAD?
GenoCAD is developed by the Peccoud Lab at Virginia Bioinformatics Institute. Up-to-date information about GenoCAD is available on www.peccoud.org. This material is based upon work supported by the National Science Foundation Grant IRI-0550100. Any opinions, findings, and conclusions or recommendations expressed in this material are those of the author(s) and do not necessarily reflect the views of the National Science Foundation.

GenoCAD Source Code
GenoCAD is distributed open source using the Apache Version 2.0 License. This license has been approved by the Open Source Initiative. The GenoCAD source code is hosted on SourceForge <http://sourceforge.net/projects/genocad/>.

VirginiaTech
Virginia Bioinformatics Institute

nsf.gov

- Peccoud team
- NSF support

Process Flow

- Parts and grammars, public or custom collections
- Design constructs
- Simulate processes

Conceptual Framework for GenoCAD

Grammar rules are made of Parts of Speech

Sentence

Subject Verb

NounPhrase

Rules make the framework, words make the sentence

The patient system adds the fuel of interest to the fire of genius

Intellectual property has the sheep life of a baroness

—Abraham Lincoln

—Bill Gates

GenoCAD uses a similar set of rules to develop biological constructs.

New Design

History

PRO RBS CDS TER

- Aspects of DNA function explained with language metaphors: transcription, translation, code
- GenoCAD lets you develop language for programming cells

Data Model, Concepts

Promoters Coding Seqs Terminators

Rule Category Category Category Category

Grammar

Promoter A Coding Seq A

Public Library Personal Library

Promoter B Coding Seq B Your constructs

peccoud.vbi.vt.edu/publications
2007: 10.1093/bioinformatics/btm446
2009: 10.1371/journal.pcbi.1000529

- Parts form the foundation, stored in project libraries
- Grammar rules specify the way the parts work in series
- Parts + Grammars give you synthetic construct designs

Further Reading

A synthetic model to design and verify synthetic genetic constructs derived from standard biological parts
 doi: 10.1093/bioinformatics/btm446

Modeling Structure-Function Relationships in Synthetic DNA Sequences using Attribute Grammars
 doi: 10.1371/journal.pcbi.1000529

Writing DNA with GenoCAD™
 doi: 10.1093/nar/gkp361

Genetic design automation: engineering fantasy or scientific renewal?
 doi: 10.1016/j.tibtech.2011.09.001

Publications: theoretical, software, ongoing development
 Cite GenoCAD if you use the tools

Getting Assistance

Help: context-sensitive help from ? Button
 Support link for asking questions or offering feedback
 Social media

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Register at GenoCAD

- Not required, but very handy
- Your preferences, parts and creations will be saved

Password Recovery or Reset



- If needed in the future, you can reset password easily

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Step 1: Parts



- Step 1: Exploring parts libraries and grammars
- Public parts and libraries samples are pre-loaded
- You will add other sources and your own project libraries
- Access to the pieces you need for subsequent steps

Parts and Parts Libraries



- Libraries will store the parts
- Public libraries are not editable by users
- Later we'll create and edit custom project libraries

Libraries contain Categories with Parts

Selected items will be displayed with relevant details
Choose: Promoter (PRO)

- Folder contains parts associated with a grammar

Examine a Part Category: Promoter

Parts list
PartID is unique

- A category may have multiple part items

Part Detail Features

Unique PartID
Name
sequence
Description

Only ATGC
(limit: ~16 million bases)

Parts can be shared across libraries

These are the features that can be located with the "search" tool later.

- Part Detail includes important features and sequence

Search for Items

search

- Locate specific parts quickly with a search

Basic Search and My Cart

The screenshot shows the GenocAD interface with a search bar and a 'My Cart' section. A search for 'all_promoters' is shown with results. Annotations highlight the search process: 'Advanced' search type, saving the search, and choosing a specific category from the results.

- Search the parts fields to locate specific items quickly
- Use * as a wildcard

Parts need Grammars

The diagram shows a 'Grammar' structure where each rule is composed of a 'Category' and a 'Part'. Below this, 'Public Library' and 'Personal Library' are shown containing various 'Part' elements. Arrows indicate that parts from these libraries are used within the grammar rules.

- Parts form the foundation, the building blocks you need
- Grammar rules specify the way the parts work in series

Grammars for Parts

The diagram illustrates how grammar rules are constructed from parts of speech. A 'Sentence' is defined as 'Subject + Verb + Object'. Specific rules are listed: R1: Sentence → Subject + Verb + Object; R2: Subject → NounPhrase; R3: Object → NounPhrase; R4: NounPhrase → NounPhrase + Modifier; R5: Modifier → PrepositionalPhrase.

- Parts form the foundation, the building blocks you need
- Grammar rules specify the way the parts work in series

Grammars

The screenshot shows the 'Grammar Summary' page in GenocAD. A list of grammars is displayed, and an annotation 'choose' points to one of the entries in the list.

- Grammars establish the design strategy
- Subject-Verb-Object
- Promoter-Cistron-Terminator

Public Grammars

Public Grammars

Grammar Summary

Name: Basic Grammar - No Simulation

Description: 1, 2 or 3 cassette(s), each with a promoter, a ribosome binding site, a coding sequence and a terminator.

Icon Set: sbol_v1_0_kon_set

Supports Attributes?: No

Categories: 12

Libraries: 1

Parts: 155

Rules: 4

Manage Grammar

- Basic Grammar—No Simulation for this example
- Characteristics of this grammar
- “Manage Grammar” for more details (advanced tutorial)

Obtain the Training Set

Obtain the Training Set

Training_Set...Parts.genocad

click

save

<http://dx.doi.org/10.6084/m9.figshare.153827>

- www.figshare.com
- Download the GenoCAD Tutorial I “Training Set”
- Click Add/Import Grammar

Upload the Training Set

Upload the Training Set

Import Grammar

You are about to import the following grammar:

Grammar Name: Training Set E. Coli Grammar

Description: This is a generic grammar for gene expression cassettes

Categories: 14

Rules: 9

Icon Set: sbol_v1_0_kon_set (EXISTING)

Choose an Option: USE EXISTING - Use the existing Icon Set. CREATE NEW - Create a new Icon Set and link it to this grammar.

Continue Import Cancel Import

Use existing

- Upload the zipped file that came from FigShare

Imported Training Set is available

Imported Training Set is available

Click Parts

An editable Grammar is now available

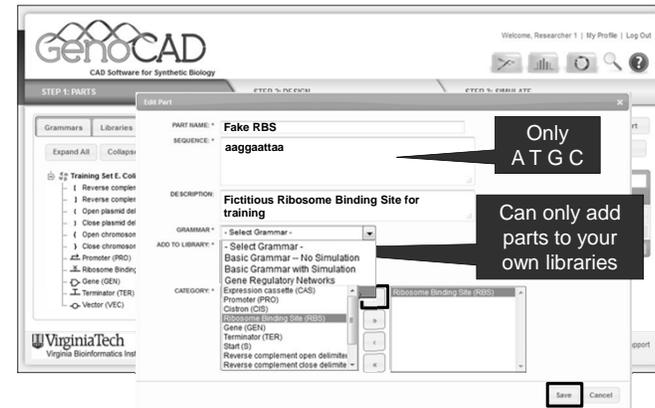
Will be used for further work

Training Set is Integrated



- The training set grammar, library, and parts are available
- Editable, so you can change or add new
- Let's add a new part as an example

Create a Custom Part



- Good strategy: create a library for each project
- Put relevant parts in that project library

User Grammar, Library, Part Created



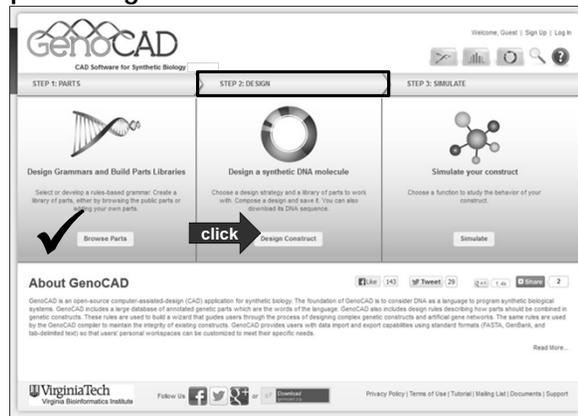
- Your custom items will be stored, now available to use
- Import parts to use and export parts for sharing or backups

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Step 2: Design Constructs



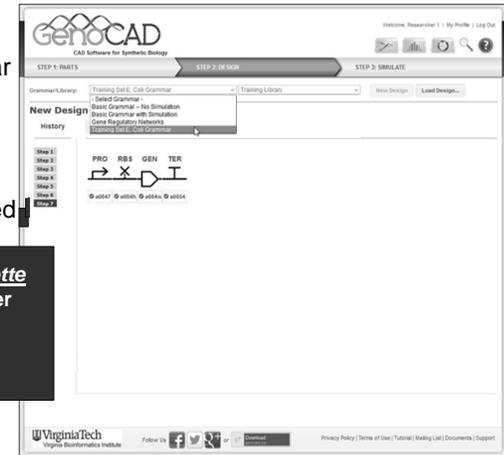
- Public and user parts, libraries, grammars in place
- Use them to create a construct with “Design” options

Design Constructs

- Choose grammar
- Choose library
- Begin to design
- Choices are listed

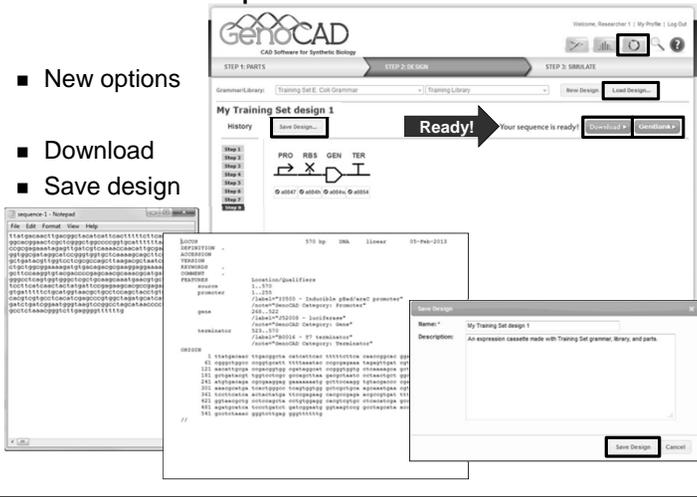
Build a simple cassette

- Inducible promoter
- RBS A
- Luciferase
- T7 terminator



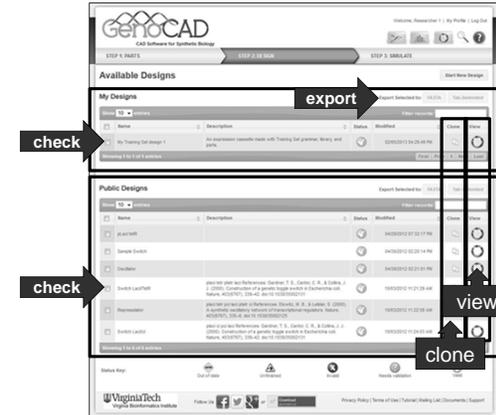
Construct is Complete

- New options
- Download
- Save design

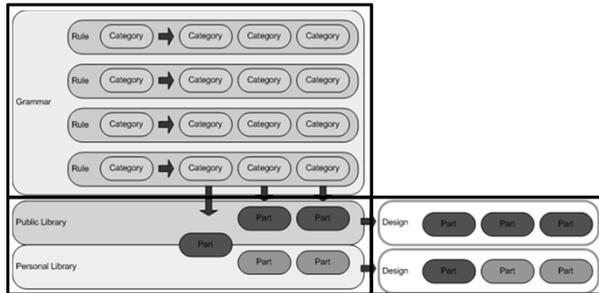


Browse for Constructs

- “Load Design” or “Available Designs” folder to see the list
- Yours + public designs are shown



Data Model



- Parts and Libraries
- Grammar and Rules
- Design your constructs

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Step 3: Simulate

The screenshot shows the GenoCAD web interface. The top navigation bar includes 'STEP 1: PARTS', 'STEP 2: DESIGN', and 'STEP 3: SIMULATE'. The main content area is divided into three columns: 'Design Grammars and Build Parts Libraries', 'Design a synthetic DNA molecule', and 'Simulate your construct'. The 'Simulate your construct' column is active, showing a 'Simulate' button. Below the main content, there is a news article titled 'A Whole-Cell Computational Model Predicts Phenotype from Genotype' with a DOI of 10.1016/j.cell.2012.05.044. A 'click' arrow points to the 'Simulate' button. At the bottom, there is a 'Status' arrow pointing to the 'Simulate' button.

- Step 3: Simulate

Constructs Ready for Simulation

The screenshot shows the COPASI and SBML web interfaces. The top part shows the COPASI interface with a 'Simulate' button and a 'COPASI' logo. Below it, there is a 'COPASI: biochemical network simulator' section with a 'www.copasi.org' link. The bottom part shows the SBML.org interface with a 'Click' arrow pointing to a 'Simulate' button and a 'www.sbml.org' link. A 'Status' arrow points to the 'Simulate' button.

- If you generate with attributes for simulation, they will be listed
- Public examples

Repressilator Example

- Design of the construct
- 3 cassettes in a network
- Parts + Grammar + Design carries key details

Simulation Sample

- Duration and interval are set
- Run Simulation to obtain the display

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GenoCAD Introduction Summary

- GenoCAD is a toolbox for synthetic biology
- Parts, grammars, designs, and simulations



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