

GenoCAD  
Advanced Topics

GenoCAD  
VirginiaTech  
Virginia Bioinformatics Institute

Computer-Assisted Design Software  
for Synthetic Biology

National Science Foundation  
WHERE DISCOVERIES BEGIN

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OpenHelix.

Version 1

GenoCAD Advanced Agenda

- Introduction and Review
- New Library with Advanced Searching
- Advanced Design
  - Copying and Reworking
  - Export GenBank format → other tools
- Grammar from Scratch
- Modifying (Editing) Grammar
- Summary
- Exercises

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

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Introduction to GenoCAD

genocad.org

STEP 1: PARTS    STEP 2: DESIGN    STEP 3: SIMULATE

Simulation Results

Introduction to:  
GenoCAD  
Sponsored Online Tutorial Suite

- Computer-assisted design software for synthetic biology

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## Register and Log In at GenoCAD

Completed first tutorial

Features we explore here require saving to your workspace

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## Conceptual Framework for GenoCAD

Grammar rules are made of Parts of Speech

Sentence

Subject Verb

Rules make the framework, words make the sentence

R1: Sentence → Subject + Verb + Object  
 R2: Subject → NounPhrase  
 R3: Object → NounPhrase  
 R4: NounPhrase → NounPhrase + Modifier  
 R5: Modifier → PrepositionalPhrase

The patient adds the fuel of interest to the fire of genius  
 ~Abraham Lincoln

Intellectual property has the shelf life of a banana  
 ~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 a language for DNA designs

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## New Project Library

Best practice: New Library for each project

Locate and reuse parts

Continue to use Training Set Grammar for now

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## Add New Library in Training Set

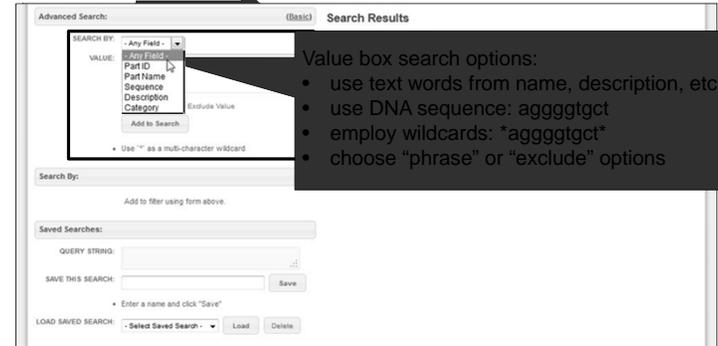


- In the Training Set, create a "new library"
- Name it "Fluors"

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## Search for Project Parts



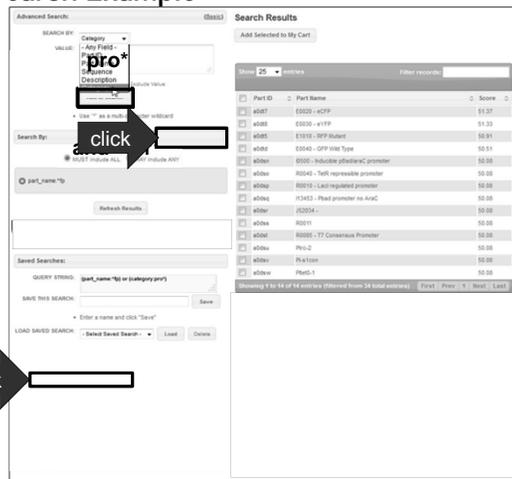
- Locate specific parts quickly with a search
- Advanced searches offer precision
- Build queries with multiple options

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## Advanced Search Example

- Set field to: *Part Name*
- Set value to: *\*fp*
- Set field to: *Category*
- Set value to: *pro\**
- Choose *MAY include*

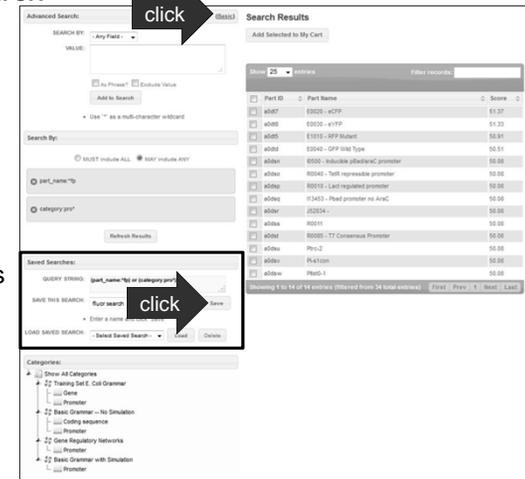


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## Save a Search

- Save searches that you might use often



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## Saved Searches and My Cart

Basic Search: (Advanced) There are now 5 parts in your Cart.

QUERY: (part\_name="Rb") or (category="pro") **click** Search Results

Search Parts

Saved Searches:

SAVE THIS SEARCH:  Save

LOAD SAVED SEARCH: fluors search Load Delete

Categories:

- Show All Categories
- Training Set E. Coli Grammar **click**
- Gene
- Promoter
- Basic Grammar - No Simulation
- Coding sequence
- Promoter
- Gene Regulatory Networks

Part ID	Part Name	Score
a0d7	E0020 - eCFP	57.19
a0d8	E0030 - eYFP	57.12
a0d5	E1010 - RFP Mutant	56.64
a0d4	E0040 - GFP Wild Type	56.17
a0dan	R0500 - Inducible pBad/lacZ promoter	55.8
a0dco	R0040 - TetR repressible promoter	55.8
a0dap	R0010 - LacI regulated promoter	55.8
a0dq	I13453 - Pbad promoter no AraC	55.8
a0dr	J52034 -	55.8
a0ds	R0011	55.8
a0dt	R0085 - T7 Consensus Promoter	55.8

- Load and run the saved search
- Highlight the "Training Set" category
- Then select the five parts shown
- Click to add to My Cart

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## My Cart

Welcome, Researcher | My Profile | Log Out

STEP 1: PARTS STEP 2: DESIGN STEP 3: SIMULATE

Grammars Libraries My Parts My Cart (5)

Expand All Collapse All Empty List

Training Set E. Coli Grammar **click**

Promoter (PRO)

Gene (GEN)

Remove Selected

Copy to Library Remove from My Cart After Copy? Export to: FASTA Unlimited

Fluors  Filter records:

Part ID	Part Name	Modified
a0d5	E1010 - RFP Mutant	07/25/2013
a0d7	E0020 - eCFP	07/25/2013
a0d8	E0030 - eYFP	07/25/2013
a0d4	E0040 - GFP Wild Type	07/25/2013
a0dan	R0500 - Inducible pBad/lacZ promoter	07/25/2013

Showing 1 to 5 of 5 entries First Prev 1 Next Last

- My Cart has my selections

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## Add More Parts

Advanced Search: Search Results

Build a query  
Part name: T7  
Category: RBS  
Join with "MAY Include"

Categories:

- Show All Categories
- Training Set E. Coli Grammar
- Gene
- Promoter
- Basic Grammar - No Simulation
- Coding sequence
- Promoter
- Gene Regulatory Networks
- Basic Grammar with Simulation
- Gene Regulatory Networks

click

- We need other parts from Training grammar
- Find T7 terminator, and an RBS
- Key point: parts need to be compatible with the grammar you intend to use
- Choose ones compatible with Training Grammar

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## Return to My Cart

STEP 1: PARTS STEP 2: DESIGN STEP 3: SIMULATE

Grammars Libraries My Parts My Cart (7)

Expand All Collapse All Empty List

Training Set E. Coli Grammar **click**

Promoter (PRO)

Gene (GEN)

Terminator (TER)

Fluors  New Library Remove Selected

Training Library  or Copy? Export to: FASTA Tab-Delimited

Fluors  Filter records:

Part Name	Modified	
a0d5	E1010 - RFP Mutant	07/25/2013
a0d7	E0020 - eCFP	07/25/2013
a0d8	E0030 - eYFP	07/25/2013
a0d4	E0040 - GFP Wild Type	07/25/2013
a0dan	R0500 - Inducible pBad/lacZ promoter	07/25/2013
a0d2	RBS F	07/25/2013
a0dk	R0016 - T7 terminator	07/25/2013

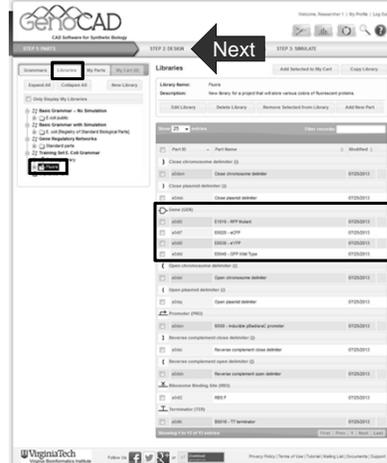
Showing 1 to 7 of 7 entries First Prev 1 Next Last

- Cart now has the items we need to design
- Select all, copy to Fluors library

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## Examine the Fluors Library

- Access the libraries tab
- Click the Fluors item
- All the parts are available
- Next let's design some color constructs



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## GenoCAD Advanced Agenda

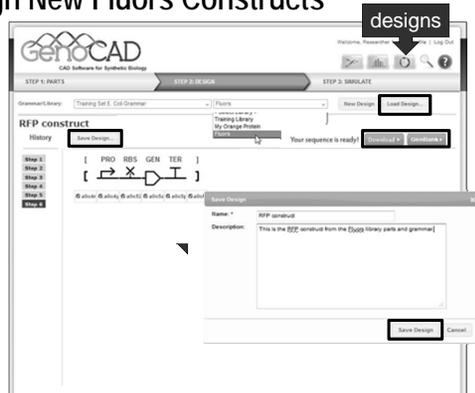
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## Design New Fluors Constructs

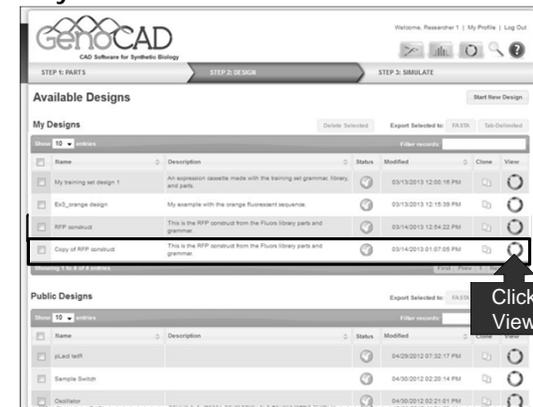


- Use the Training Set Grammar + Fluors Library
- This time let's reverse the orientation, use PCT-

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## Quickly Clone a Construct



- From Designs list you can quickly "clone" copies
- Click to "clone" the RFP construct

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## Work with a Cloned Design

The screenshot shows the GenoCAD web interface. At the top, there are navigation tabs for 'STEP 1: PARTS', 'STEP 2: DESIGN', and 'STEP 3: SIMULATE'. Below this, there's a 'YFP construct' section with a 'Save Design...' button. The main area is a 'My Designs' table with columns for Name, Description, Status, Modified, Clone, and View. The 'YFP construct' row is highlighted, and its 'View' button is circled in red. A red box labeled 'designs' points to the top right of the interface.

- You can quickly swap out pieces
- Generate similar constructs easily

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## Exporting GenBank Format

The screenshot shows the VectorEditor web tool interface. It features a 'Your sequence is ready!' message with a 'Download' button and a 'GenBank' button. A red box highlights the 'GenBank' button. A red box labeled 'bit.ly/GBtable' points to the 'GenBank' button. A red box labeled 'code.google.com/p/vectoreditor/' points to the 'Download' button. The interface also shows a 'Summary' section with 'Project Information' and 'Labels'.

- Categories may be mapped to GenBank features
- Can use this to visualize features in GenBank-compliant tools
- Illustrated with VectorEditor Demo web tool

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## Obtain YFP GenBank Format File

The screenshot shows the GenoCAD web interface. At the top, there are navigation tabs for 'STEP 1: PARTS', 'STEP 2: DESIGN', and 'STEP 3: SIMULATE'. Below this, there's an 'Available Designs' section with a 'Start New Design' button. The main area is a 'My Designs' table with columns for Name, Description, Status, Modified, Clone, and View. The 'YFP construct' row is highlighted, and its 'View' button is circled in red. A red box labeled 'Click View' points to the 'View' button.

- Obtain the YFP design from My Designs
- Click "View" to access GenBank output

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## Exporting with GenBank Features

- Select the GenBank button
- Obtain your text file
- Examine the Features area

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## Upload the YFP File

- Access VectorEditor <http://bit.ly/VectorEditor>
- Import the YFP construct file
- View the features

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## Grammar from Scratch

- Can create a new grammar to suit project needs
- Use them to create a construct with “Design” options

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## A Blank Grammar Template

Welcome, Researcher 1 | My Profile | Log Out

STEP 1: PARTS STEP 2: DESIGN STEP 3: SIMULATE

### Create New Grammar

Create a new grammar by completing and submitting the following form:

Name: \* test new grammar

Description: \*

Image Set: \* biobricks\_icon\_set

Preview **click**

biobricks\_icon\_set  
- select image set -  
biobricks\_icon\_set  
genoguard\_icon\_set  
mar\_icon\_set  
main\_icon\_set\_nograd  
abol\_icon\_set  
abol\_v1\_0\_icon\_set  
Ca\_grammar2007  
test\_vsv

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- Name and describe a grammar, choose an icon set
- Brand new grammar is created

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## Build a Grammar

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STEP 1: PARTS STEP 2: DESIGN STEP 3: SIMULATE

### Manage Grammar

Name: Researcher 1 new grammar

Description: creating a grammar from scratch

Starting Category: Start | Transcription Unit (S)

Icon Set: biobricks\_icon\_set

Categories: **Manage Categories**

Category Detail

Letter: \*

Description: \*

Genbank Qualifier: - Select Genbank Qualifier -

Icon: - Select Icon -

Save Cancel

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- The new grammar has only default categories
- Just add new categories and rules

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## Copy a Grammar

Welcome, Researcher 1 | My Profile | Log Out

STEP 1: PARTS STEP 2: DESIGN STEP 3: SIMULATE

Grammars Libraries My Parts My Cart (0) Grammar Summary **Manage Grammar**

Add / Import Grammar

Public Grammars

- Basic Grammar - No Simulation
- Basic Grammar with Simulation
- Gene Regulatory Networks
- User Grammars
- Training Set E. Coli Gram
- Researcher 1 new grammar

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Manage Grammar

Name: Basic Grammar -- No Simulation

Description: 1, 2 or 3 cassettes, each with a promoter, a ribosome binding site, a coding sequence and a terminator

Starting Category: Start | Transcription Unit (S)

Icon Set: biobricks\_icon\_set

Copy Grammar (Basic Grammar -- No Simulation)

Name: \* Copy of Basic Grammar -- No Simulation

Description: \* 1, 2 or 3 cassettes, each with a promoter, a ribosome binding site, a coding sequence and a terminator

Starting Category: \* Start | Transcription Unit (S)

Image Set: \* biobricks\_icon\_set

Preview

Include Libraries: E coli public

Copy

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- Another way to create a new grammar: copy one
- It will then become editable to modify for your needs

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## Export a Grammar

Welcome, Researcher 1 | My Profile | Log Out

STEP 1: PARTS STEP 2: DESIGN STEP 3: SIMULATE

Grammars Libraries My Parts My Cart (0) Grammar Summary **Manage Grammar**

Add / Import Grammar

Public Grammars

- Basic Grammar - No Simulation
- Basic Grammar with Simulation
- Gene Regulatory Networks
- User Grammars
- Training Set E. Coli Gram
- Researcher 1 new grammar

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Manage Grammar

Name: Basic Grammar -- No Simulation

Description: 1, 2 or 3 cassettes, each with a promoter, a ribosome binding site, a coding sequence and a terminator

Starting Category: Start | Transcription Unit (S)

Icon Set: biobricks\_icon\_set

Export Grammar (Basic Grammar -- No Simulation)

Name: \* Basic Grammar -- No Simulation

Description: \* 1, 2 or 3 cassettes, each with a promoter, a ribosome binding site, a coding sequence and a terminator

Starting Category: \* Start | Transcription Unit (S)

Image Set: \* biobricks\_icon\_set

Export

Category: \*

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- Another way to work with a grammar: export
- Any grammar can also be exported and shared

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## GenoCAD Advanced Agenda

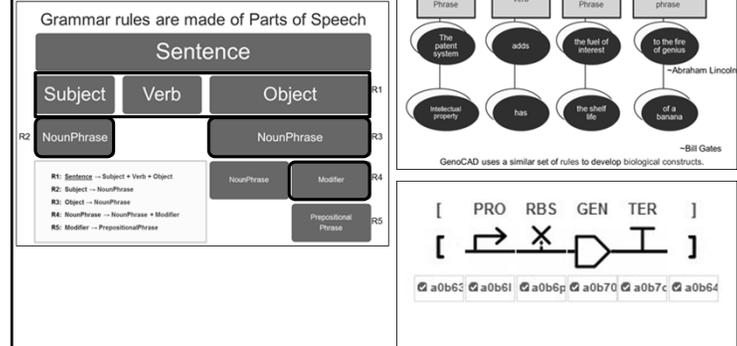
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## Modifying Grammars



- Grammars establish the expression strategy
- Subject–Verb–Object
- Promoter–Cistron–Terminator

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## Manage Grammar

- Access the Grammars tab
- Select Training Set grammar
- Click “Manage Grammar” to examine rules

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## Grammars

- Categories: parts characteristics
- Rules: specify the number, order, orientation, etc

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## Add Rules to a Grammar

- Cistron with histidine tags need rules: CIS → RBS GEN HIS
- One tag at the end of a cistron (histag-C)

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## New Rule is Available, Old Rules can be edited

- Cistron-using designs can now have his-tag
- HisTag is now a terminal category because it is used

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## Rule Editing has Consequences

- Change to rbgn rule affects existing constructs
- View the "Copy of RFP construct"

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## Validation Status

- Return to the Design list
- Note the change in status
- Examine the status key
- Re-work the design by clicking the steps again until complete

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## GenoCAD Summary

The screenshot displays the GenoCAD web application interface. At the top, it says 'GenoCAD CAD Software for Synthetic Biology' and includes a navigation bar with 'STEP 1: PARTS', 'STEP 2: DESIGN', and 'STEP 3: SIMULATE'. Below this, there are three main panels: 'New Design' on the left with a tree view of grammars and parts, 'History' in the center showing a sequence of operations like 'PROG', 'PROG', 'ODE', and 'VIEW', and 'Simulation Results' on the right showing a line graph of simulation data. The footer includes the Virginia Tech logo and social media links.

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

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