

WEININGER WORKS™ OPEN ACCESS METHOD: Molecular Locks

Overview

Configuration, Sensitivity, and Specificity

Circuits

Open Access

Molecular Lock Overview

Molecular Locks:

- were invented, patented, and developed by Arthur Weininger and Susan Weininger;
- are protein assemblies that cooperatively lock onto specific target nucleic acids (DNA or RNA); and
- form the basis of our **Molecular Lock Pathogen Shield (MOLOPS)** system.

MOLOPS nucleic acid detection components:

- can be cost-effectively made in bacteria;
- can be easily tested and evaluated in gel retardation assays;
- are highly stable to environmental factors (e.g. temperature);
- can be used on crude lysates; and
- are able to be implemented in many formats (e.g. dipstick or electronic).

MOLOPS nucleic acid silencing application components:

- can be transferred to cells as proteins or encoded in deliverable nucleic acids; and
- most often are designed to target:
 - replication control sequences that are upstream of coding regions (e.g. HIV LTR); or
 - promoters that control disease-causing or disease-permitting genes (e.g. pathogenic Burkholderia pseudomallei toxin protein and drug resistance protein promoters).

We believe that it is critical that a global **MOLOPS** surveillance system be set up to identify, characterize, and inactivate pathogenic biota. The detection of pathogenic biota and the silencing of pathogenic promoters and control regions provide the basis for a broad pathogen shield.

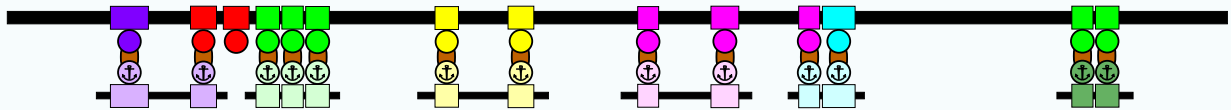
Molecular Lock Configuration, Sensitivity, and Specificity

Molecular Locks are molecular assemblies that are engineered to bind specifically to nucleic acid targets. Target specificity is obtained even if the target is comprised of commonly occurring sequences. Molecular Lock components can be used to protect or isolate the target. In tests, non-target nucleic acids can be eliminated without degrading or reducing the target nucleic acids.

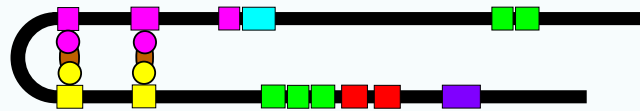
Configuration

Molecular Lock oligomerization domains are selected so that nucleic acid binding domains cooperatively bind to the target in a specific geometry.

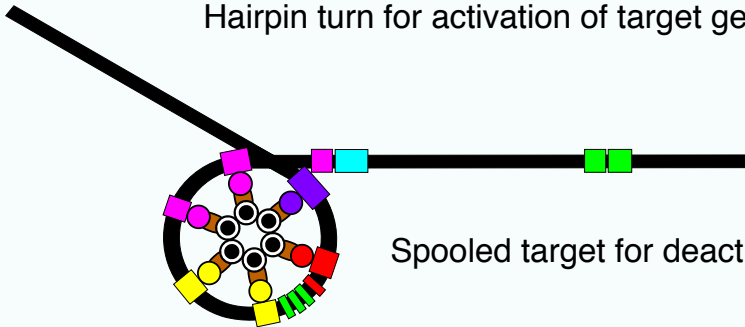
Molecular Lock Configurations



Anchored target ("lockbox") for immobilization, detection and counting of target genes



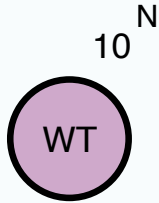
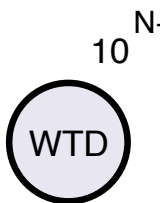
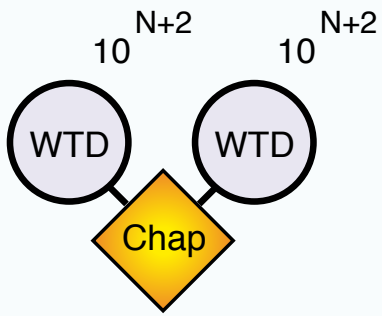
Hairpin turn for activation of target genes



Spooled target for deactivation of target genes

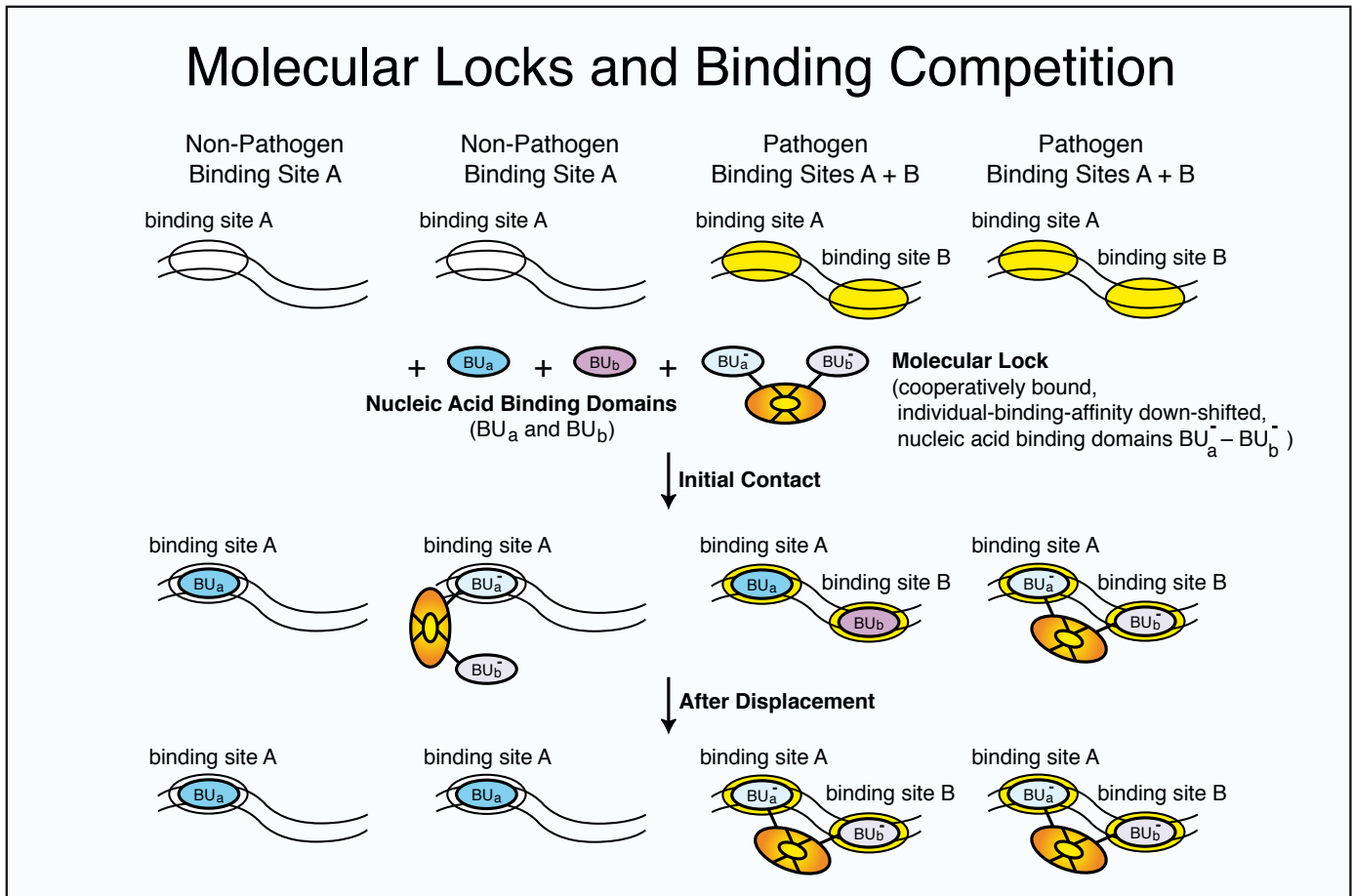
Sensitivity

The binding affinity of a molecular assembly that binds cooperatively with two binding domains is on the order of the square of the binding affinity of a molecule binding with only one of the domains. Downshifting the binding affinity of each of the Molecular Lock components allows the assembled block to bind tightly to the target even if each subcomponent would be weakly bound individually. This is an important feature both *in vitro* and *in vivo*.

Wild-Type Protein	Wild-Type Protein Downshifted	Cooperatively Binding Molecular Lock
		
10^N (e.g. 10^{-9} M)	10^{N+2} (e.g. 10^{-7} M)	$(10^{N+2})^2$ (e.g. 10^{-14} M)

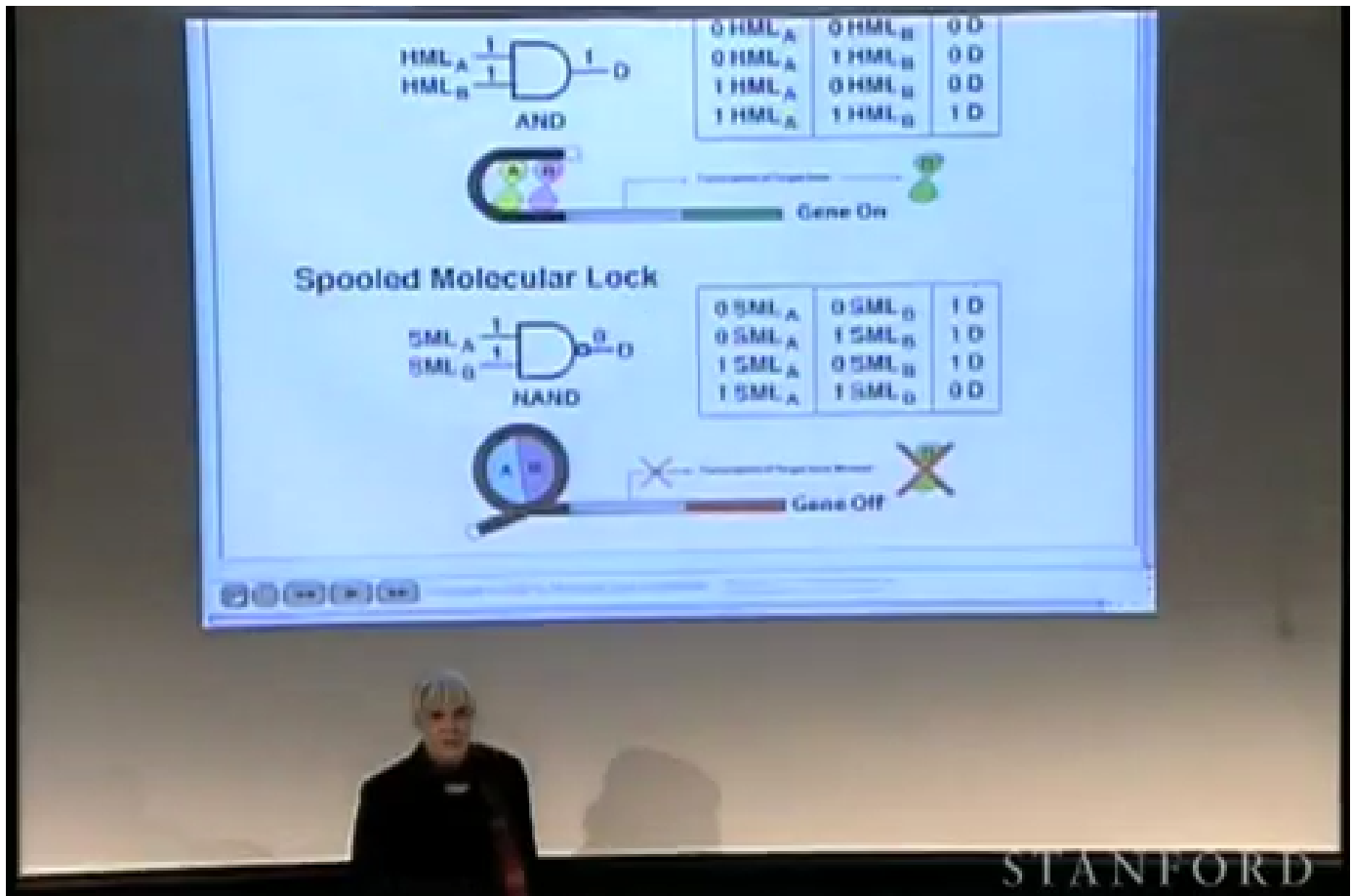
Specificity

Molecular Locks formed from more than one binding component can select specific nucleic acid targets—even when a portion of the target is found elsewhere in a non-target sequence.



Molecular Lock Circuits

Molecular Locks can also be used to characterize molecular circuits. Characterized molecular circuits can be used to design specific or broad Molecular Locks.



https://weiningerworks.com/Weininger__Stanford_talk_2009_Oct_14__VIDEO.mp4#t=126

[Download video](#) or right mouse down (on video) to "Save As..."

**"Construction of De Novo Biological Process Control Circuits:
Parts & Engineering Principles" (PDF)**

Susan Weininger

**EE 380 Computer Systems Colloquium
Stanford University
14 October 2009**

Molecular Lock Method Open Access

Molecular Lock method patents have been broadly issued to Arthur Weininger and Susan Weininger. These patents have now expired. The Molecular Lock method described in the expired patents is now an Open Access Method. Note that individual Molecular Locks may still be individually protected as composition patents.

Open Access Methods (Definition and Disclaimers)

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