sRNA triggered translational OFF switch

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34th TBI Winterseminar

February, 2019

Design Idea

sRNA (y)

- leading A for efficient transcription
- apply terminator design principles[1]

Interaction

- optimize for stable interaction without disrupting other constraints

5’ UTR (x)

- result from another design attempt
- high reporter gene expression

$$f(xy) = 0.01 \times (G(y|\Phi_{terminator}) - G(y|\Phi))^2 + (G(xy|\phi_{unbound}) + G(xy|\phi_{bound}) - 2 \cdot G(xy|\Phi))$$

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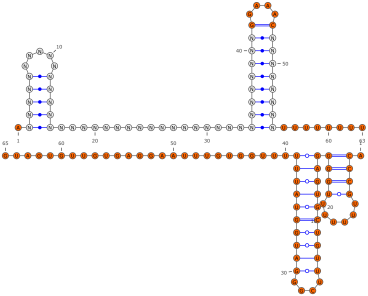

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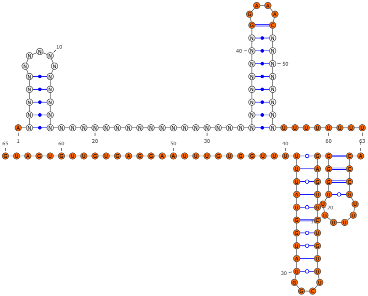

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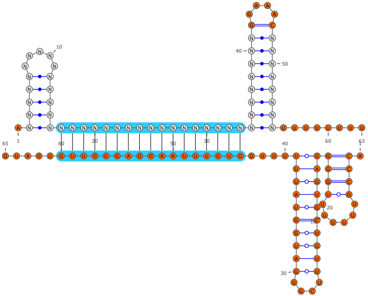

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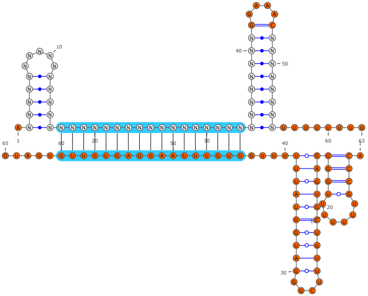

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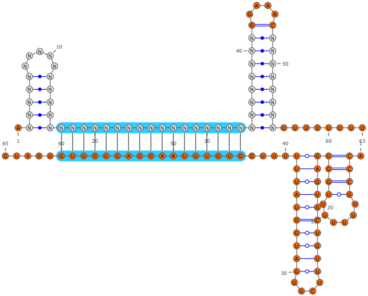

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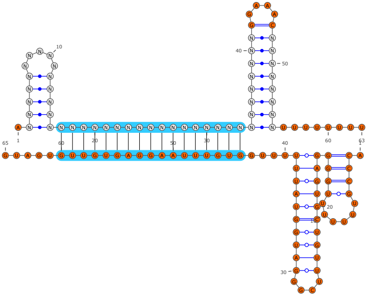

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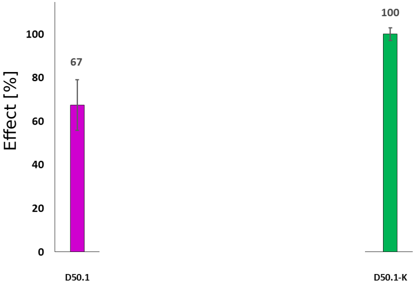

$$\text{Effect} = \frac{\langle OFF \rangle}{\langle ON \rangle} = \frac{p_u \cdot \langle H \rangle + p_b \cdot \langle L \rangle}{\langle H \rangle}$$

If $\langle H \rangle = 800$, $\langle L \rangle = 50$ and

Effect = 67%

$\Rightarrow$**35% of all targets are bound**

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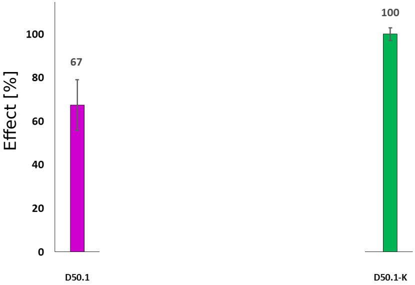

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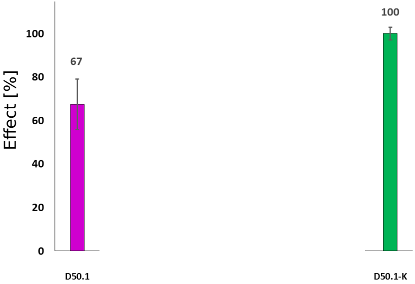

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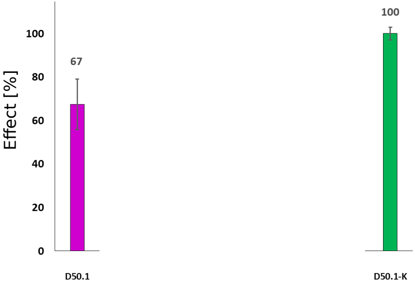

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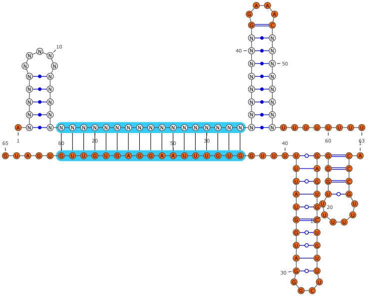

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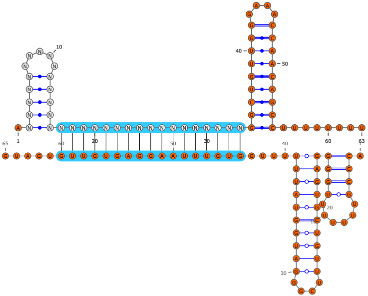

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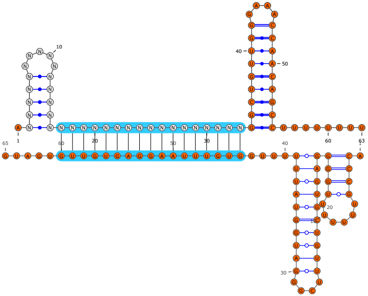

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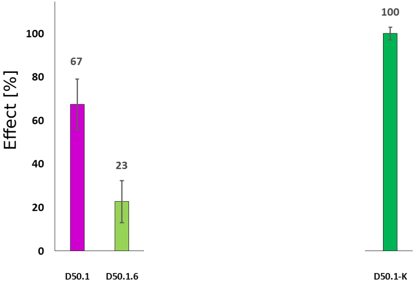

If $\langle H \rangle = 800$, $\langle L \rangle = 50$ and Effect = 23%

$\Rightarrow$ **82% of all targets are bound**

Extend the binding region

$\rightarrow$ **confusing results**

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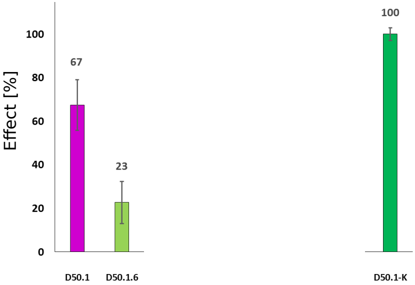

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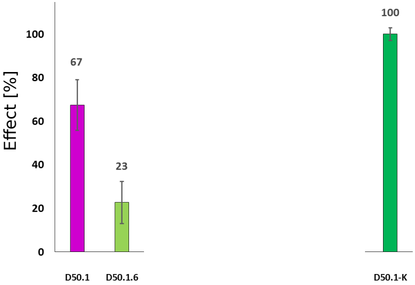

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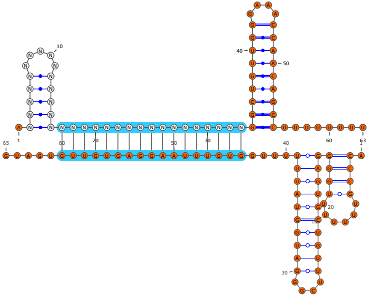

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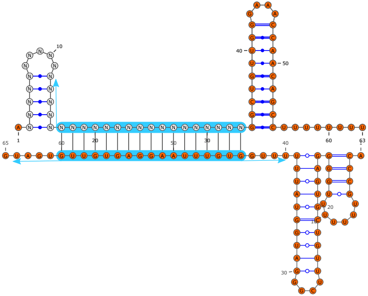

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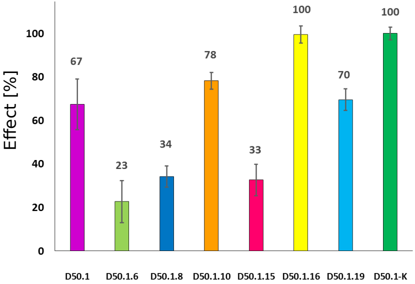

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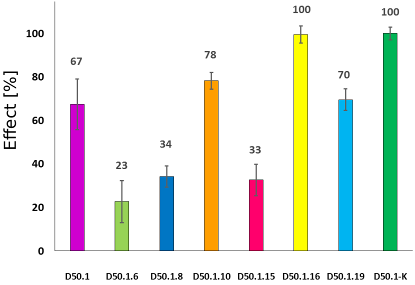

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2. How to verify D50.1.6 regulation?
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   - Is it possible to measure duplex concentration?
3. What is wrong with the assumption:
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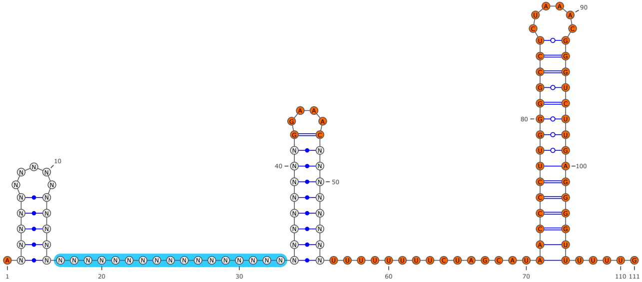

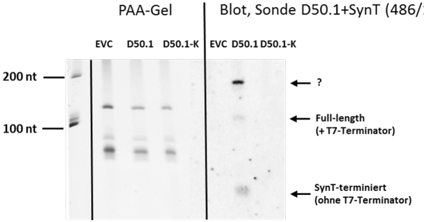

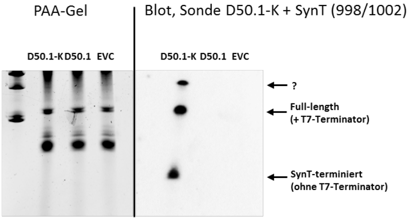

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Thanks to...

lab members:

- **Stefan Hammer**
- Felix Kühnl
- Peter F. Stadler
- Manuela Geiß

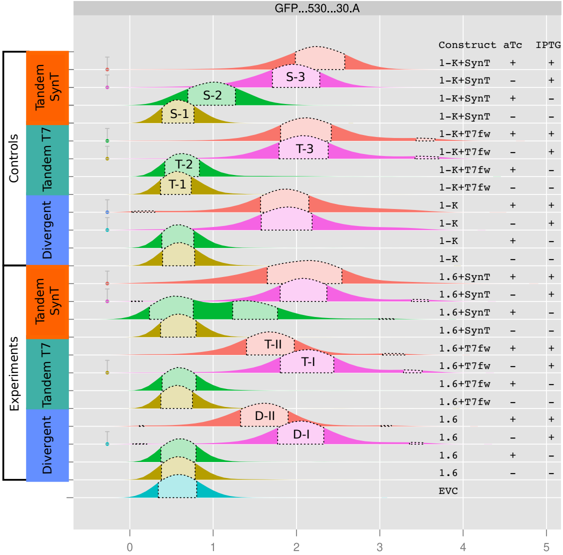
- Petra Pregel
- Jens Steuck

UNIVERSITÄT
LEIPZIG

collaborators:

- Anna Ender, Leipzig
- Chris Günzel, Leipzig
- Mario Mörl, Leipzig
- Christina Weinberg, Leipzig
- **Ilka Axmann, Düsseldorf**
- **Alice Pavlovski, Düsseldorf**
- Sebastian Will, Vienna
- **Christoph Flamm, Vienna**
- **Ivo L. Hofacker, Vienna**
- Yann Ponty, Palaiseau
- Michael Ryckelynck, Strasbourg

Terminator Efficiency Estimation



SynT efficiency = 88%

$$p_t = \frac{M_{S_1} - M_{S_3}}{M_{S_1} - M_{S_3}}$$