Monday Sept 19th - Morning - Welcome/Introduction			
10:30	11:00		**Coffee break**
11:00	12:00		**Word from the organizers + General intro**
12:00	14:00		**Lunch break**
Monday Sept 19th - Afternoon - Design stories (chair: Yann Ponty)			
14:00	15:30	#22	Sven Findeiß
			Get away from Plug and Pray
15:30	16:15		**Coffee break**
16:15	16:45	#5	Jan Gorodkin
			Two design stories: probes for SARS-CoV-2 detection and CRISPR/Cas9 gRNAs
16:45	17:30	#20	Sarah Berkemer
			Design of RNA tandem repeats creating RNA droplets forming liquid-liquid phase separation
Tuesday Sept 20th - Morning - Molecular biology (chair: Christoph Flamm)			
9:00	9:45	#3	Danny Barash
			Eukaryotic riboswitch detection using inverse RNA folding
9:45	10:30	#10	Sebastian Will
			Infrared: A sampling framework for RNA design (and beyond)
10:30	11:00		**Coffee break**
11:00	11:30	#1	Philippe Nghe
			Discovering RNA Self-Reproducers By In Silico And In Vitro Screening
11:30	12:00	#8	Katja Petzold
			RNA dynamics: one basepair at a time
12:00	14:00		**Lunch break**
Tuesday Sept 20th - Afternoon - Molecular computing (chair: Christoph Flamm)			
14:00	14:45	#13	Cody Geary
			Designing RNA during the DNA Origami revolution
14:45	15:30	#14	Ebbe Andersen
			Structural basis of RNA origami design, folding and flexibility
15:30	16:15		**Coffee break**
16:15	17:00	#15	Shinnosuke Seki
			Single-Stranded Architectures for RNA Co-Transcriptional Folding
17:00	17:30	#27	Stefan Badelt
			On the compilation of multi-stranded nucleic acids circuits
17:30	18:00	#28	Harold Fellerman
			Computing with nucleic acids
Wednesday Sept 21st - Morning - ML design (chair: Vladimir Reinharz)			
9:00	9:30	#18	Jorge Fernandez-de-Cossio-Diaz
			Generative modelling of riboswitches with restricted Boltzmann machines
9:30	10:00	#6	Bruno Sargueil
			Differential SHAPE probing for predict pseudoknot and non-canonical interactions
10:00	10:30	#29	Ivo Hofacker
			Experiments in Deep Learning for RNA Secondary Structure Prediction
10:30	11:00		**Coffee break**
11:00	11:30	#25	Frederick Runge
			Learning to Design RNA
11:30	12:00	#16	Andrew E. Torda
			Was the election stolen?
Thursday Sept 22nd - Morning - Combinatorial design (chair: Ronny Lorenz)			
9:00	9:45	#11	Yann Ponty
			Minimalistic RNA inverse folding
9:45	10:30	#19	Christine Heitsch
			What can geometric combinatorics say about RNA design?
10:30	11:00		**Coffee break**

11:00	11:30	#12	Hua-Ting Yao
	Forbidden RNA motifs and the cardinality of secondary structure space		
11:30	12:00	#21	Maciej Antczak
	Datasets for benchmarking RNA design algorithms		
12:00	14:00		**Lunch break**
Thursday Sept 22nd - Afternoon - 3D & design (chair: Marta Szachniuk)			
14:00	14:45	#7	Petr Sulc
	Coarse-grained modeling for RNA nanotechnology		
14:45	15:30	#4	Nicolas Schabanel
	ENSnano: a 3D DNA nanostructure design software for Windows, Mac OS and linux		
15:30	16:15		
16:15	16:45	#9	Samuela Pasquali
	Physical modeling of RNA polymorphism		
16:45	17:30	#26	Vladimir Reinharz
	Challenges in designing RNA non-canonical modules		
Friday Sept 23rd - Morning - Dynamic landscapes design (chair: Ivo Hofacker)			
9:20	10:15	#30	Stefan Badelt
	Simulations of cotranscriptional folding explain the impact of sequence mutations		
10:30	11:00		**Coffee break**
11:00	11:30	#24	Maria Waldl
	Kinetic features of RNA-RNA interactions		
11:30	12:00	#23	Felix Kuehnl
	BarMap-QA: cotranscriptional folding with quality assurance		
12:00	14:00		**Lunch break + Departure**

Talk #1 - Philippe Nghe - Discovering RNA Self-Reproducers By In Silico And In Vitro Screening

The RNA world hypothesis proposes that RNAs carry catalytic activity necessary for primordial evolution. A first necessary condition for evolution is reproduction. Whether self-reproduction is rare or common in the space of RNA sequences is central to assess the plausibility of this scenario. To date, two ribozymes have been shown to autocatalytically sustain their self-reproduction in the laboratory, starting from RNA oligomers: the Azoarcus ribozyme derived from the group I intron family (Hayden and Lehman 2006) and a fragmented ligase (Lincoln and Joyce 2009). In this project, we assess the probability of self-reproducing RNAs in sequence space by using as a starting point the Azoarcus ribozyme that can autocatalytically self-reproduce.
We show that combining in silico and in vitro screening allows for the discovery of a large number of artificial self-reproducing ribozymes. For this, the strategy consists of: i) Identifying natural self-reproducing GIIs; ii) Applying physics-based and machine learning methods to generate artificial candidates for self-reproduction; iii) Testing designed sequences for self-reproduction using high-throughput sequencing; v) characterizing the representative self-reproducers. We find that generative models that combine statistical signatures from pair correlations and secondary structure prediction are efficient at producing functional ribozymes more than 60 nucleotides away from the original sequence, whereas random mutations destroy activity after only a few. These methods interpolate the natural diversity found in group I introns, from which self-reproducers can be successfully re-engineered. This overall shows that self-reproduction is not an exceptional property of a few laboratory-made RNAs, but is relatively widespread in the sequence space.

Joint work with: Lambert, Camille ; Opuu, Vaitea ; Calvanese, Francesco ; Weigt, Martin ; Smerlak, Matteo ; Nghe, Philippe

Talk #3 - Danny Barash - Eukaryotic riboswitch detection using inverse RNA folding

The inverse RNA folding problem for designing sequences that fold into a given RNA secondary structure was introduced in the early 1990's in Vienna. By an extension of this problem we use a coarse-grained approach to possibly detect novel eukaryotic riboswitches. The approach can tentatively be used for other domains and applications,

Joint work with: Mukherjee, Sumit; Drory, Matan; Barash, Danny

Talk #4 - Nicolas Schabanel - ENSnano: a 3D DNA nanostructure design software for Windows, Mac OS and linux

ENSnano takes up the concept of others DNA/RNA nanostructures design software like cadnano and scadnano, and introduces the following features:
- A smooth and intuitive design interface
- Fast design and handling of large structures
- Custom organisation of the 2D view
- 3D cross-over recomandation
- A new grid-based 3D organisation of helices
- Realtime 3D visualisation and editing
- Export of strand sequences to excel files for ordering
- Import of designs from cadnano and scadnano, with 3D structure guessing and automatic grid assignement
- Export to OxDNA for physical simulation, an export to MrDNA is also planed.
- Cross-platform: Windows, MacOS and Linux
- Curved DNA/RNA designs
- Experimental validations

ENSnano is developed by Nicolas Levy and Nicolas Schabanel.

Joint work with: Levy, Nicolas; Schabanel, Nicolas

Talk #5 - Jan Gorodkin - Two design stories: probes for SARS-CoV-2 detection and CRISPR/Cas9 gRNAs

I will present two design cases. The first case concern non-enzymatic isothermal strand displacement and amplification for rapid detection of SARS-CoV-2, which we accomplished through design of DNA probes that opens and binds to targeted locations of the SARS-CoV-2 genome. Through RNA folding considerations, we show why one of two probes are more successful and makes the detection possible. In the second case, design of CRISPR/Cas9 guide RNA (gRNA) are made from first generating cleavage efficiency data and subsequently train a deep learning-based neural network which has cutting-edge performance tested on independent data sets.

Joint work with: Gorodkin J, Mohammadniaei M, Zhang M, Ashley J, Christensen UB, Friis-Hansen LJ, Gregersen R, Lisby JG, Benfield TL, Nielsen FE,

Talk #6 - Bruno Sargueil - Differential SHAPE probing for predict pseudoknot and non-canonical interactions

Sargueil, B ; De Bisschop, G; Hardouin, P; Lyonnet, FX ; Frezza, E; Masquida, B ; Ponty, Y, Will, S ; Cocco, S ; Monasson, R; Cossio, J and Giocchino, A

The development of reliable RNA design processes requires experimental validation. RNA structure modelling from chemical probing experiments has made tremendous progress, however accurately predicting large RNA structures is still challenging for several reasons. In particular interactions such as pseudoknots and non-canonical base pairs which are not captured by the available incomplete thermodynamic model are hardly predicted efficiently. To identify nucleotides involved in pseudoknots and non-canonical interactions, we scrutinized the SHAPE reactivity of each nucleotide of a benchmark RNA under multiple conditions. We show that probing at increasing temperature was remarkably efficient at pointing to non-canonical interactions and pseudoknot pairings. We will discuss the possibility to inform the modelling software with such information. The SHAPE probing technology was then use to screen for RNA computationally designed to interact with a small molecule. Updated results will be presented.

Joint work with: Sargueil, B ; de Bisschop, Hardouin, P; Lyonnet, FX ; Frezza, E; Ponty, Y, Will, S ; Cocco, S ; Monasson, R; Cossio, J; Giocchi

Talk #7 - Petr Sulc - Coarse-grained modeling for RNA nanotechnology

Nucleic acid nanotechnology uses designed DNA or RNA strands that self-assemble into larger complexes and nanodevices. Computer modeling and simulations can provide crucial insights into function and design of such nanostructures. However, the sizes (up to thousands of base pairs) and timescales of their assembly (minutes to hours) of such nanodevices presents major challenge for modeling approaches. Here, we will present a coarse-grained model, oxDNA/oxRNA, specifically designed to simulate DNA and RNA nanotechnology, and we will demonstrate its application to RNA strand displacement reaction, a key mechanism in active nanotechnology devices which has recently been also identified to occur during RNA folding in vivo. We will then discuss applications of our modeling platform for inverse design of multicomponent nanostructure assemblies: how to design individual nucleic acid building blocks that self-assemble reliable into target mutlicomponent structure while avoiding kinetic traps and alternative free-energy minima? We show that through combination of multiscale modeling and mapping of the inverse design problem to Boolean Satisfiability Problem (SAT), it is possible to design nanostructures that assemble large-scale 3D assemblies, opening ways to use nucleic acids to biotemplated manufacturing.

Joint work with: Sulc, Petr;

Talk #8 - Katja Petzold - RNA dynamics: one basepair at a time

Many functions of RNA depend on rearrangements in secondary structure that are triggered by external factors, such as protein or small molecule binding. These transitions can feature on one hand localized structural changes in base-pairs or can be presented by a change in chemical identity of e.g. a nucleo-base tautomer [1]. We use and develop R1ρ relaxation-dispersion NMR methods [2] for characterizing transient structures of RNA that exist in low abundance (populations <10%) and that are sampled on timescales spanning three orders of magnitude (µs to s).

The characterization of transient structures in microRNA miR-34a targeting the mRNA of Sirt1 [3] will be discussed and a first glimpse into ribosomal dynamics will be provided. We have trapped these short-lived states and characterized their structure and impact on function.

Reference:
[1] I.J. Kimsey, K. Petzold, B. Sathyamoorthy, Z.W. Stein and H.M. Al-Hashimi Nature, 519 (7543), pp 315-320, 2015
[2] J. Schlagnitweit, E. Steiner, H. Karlsson and K. Petzold, Chemistry – A European Journal; 24(23):6067-6070, 2018. & M. Marušić, J. Schlagnitweit and K. Petzold, ChemBioChem 2019, 20, 2685-2710
[3] L. Baronti, I. Guzzetti†, P. Ebrahimi†, S. Friebe Sandoz†, E. Steiner†, J. Schlagnitweit, B. Fromm, L. Silva, C. Fontana, A. Chen and K. Petzold, Nature 2020, 583, 139-144

Joint work with: Petzold, Katja and the entire PetzoldLab (alumni and current)

Talk #9 - Samuela Pasquali - Physical modeling of RNA polymorphism

RNA molecules are characterized by the existence of a multitude of stable states that that result in a frustrated energy landscape, where the observed structures depend sensibly on experimental conditions and can depend on the initial, unfolded, structure.
Using both atomistic and coarse-grained physical models for RNAs, combined with enhanced sampling methods, we investigate the energy landscape of these systems to understand what are the most relevant structures in the different conditions. Using a few significant examples we show how the combination of these methods allowed us to rationalize the experimental evidence showing the concurrent existence of multiple states [1,2].
The coarse-grained model we develop [3] is also a useful starting point to couple simulations with experimental data, moving toward intergrative modeling.
We have recently developed a simulation technique allowing to bias MD coarse-grained simulations with SAXS data on-the-fly [4], and a theoretical framework to perform fast constant pH simulations where we can model the system considering the exchange of charges with the solvent [5]. These developments allow us to account for the environment to obtain reasonable structures to then be studied more thoroughly with high-resolution modeling.

References:
1.K Röder, G Stirnemann, AC Dock-Bregeon, DJ Wales, S Pasquali, Structural transitions in the RNA 7SK 5′ hairpin and their effect on HEXIM binding, Nucleic Acids Research 48 (1), 373-389 (2020)
2.K Röder, AM Barker, A Whitehouse, S Pasquali, Investigating the structural changes due to adenosine methylation of the Kaposi's sarcoma-associated herpes virus ORF50 transcript, PLOS Computational Biology 2022, 18(5):e1010150, doi: 10.1371/journal.pcbi.1010150, PMID: 35617364
3.T. Cragnolini, Y. Laurin, P. Derreumaux, S. Pasquali, The coarse-grained HiRE-RNA model for de novo calculations of RNA free energy surfaces, folding, pathways and complex structure predictions, J. Chem. Theory Comput., 11, 3510 (2015)
4.L Mazzanti, L Alferkh, E Frezza, S Pasquali, Biasing RNA coarse-grained folding simulations with Small--Angle X--ray Scattering (SAXS) data, BioXiv doi: 10.1101/2021.03.29.437449 (2021)
5.S. Pasquali, E. Frezza, F.L. Barroso da Silva, Coarse-grained dynamic RNA titration simulations, Interface Focus 9: 20180066 (2019)

Joint work with: Samuela Pasquali, Konstantin Roeder

Talk #10 - Sebastian Will - Infrared: A sampling framework for RNA design (and beyond)

Infrared is a modeling framework for efficient targeted sampling and optimization. It was originally developed for implementing complex sequence design approaches with multiple objectives and side constraints, e.g. design of sequences with multiple RNA target structures while controlling the GC-content (RNARedPrint). Due to its declarative, compositional application programming/modeling interface, Infrared allows extending existing design tools to solve very specific design tasks, e.g. optimizing codon-usage while targeting RNA structures and (possibly) additional constraints. In the same way, it enables rapid development of completely new design tools like RNAPOND (and, due to its generality, even methods beyond design, e.g. alignment of RNAs with pseudoknots). A main feature of the system is its automatic adaptation to the complexity of the declaratively modeled task. For this purpose, the system implicitly derives fixed-parameter-tractable sampling and optimization algorithms using tree-decomposition. The talk outlines main properties and background of the system, its elementary usage, and presents concrete examples of design applications.

Joint work with: Will, Sebastian; Ponty, Yann; Yao, Hua-Ting

Talk #11 - Yann Ponty - Minimalistic RNA inverse folding

We consider the Combinatorial RNA Design problem, a minimal instance of RNA inverse folding. We consider two free-energy models where the contributions of base pairs are additive: the purely combinatorial Watson-Crick model, which only allows equally contributing A-U and C-G base pairs, and the real-valued Nussinov-Jacobson model, which associates arbitrary energies to A-U, C-G and G-U base pairs.

We first provide a complete characterization of designable structures using restricted alphabets and, in the four-letter alphabet, provide a complete characterization for designable structures without unpaired bases. When unpaired bases are allowed, we characterize extensive classes of (non-)designable structures, and prove the closure of the set of designable structures under the stutter operation. Membership of a given structure to any of the classes can be tested in O(n) time, and so is the generation of a solution sequence for positive instances.

Finally, we consider a structure-approximating relaxation of the design, and provide a O(n) algorithm which, given a structure S that avoids two trivially non-designable motifs, transforms S into a designable structure constructively by adding at most one base-pair to each of its stems.

Joint work with: Ponty, Yann; Hales, Jozef; Héliou, Alice; Manuch, Jan; Stacho, Ladislav

Talk #12 - Hua-Ting Yao - Forbidden RNA motifs and the cardinality of secondary structure space

The problem of RNA design attempts to construct RNA sequences that perform a predefined biological function, identified by several additional constraints. One of the foremost objectives of RNA negative design is that the designed RNA sequence should adopt a predefined target secondary structure preferentially to any alternative structure, according to a given metrics and folding model. It was observed in several works that some secondary structures are undesignable, i.e. no RNA sequence can fold into the target structure while satisfying some criterion measuring how preferential this folding is compared to alternative conformations.
We show that the proportion of designable secondary structures decreases exponentially with the size of the target secondary structure, for various popular combinations of energy models and design objectives. This exponential decay is, at least in part, due to the existence of forbidden motifs, which can be generically constructed, and jointly analyzed to yield asymptotic upper bounds on the number of designable structures. Moreover, we define a lower bound of the structural ensemble defect. We show that, across uniformly distributed secondary structures, such a lower bound has a Normal limiting distribution with the expected value and the variance both linear to the size of the secondary structure.

Joint work with: Yao, Hua-Ting; Chauve, Cedric; Regnier, Mireille; Ponty, Yann

Talk #13 - Cody Geary - Designing RNA during the DNA Origami revolution

RNA is the punk-brother of DNA. While DNA plays by rules, RNA is more rebellious. The diverse structural features of RNA that make it a powerfully-functional molecule in biology also make it difficult to tame and rationally-design.

In contrast to engineered DNA nanostructures such as DNA origamis, natural RNA molecules in cells must fold under non-equilibrium conditions; the RNAs fold continuously while the strand is still emerging from the polymerase. While design of staple strands to produce DNA origami nanostructures can be easily automated by simple algorithms, producing a single-stranded RNA origami requires the entire sequence of the RNA to be designed by inverse folding, which is computationally much more challenging.

Our RNA design software ROAD begins with a random starting sequence, and over many iterations mutates that sequence to improve its folding into a target fold. ROAD uses both positive and negative design cycles to perform a gradient descent based on an adapting scoring function. The strategy is based on in vitro selection methods where the selection conditions gradually become more difficult over successive rounds.

Joint work with: Geary, Cody; Grossi, Guido; McRae, Ewan K.S.; Rothemund, Paul W. K.; Andersen, Ebbe S.

Talk #14 - Ebbe Andersen - Structural basis of RNA origami design, folding and flexibility

The research field of RNA nanotechnology develops methods for the rational design of self-assembling RNA nanostructures with applications in nanomedicine and synthetic biology. Inspired by the cotranscriptional folding of biological RNA molecules, we developed the RNA origami method to design RNA nanostructures compatible with cotranscriptional folding [1,2], advantageous for large-scale production in vitro and expression in vivo. However, advancing this technology further will require a better understanding of RNA structural properties and the non-equilibrium dynamics of the cotranscriptional folding process. Here, we use cryogenic electron microscopy to study a panel of RNA origami structures at sub-nanometer resolution revealing structural parameters of kissing loop and crossover motifs, that are further used to optimize designs by reduction of internal strain and global twist. In three-dimensional bundle designs, we discover a novel kinetic folding trap that forms during cotranscriptional folding and is only released 10-12 hours after transcription start. We characterize the conformational landscape of RNA origamis to reveal the RNA flexibility of helices and structural motifs. Finally, we demonstrate that large distinctive RNA origami shapes are visible by cryo-electron tomography pointing to potential use as markers in cellular environments. Our results improve understanding of RNA structure, folding, and dynamics, providing a basis for rational design of genetically encoded RNA nanodevices.

References:

[1] Geary, C., Rothemund, P. W. & Andersen, E. S. A single-stranded architecture for cotranscriptional folding of RNA nanostructures. Science 345, 799-804, doi:10.1126/science.1253920 (2014).
[2]Geary, C., Grossi, G., McRae, E. K. S., Rothemund, P. W. K. & Andersen, E. S. RNA origami design tools enable cotranscriptional folding of kilobase-sized nanoscaffolds. Nat Chem, doi:10.1038/s41557-021-00679-1 (2021).

Joint work with: McRae; Rasmussen; Liu; Bøggild; Nguyen; Sampedro Vallina; Boesen; Pedersen; Ren; Geary; Andersen

Talk #15 - Shinnosuke Seki - Single-Stranded Architectures for RNA Co-Transcriptional Folding

Oritatami (folding in Japanese) is a mathematical model of computation by co-transcriptional folding we proposed in 2016 and have been studying, primarily on its computational power. In this model, RNA co-transcriptional folding is generalized so that the bases (called “beads” herein) can be of arbitrarily defined, finitely-many types that may have arbitrary affinities with each other (rather than just the four bases in RNA with their fixed set of affinities), but restricted on the 2D plane. In this talk, we present the latest universal oritatami architecture that enables us to compute all computable functions (Turing universality) co-transcriptionally, with particular emphasis on simplicity of mechanisms it employs to read/write a bit, to store information, and to merge computational paths (erasure).

Joint work with: Daria Pchelina, Nicolas Schabanel, Shinnosuke Seki, and Guillaume Theyssier

Talk #16 - Andrew E. Torda - Was the election stolen?

RNA sequence design makes more promises than an American election candidate. To continue the analogy, we have made promises and broken them. As the chemist George Bush (snr) said, read my lips. We have promised our collaborators that we will deliver sequences which fold up like tRNA's, but are more stable, enjoy strange anti-codons and can jump over stop codons. We may not have delivered completely.

We have been using methods which treat sequence design as a continuous problem. En route to a real sequence, a site can be undecided about the base it wants to be. one could see this as sequence-particles moving in a 4-dimensional space, and trying to minimise their score in the nearest neighbour model. At the same time, they have numerical incentives to dissuade them from folding into wrong structures.

If you want to build a molecule which does a biological job, the problem becomes simpler and harder. The problem might be simpler in that you accept that you will not design a sequence from scratch. One probably wants some or much of a natural molecule. In our formulation, one uses harmonic restraints on base types at certain positions. The design problem might become harder in that you have to decide which positions in the sequence should be kept native. We have applied a mixture of intense literature research, expert intuition and blind guesswork with unjustified optimism.

Joint work with: Torda, Andrew E.; Matthies, Marco C.

Talk #17 - Marco C. Matthies - Differentiable dynamic programming for RNA sequence design

Representing nucleotides with vectors of real numbers instead of symbols from an alphabet allows one to view the RNA sequence design problem as a continuous optimisation problem. If the design objective is differentiable with respect to the sequence vector representation, gradients can be used to guide the search for good sequences.

We use 4-component vectors at each site of a sequence to represent single-site nucleotide probability distributions. A variant of McCaskill's partition function algorithm for the nearest-neighbour model can be used to calculate expectation values for sequence probability distributions. Together with a previously introduced method of calculating expected energy for sequence distributions, we can approximate the expected probability of a sequence ensemble folding into a given target structure. We use this as our design objective.

Gradients for sequence optimisation are calculated by forward-mode automatic differentiation. Optimisation follows gradients in sequence probability space until it converges to a discrete sequence. This is a work in progress and some preliminary results will be presented on the performance of the sequence design method.

Joint work with: Matthies, Marco C.; Torda, Andrew E.

Talk #18 - Jorge Fernandez-de-Cossio-Diaz - Generative modelling of riboswitches with restricted Boltzmann machines

Restricted Boltzmann machines (RBM) are energy-based latent variable generative models, consisting of two layers, that can offer interpretable representations of complex data. Recently they have been applied to modelling protein sequence data. In this talk, I will present evidence suggesting RBM are effective generative models of structured RNA. In particular, I consider the SAM riboswitch family, which regulates expression of downstream bacterial mRNAs by adopting competing structural conformations in response to the presence of a cellular metabolite. The RBM automatically infers relevant statistical features from the sequence data, such as conservation patterns, complementarity constraints consistent with the secondary structure, and the presence of a pseudoknot. The functionality of designed sequences has been validated experimentally by SHAPE mapping.

Joint work with: Fernandez-de-Cossio-Diaz, J; Di Gioacchino, A; Cocco, S; Monasson, R; Sargueil, B; Ponty, Y; Marchand, B; Hardouin, P; Lyonnet F

Talk #19 - Christine Heitsch - What can geometric combinatorics say about RNA design?

Branching is a critical characteristic of RNA design, yet can be challenging to validate with thermodynamic optimization approaches. Using mathematical methods (convex polytopes and their normal fans), we can improve prediction accuracy on well-defined families while also illuminating why the general problem is so difficult.

Joint work with: Heitsch, Christine; Poznanovi\'c, Svetlana; et. al.

Talk #20 - Sarah Berkemer - Design of RNA tandem repeats creating RNA droplets forming liquid-liquid phase separation

Various genetic disorders are caused by expansion of short tandem repeats as they aggregate in cells and form so-called RNA droplets or foci. However, themolecular mechanisms of RNA foci formation remains unclear. The aim of being able to design RNA tandem repeats and model RNA foci formation is twofold:
it will help understand the mechanisms and therapies related to genetic disorders such as Huntigton's disease but at the same time serve as a method to spatial engineering inside cells as RNA droplets cause a liquid-liquid phase separation which can serve as process isolation and help to organize proteins and multienzyme pathways without fine-tuning RNA expression levels.

Phase-separating RNA molecule complexes are contructed from small repeating sequences, e.g. triplet repeats. Visualization of RNA foci is conducted by tagging droplets with e.g. GFP and corresponding adapters such as the MS2 aptamer.

Previous studies successfully showed the formation of RNA foci using various types of RNA triplet repeats and even longer repeat sequences where the formation of G-quadruplexes seems to be an important part for the interaction between two tandem repeat RNAs [1,2,3,4].

Existing studies could experimentally show which RNA triplets are the most successful in forming RNA foci, however, the structure of RNA foci and their dynamics are not yet understood. Additionally, the liquid-liquid phase separation opens numerous possibilities for spatial engineering inside the cells, but we still lack the knowledge of structural and chemical properties of the RNA droplets and the space inside the foci. By designing RNA molecules that form droplets, we need to take into account interactions of more than two RNA sequences as well as possible interactions with binding proteins. Hence, we aim to develop design strategies for interacting short tandem RNA repeats and explore properties of RNA droplets and their formation.

[1]Haotian Guo et al, https://www.biorxiv.org/content/10.1101/2020.07.02.182527v2.full
[2] Jain and Vale, 2017, https://doi.org/10.1038/nature22386
[3] Nguyen, Hori & Thirumalai 2021: https://doi.org/10.1101/2021.02.20.432119
[4] Isiktas et al, 2022 https://www.biorxiv.org/content/10.1101/2022.04.11.487960v1.full

Joint work with: Sarah J Berkemer, Ariel B Lindner, Yann Ponty, Carla Tous-Mayol

Talk #21 - Maciej Antczak - Datasets for benchmarking RNA design algorithms

In this talk, we will present the databases developed to support benchmarking of bioinformatics algorithms targeting RNA, including the ones for RNA design. RNAsolo (https://rnasolo.cs.put.poznan.pl/) collects experimentally determined 3D RNA structures from RNAs alone, protein-RNA complexes, and DNA-RNA hybrids and organizes them into classes of equivalent structures. Their sequences and tertiary structures are grouped in 192 benchmark sets ready for download and automated processing. RNAloops (https://rnaloops.cs.put.poznan.pl/) aims to facilitate the study of multiloops in RNA molecules. It collects n-way junctions found in experimental RNA structures and allows to search them by sequence, secondary structure topology, or structure parameters. Both data sources address RNA-related studies by providing reliable sequence and structure data and efficient search facilities.

Joint work with: Antczak, Maciej; Szachniuk, Marta

Talk #22 - Sven Findeiß - Get away from Plug and Pray

I will talk about the collaborative projects with the group of Mario Mörl (Biochemistry department at Uni. Leipzig) on transcription termination regulating riboswitches and how we put tRNA processing under ligand control. The presentation will summarize how the corresponding design models have been developed, implemented, and analyzed in silico, as well as the biochemical investigations in vitro and in vivo. I will not only show the success story but the main emphasis will be on the problems we faced, how we solved them, and especially the issues that remain.

Joint work with: Findeiß, Sven

Talk #23 - Felix Kuehnl - BarMap-QA: cotranscriptional folding with quality assurance

Joint work with: Findeiß, Sven et al

Talk #24 - Maria Waldl - Kinetic features of RNA-RNA interactions

TBA

Joint work with: TBA

Talk #25 - Frederick Runge - Learning to Design RNA

TBA

Joint work with: TBA

Talk #26 - Vladimir Reinharz - Challenges in designing RNA non-canonical modules

TBA

Joint work with: TBA

Talk #27 - Stefan Badelt - On the compilation of multi-stranded nucleic acids circuits

Joint work with: TBA

Talk #28 - Harold Fellerman - Computing with nucleic acids

Joint work with: TBA

Talk #29 - Ivo Hofacker - Experiments in Deep Learning for RNA Secondary Structure Prediction

Joint work with:

Talk #30 - Stefan Badelt - Simulations of cotranscriptional folding explain the impact of sequence mutations

Joint work with: