CURRICULUM VITAE

Fyodor A. Kondrashov

PERSONAL
Born on 8 May 1979 in the former Soviet Union, resided in the USA 1990-2008, in Spain 2008-2017 and in Austria since 2017. Fluent in English and Russian, conversational Spanish.

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EDUCATION

2005 – 2008	PhD degree in Biology from University of California at San Diego.
2003 – 2004	Master of Arts degree in Population Biology from University of California at Davis.
1996 – 2000	Bachelor of Arts degree in Biology and Ecology from Simon's Rock College.

RESEARCH EXPERIENCE AND POSITIONS

Since Oct. 2017	Professor, IST Austria
Since 2012	Scientific Director of the School of Molecular and Theoretical Biology
2011 – on leave	ICREA Research Professor at the CRG, a tenure position
2008 – 2017	Junior Group Leader at the Center for Genomic Regulation
2005 – current	Summer field work expeditions in Siberia and the Arctic
2000 – 2003	Research Scientist, NCBI, NIH.

RESEARCH GRANTS AND AWARDS (Total raised 4,132,248 EURO, $650,000 USD)

2019 – 2023	ERC Consolidator Grant from the European Commission, Grant Agreement # 771209 ChrFL. **1,998,280 EURO**
2016 – 2019	Plan Estatal (BFU2015-68723-P) from the Spanish Ministry of Economics and Competitiveness, **284,592 EURO**
2014 – 2015	Agéncia de Gestió d´Ajuts Universitaris i de Recerca (AGAUR), a joint grant with Lucas Carey and Jordi Garcia-Ojalvo (coordinator) from the UPF, total 48,000 EURO (**28,800 EURO** for our lab).
2014 – 2018	ERC Starting Grant from the European Commission, Grant Agreement #335980–EinME. **1,461,576 EURO**
2013 – 2015	Plan Nacional Grant (BFU2012-31329) from the Spanish Ministry of Economics and Competitiveness, **184,000 EURO**
2012 – 2017	Howard Hughes Medical Institute International Early Career Scientist Award #55007424, **$650,000**
2011 – 2013	EMBO Young Investigator Award, **45,000 EURO**
2010	The Theodosius Dobzhansky Prize from the Society for the Study of Evolution

2010 – 2012 Plan Nacional Grant (BFU2009-09271) from the Spanish Ministry of Science and Innovation, **130,000 EURO**
2008 EMBO long term post doctoral fellowship (declined).
2005 – 2008 National Science Foundation Graduate Research Fellow.
2003 Darwin Trust Fund Fellowship (declined).

EDUCATIONAL GRANTS (Total raised $1,443,753.05 USD, 330,000 EUR)
2019 Zimin Foundation grant for the School of Molecular and Theoretical Biology, $**443,000 USD**
2018 – 2020 Howard Hughes Medical Institute educational seed grant for the School of Molecular and Theoretical Biology, **$63,000**
2018 Zimin Foundation grant for the School of Molecular and Theoretical Biology, $**323,139 USD**
2018 Donation to the School of Molecular and Theoretical Biology from Charities Aid Foundation (CAF), $**109,414.05 USD**
2017 Zimin Foundation grant for the School of Molecular and Theoretical Biology, $**406,200 USD**
2016 Zimin Foundation grant for the School of Molecular and Theoretical Biology, **330,000 EURO**
2015 – 2017 Howard Hughes Medical Institute educational seed grant for the School of Molecular and Theoretical Biology, **$63,000 USD**
2014 Howard Hughes Medical Institute educational seed grant for the 2014 School of Molecular and Theoretical Biology, **$21,000 USD**
2013 Howard Hughes Medical Institute educational seed grant for the 2013 School of Molecular and Theoretical Biology, **$15,000 USD**

REVIEW EXPERIENCE
Biofizika, Bioinformatics, Biology Direct, BMC Bioinformatics, BMC Evolutionary Biology, BMC Genomics, Cell, Cell Reports, Comparative and Functional Genomics, eLife, Evolution, Future Microbiology, Gene, Genetical Research, Genetics, Genetics Research, Genome Biology, Genome Biology and Evolution, Genome Research, Genomics, Heredity, Human Molecular Genetics, In Silico Biology, Journal of Molecular Evolution, Molecular Biology and Evolution, Molecular Phylogenetics and Evolution, Nature, Nature Chemical Biology, Nature Genetics, Nature Reviews Genetics, Nucleic Acid Research, Philosophical Transactions Royal Society B, PLOS Biology, PLOS Genetics, PLOS One, PNAS, RNA Journal, Science, Trends in Ecology and Evolution, Trends in Genetics.

PROFESSIONAL COMISSIONS OF TRUST
2006 – 2016 Biology Direct: Member of the Editorial Board
2013 – 2018 Biology Direct: Section Editor, Evolutionary Biology
2018 ERC LS2 Starting Grant Panel Member

GEOGRAPHY OF INVITED AND CONFERENCE PRESENTATIONS
Brisbane (**Australia**); Klosterneuburg, Vienna (**Austria**); Toronto (**Canada**); Suzhou (**China**); Nove Hrady (**Czech Republic**); Copenhagen (**Denmark**); Helsinki (**Finland**); Marseille (**France**);

Berlin, Cologne, Heidelberg, Konstanz, Mainz, Munich, Leipzig (**Germany**); Szeged (**Hungary**); Bangalore (**India**); Rehovot, Sede Boker (**Israel**); Bergamo, Bertinoro, Milan (**Italy**); Hayama, Okinawa (**Japan**); Goniadz, Krakow, Poznan, Torun, Warsaw (**Poland**); Lisbon, Porto (**Portugal**); Atkarsk, Chelyabisk, Kazan, Khanty-Mansiysk, Krasnoyarsk, Mias, Moscow, Novosibirsk, Pushchino, Rostov-on-Don, Saratov, Taganrog, Zvenigorod (**Russia**); Singapore (**Singapore**); Barcelona, Girona, Granada, Madrid, Valencia (**Spain**); Basel, Lausanne, Sessa, Zurich (**Switzerland**); Stockholm (**Sweden**); Taipei (**Taiwan**); Ankara, Istanbul (**Turkey**); Bath, Brighton, Cambridge, Edinburgh, Liverpool, London, Reading (**UK**); Arlington, Berkeley, Bethesda, Boston, Chicago, Dallas, Davis, Ithaca, Los Angeles, New Haven, New York, Norfolk, Kansas City, Portland, Rockville, San Diego, San Francisco, Tucson (**USA**).

RESEARCH REFERENCES

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PUBLICATIONS

76. Slavskii SA, Shashkova TI, Bazykin G, Axenovich TI, Kondrashov FA, Aulchenko YS. Human height is a multiplicative, but not an additive, trait. *Nature Genetics* (submitted).

75. Garriga Nogales G, Tommaso P, Magis C, Erb I, Laayouni H, Kondrashov FA, Floden E, Notredame C. Fast and accurate large multiple sequence alignments using root-to-leave regressive computation. *Nature Biotechnology* (submitted).

74. Konczal M, Zapata L, Camara F, Vlasova A, Lyulina AS, Bello C, Fraïsse C, Derelle R, Tutukina MN, Plyuscheva M, Fontsere C, Tomkovich PS, Yakushev NN, Shepelev IA, Arkhipov VYu, Zöckler C, Digby R, Loktionov EY, Lappo EG, Ossowski S, Marques T, Guigo R, Syroechkovskiy EE, Kondrashov FA. Population genomics of the critically endangered spoon-billed sandpiper. *Nat Ecol Evol* (in revision).

73. Pokusaeva VO, Usmanova DR, Putintseva EV, Espinar L, Sarkisyan KS, Mishin AS, Bogatyreva NS, Ivankov DN, Povolotskaya IS, Filion GJ, Carey LB, Kondrashov FA. Experimental assay of a fitness landscape on a macroevolutionary scale. *PLOS Genetics* (accepted). https://www.biorxiv.org/content/10.1101/222778v2

72. Pich i Rosello O, Vlasova AV, Shichkova PA, Markov Y, Vlasov PK, Kondrashov FA. Genomic analysis of human polymorphisms affecting drug-protein interactions. https://www.biorxiv.org/content/10.1101/119933v1

71. Kotlobay A, Sarkisyan KS, Mokrushina Y, Marcet-Houben M, Serebrovskaya EO, Markina NM, Gonzalez Somermeyer L, Gorokhovatsky AY, Vvedensky A, Purtov KV, Petushkov VN, Rodionova NS, Chepurnyh TV, Fakhranurova LI, Guglya EB, Ziganshin RH, Tsarkova AS, Kaskova ZM, Shender V, Abakumov M, Abakumova TO, Povolotskaya IS, Eroshkin FM, Zaraisky AG, Mishin AS, Dolgov SV, Mitiouchkina TYu, Kopantzev EP, Waldenmaier H, Oliveira AG, Oba Y, Barsova E, Bogdanova EA, Gabaldón T, Stevani CV, Lukyanov S, Smirnov IV, Gitelson JI, Kondrashov FA, Yampolsky I. (2018) A genetically encodable bioluminescent system from fungi. *PNAS*, **115**(50):12728-12732.

70. Usmanova DR, Bogatyreva NS, Ariño Bernad J, Eremina AA, Gorshkova AA, Kanevskiy GM, Lonishin LR, Meister AV, Yakupova AG, Kondrashov FA, Ivankov DN. (2018) Self-consistency test reveals systematic bias in programs for prediction change of stability upon mutation. *Bioinformatics*. **34**, 3653-3658.

69. Zapata L, Pich O, Serrano L, Kondrashov FA, Stephan Ossowski S, Schaefer MH. (2018) Negative selection in tumor genome evolution acts on essential cellular functions and the immunopeptidome. *Genome Biol.* **19**, 67

68. Antipov SS, Tutukina MN, Preobrazhenskaya EV, Kondrashov FA, Patrushev MV, Toshchakov SV, Dominova I, Shvyreva US, Vrublevskaya VV, Morenkov OS, Sukharicheva NA, Panyukov VV, Ozoline ON. (2017) The nucleoid protein Dps binds genomic DNA of Escherichia coli in a non-random manner. *PLoS ONE* **12**, e0182800.

67. Saint-Léger A, Bello C, Dans PD, Torres A, Camacho N, Orozco M, Kondrashov FA, Ribas de Pouplana L. (2016) Saturation of recognition elements blocks evolution of new tRNA identities. *Science Advances*. **2**, e1501860.

66. Sarkisyan KS, Bolotin DA, Meer MV, Usmanova DR, Mishin AS, Sharonov GC, Ivankov DN, Bozhanov NG, Baranov MS, Soylemez O, Bogatyreva NS, Vlasov PK, Egorov ES, Logacheva MD, Kondrashov AS, Chudakov DM, Putintseva EV, Mamedov IZ, Tawfik DS, Lukyanov KA, Kondrashov FA. (2016) Local fitness landscape of the green fluorescent protein. *Nature*. **533**, 397-401.

65. Rivkina E, Petrovskaya L, Vishnivetskaya T, Krivushin K, Shmakova L, Tutukina M, Meyers A, Kondrashov F. (2016) Metagenomic analyses of the late Pleistocene permafrost - additional tools for reconstruction of environmental conditions. *Biogeosciences* **13**, 2207-2219.

64. Howe K, Schiffer PH, Zielinski J, Wiehe T, Laird GK, Marioni J, Soylemez O, Kondrashov FA, Leptin M. (2016) Structure and evolutionary history of a large family of NLR proteins in the zebrafish. *Open Biology*. **6**, 4

63. Kretz CA, Dai M, Soylemez O, Yee A, Desch K, Siemieniak D, Tomberg K, Kondrashov FA, Meng F, Ginsburg D. (2015) Massively parallel enzyme kinetics reveals the substrate recognition landscape of ADAMTS13. *Proceedings of the National Academy of Sciences USA*, **112**, 9328-9333.

62. Arkhipova OV, Meer MV, Mikoulinskaia GV, Zakharova MV, Galushko AS, Akimenko VK, Kondrashov FA. (2015) Recent Origin of the Methacrylate Redox System in Geobacter sulfurreducens AM-1 through Horizontal Gene Transfer. *PLoS One*. **10**, e0125888

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60. Kondrashov DA, Kondrashov FA. (2015) Topological features of rugged fitness landscapes in sequence space. *Trends in Genet*. **31**, 24-33

59. Pougach K, Voet A, Kondrashov FA, Voordeckers K, Christiaens JF, Baying B, Benes V, Sakai R, Aerts J, Zhu B, Van Dijck P, Verstrepen KJ. (2014) Duplication of a promiscuous transcription factor drives the emergence of a new regulatory network. *Nat Commun*. **5**, 4868

58. Seplyarskiy VB, Logacheva MD, Penin AA, Baranova MA, Leushkin EV, Demidenko NV, Klepikova AV, Kondrashov FA, Kondrashov AS, James TY. (2014) Crossing-over in a

hypervariable species preferentially occurs in regions of high local similarity. *Mol Biol Evol*. **31**, 3016-3025.

57. Pich i Rosello O, Kondrashov FA. (2014) Long-term asymmetrical acceleration of protein evolution after gene duplication. *Genome Biol Evol*. **6**, 1949-1955.

56. Ivankov DN, Finkelstein AV, Kondrashov FA. (2014) A structural perspective of compensatory evolution. *Cur Opinion Struc Biol*. **26**, 104–112

55. Moroz LL, Kocot KM, Citarella MR, Dosung S, Norekian TP, Povolotskaya IS, Grigorenko AP, Dailey C, Berezikov E, Buckley KM, Ptitsyn A, Reshetov D, Mukherjee K, Moroz TP, Bobkova Y, Yu F, Kapitonov VV, Jurka J, Bobkov YV, Swore JJ, Girardo DO, Fodor A, Gusev F, Sanford R, Bruders R, Kittler E, Mills CE, Rast JP, Derelle R, Solovyev VV, Kondrashov FA, Swalla BJ, Sweedler JV, Rogaev EI, Halanych KM, Kohn AB. (2014) The ctenophore genome and the evolutionary origins of neural systems. *Nature*. **510**, 109-114.

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53. Eliseeva IA, Vorontsov IE, Babeyev KE, Buyanova SM, Sysoeva MA, Kondrashov FA, Kulakovskiy IV. (2013) In silico motif analysis suggests an interplay of transcriptional and translational control in mTOR response. *Translation* **1**, e27469

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51. Arkhipov V.Yu. Noah, N., Koschkar, S., Kondrashov, F.A. (2013) Birds of Mys Shmidta, north Chukotka, Russia. *Forktail* **29**, 25-30.

50. Breen, M.S., Kemena, C., Vlasov, P.K., Notredame, C., Kondrashov, F.A. (2013) Reply to: The role of epistasis in protein evolution. *Nature* **497**, E2-E3.

49. Soylemez O, Kondrashov FA (2012). Estimating the rate of irreversibility in protein evolution. *Genome Biol Evol*. **4**, 1213-1222.

48. Breen MS, Kemena C, Vlasov PK, Notredame C, Kondrashov FA. (2012) Epistasis as the primary factor in molecular evolution. *Nature* **490**, 535-538. [Featured on Faculty of 1000]

47. Kondrashov FA (2012). Gene duplication as a mechanism of genomic adaptation to a changing environment. *Proc Biol Sci*. **279**, 5048-5057.

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44. Breen MS, Kondrashov FA (2010). Mitochondrial pathogenic mutations are population-specific. **Biol Direct**. **5**, 68.

43. Povolotskaya IS, Kondrashov FA (2010). Sequence space and the ongoing expansion of the protein universe. *Nature*. **465**, 922-926. [Featured on Faculty of 1000]

42. Kondrashov FA, Kondrashov AS (2010). Measuring spontaneous mutation rates in the recent past and the near future. *Philos. Trans. R. Soc. Lond. B Biol. Sci*. **365**, 1169-1176.

41. Meer MV, Kondrashov AS, Artzy-Randrup Y, Kondrashov FA (2010). Compensatory evolution in mt-tRNAs navigates valleys of low fitness. *Nature*. **464**, 279-282.

40. Innan H, Kondrashov FA (2010) The evolution of gene duplications: classifying and distinguishing between models. *Nat. Rev. Genet*. **11**, 97-108. [Featured on Faculty of 1000]

39. Kondrashov AS, Povolotskaya IS, Ivankov DN, Kondrashov FA (2010). Rate of sequence divergence under constant selection. *Biology Direct*. **5**, 5. [Highly Accessed]

38. Alkalaeva E, Eliseev B, Ambrogelly A, Vlasov P, Kondrashov FA, Gundllapalli S, Frolova L, Söll D, Kisselev L (2009) Translation termination in pyrrolysine-utilizing archaea. *FEBS Lett*. **583**, 3455-3460.

37. Schmidt S, Gerasimova A, Kondrashov FA, Adzuhbei IA, Kondrashov AS, Sunyaev S (2008) Hypermutable nonsynonymous sites are under stronger negative selection. *PLoS Genet*. **4**, e1000281.

36. Assis R, Kondrashov AS, Koonin EV, Kondrashov FA. (2008) Nested genes and increasing organizational complexity of metazoan genomes. *Trends Genet*. **24**, 475-478.

35. Donaldson ZR, Kondrashov FA, Putnam A, Bai Y, Stoinski TL, Hammock EA, Young LJ. (2008) Evolution of a behavior-linked microsatellite-containing element in the 5' flanking region of the primate AVPR1A gene. *BMC Evol Biol*. **8**, 180.

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33. Bazykin GA, Kondrashov FA, Brudno M, Poliakov A, Dubchak I and Kondrashov AS (2007) Extensive parallelism in protein evolution. *Biology Direct* **2**, 20 [Highly Accessed]

32. Plotnikova OV, Kondrashov FA, Vlasov PK, Ginter EK and Rogaev EI (2007). Conversion and compensatory evolution of the γ-crystallin genes and identification of a cataractogenic mutation that reverses the sequence of the human CRYGD gene to an ancestral state. *Am. J. Hum. Genet*. **81**, 32-43

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28. Kondrashov FA, Ogurtsov AY, Kondrashov AS. (2006) Selection in favor of nucleotides G and C diversifies evolution rates and levels of polymorphism at mammalian synonymous sites. *Journal of Theoretical Biology* **240**, 616-626.

27. Kondrashov FA and Kondrashov AS. (2006) Role of selection in fixation of gene duplications. *Journal of Theoretical Biology* **239**, 141-151.

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25. Yampolsky LY, Kondrashov FA and Kondrashov AS. (2005) Distribution of the strength of selection against amino acid replacements in human proteins. Human Molecular Genetics 14, 3191-3201. [Featured on Faculty of 1000]

24. Kondrashov FA. (2005) Prediction of pathogenic mutations in mitochondrially encoded human tRNAs. *Human Molecular Genetics* **14**, 2415-2419.

23. Kondrashov FA. (2005) Analysis of monomer sequences in protein and tRNAs and the manifestation of compensated pathogenic deviations in their evolution. *Biofizika* **50**, 389-395.

22. Kondrashov FA. (2005) Convergent evolution of secondary structure of mitochondrial cysteine tRNA in the nine-banded armadillo Dasypus novemcinctus. *Biofizika* **50**, 396-403.

21. Jordan IK, Kondrashov FA, Adzhubei IA, Wolf YI, Koonin EV, Kondrashov AS and Sunyaev S. (2005) A universal trend of amino acid gain and loss in protein evolution. *Nature* **433**, 633-638. [Featured on Faculty of 1000]

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18. Bazykin GA, Kondrashov FA, Sunyaev S, Ogurtsov AY and Kondrashov AS. (2004) Positive selection at sites of multiple amino acid replacements since rat-mouse divergence. *Nature* **429**, 558-562. [Featured on Faculty of 1000]

17. Castillo-Davis C, Kondrashov FA. Hartl DL and Kulathinal RJ. (2004) The functional genomic distribution of protein divergence in two animal phyla: coevolution, genomic conflict, and constraint. *Genome Res*. **14**, 802-811.

16. Kondrashov FA, Ogurtsov AY and Kondrashov AS. (2004) Bioinformatical assay of human gene morbidity. *Nucleic Acids Res*. **32**, 1731-1737.

15. Panchenko AR, Kondrashov FA and Bryant S. (2004) Prediction of functional sites by analysis of sequence and structure conservation. *Protein Science* **13**, 884-892

14. Sunyaev S, Kondrashov FA, Bork P and Ramensky V. (2003) Impact of selection, mutation rate and genetic drift on human genetic variation. *Human Molecular Genetics* **12**, 3325-3330.

13. Kondrashov FA and Koonin EV. (2003) Evolution of alternative splicing: deletions, insertions and origin of functional parts of proteins from intron sequences. *Trends in Genetics* **19**, 115-119.

12. Kondrashov AS, Sunyaev S and Kondrashov FA. (2002) Dobzhansky-Muller incompatibilities in protein evolution. *Proceedings of the National Academy of Sciences USA* **99**, 14878-14883. [Featured on Faculty of 1000]

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10. Perelygin AA, Kondrashov FA, Rogozin IB and Brinton MA. (2002) Evolution of the mouse polyubiquitin C gene. *Journal of Molecular Evolution* **55**, 202-210.

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7. Kondrashov FA and Koonin EV. (2001) Origin of alternative splicing by tandem exon duplication. *Human Molecular Genetics* **10**, 2661-2669

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5. Kondrashov FA and Kondrashov AS. (2001) Multidimensional epistasis and the disadvantage of sex. *Proceedings of the National Academy of Sciences USA* **98**, 12089-12092.

4. Wolf YI, Kondrashov FA and Koonin EV. (2001) Footprints of primordial introns on the eukaryotic genome: still no clear traces. *Trends in Genetics* **17**, 499-501.

3. Rogozin IB, Kondrashov FA and Glazko GV. (2001) Use of mutation spectra analysis software. *Hum Mutat.* **17**, 83-102.

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1. Kondrashov AS and Kondrashov FA. (1999) Interactions among quantitative traits in the course of sympatric speciation. *Nature* **400**, 351-354.

Book Chapters and News and Views:

1. Kondrashov FA (2005). In search of the limits of evolution. *Nature Genetics* **37**, 9-10 (news and views).

2. Kondrashov FA (2010). Gene Dosage and Duplication. in Evolution after Gene Duplication. Eds. Dittmar K and Liberles D (Wiley-Blackwell, Hoboken, New Jersey).

RESEARCH STATEMENT

General

Throughout my research career I have utilized an interdisciplinary approach to study various evolutionary and functional aspects of genes and genomes. My research used aspects of functional genomics, population genetics, systems biology, molecular evolution, medical genetics and bioinformatics. Until I started my own laboratory in 2008 my research has been almost exclusively theoretical and computational, however, in the last several years I made a strong push to encompass experimental and translational components. Because of the interdisciplinary nature of my research, I mostly work within small teams that include researchers of different disciplines. Similarly, my laboratory is a diverse group of researchers that includes physicists, mathematicians, cell biologists, evolutionary biologists and bioinformaticians. Thus, my work has been almost exclusively collaborative.

Main research question

My primary interest is understanding how species, their genes and genomes evolve and the forces that drive this evolution. One of the main ways in which I worked to understand evolution is

through the elucidation of the genotype to phenotype connection, which in evolutionary biology is referred to as the fitness landscape. How the phenotype (fitness) is shaped by the genotype is the underlying basis for a wide array of issues in biology. Whether or not a mutation affects human health, what are the forces shaping natural variability of a population, what are the gene circuits shaping fruit fly wing morphology – these are all questions, among many, that can be formulated in the framework of the fitness landscape. In our work we strive to bridge the gap between microevolution (population genetics) and macroevolution (on a molecular level) to understand the fitness landscapes. Conversely, we also study how different aspects of the fitness landscape shape micro- and macroevolutionary processes.

Using proteins as a model unit of the genotype, we used computational and experimental approaches to study the fitness landscape. We tested the null hypothesis is that the fitness landscape is simple, whereby mutations affect fitness independently of each other. Alternatively, mutations interact with each other, a phenomenon called epistasis, to contribute to fitness, possibly, in quite complicated ways. On a macroevolutionary scale, many of our empirical observations appear to counter the null hypothesis. Specifically, counter to the null hypothesis, protein sequences appear to diverge slower and farther (Povolotskaya and Kondrashov, Nature, 2010), many more amino acid residues appear to be useful per site (Breen et al, Nature, 2012), amino acids appear to change frequency slower (Jordan et al., Nature, 2004), rates of parallel and convergent evolution appear to show different dynamics than expected (Bazykin et al., Biology Direct, 2007; Povolotskaya and Kondrashov, Nature, 2010; Soylemez and Kondrashov, GBE, 2012) finally, unexpectedly, human disease mutations were found in wildtype of other species (Kondrashov et al., PNAS, 2002; Ken and Kondrashov, Nature Genetics, 2004; Plotnikova et al., Am J Hum Genet, 2007).

The overwhelming evidence we, and others, have gathered over the years in rejection of the null hypothesis has led us to investigate the issue theoretically and experimentally. In our first, among several planned, experimental assays of the fitness landscapes we have managed to describe the local fitness landscape, that is one that describes only a few interacting mutations, of the green fluorescent protein (Sarkisyan, et al., Nature, 2016), confirming that epistasis is necessary to describe the landscape even on a relatively local scale. We followed our work on the GFP with a larger scale fitness landscape that considered a fitness landscape on a macroevolutionary scale. Selecting His3 as a model protein, we considered the fitness of His3 sequences that were composed of shuffled amino acid states found in different orthologues of His3. Remarkably, we found that 85% of all amino acid states that were fixed across half a billion years of evolution were associated with high fitness in some combinations and with low fitness in other combinations (Pokusaeva, et al. PLOS Genetics, in review). Therefore, it appears that evolutionary trajectories traverse rugged areas of the sequence space and that the order in which amino acid substitutions occur is not arbitrary. Interestingly, we also showed that in the case of His3, assuming that amino acid states contribute to multiple linear predictors of fitness usually outperformed a model where amino acid states contribute to just a single linear predictor. We conclude that the genotype to phenotype relationship is multidimensional, such that the highly multidimensional sequence space cannot be projected into a monotonic function, or even a smooth function with several maxima. We are currently following up these studies with further experimental work in GFP, His3 and other model proteins.

Theoretically, we have been investigating the role of complex fitness landscapes on rates of adaptive substitutions in evolving populations (Kondrashov and Kondrashov, 2002), we devised a new theoretical approach bridging micro- and macroevolutionary levels modeling the impact of the null hypothesis on sequence divergence from a population genetics perspective (Kondrashov et al., Biology Direct, 2010). Finally, we are working towards a unifying theory of molecular evolution that models sequence divergences explicitly incorporating epistatic interactions (Usmanova et al., MBE, 2015), although most of this work is at its infancy.

Our further work on the topic is bound to include a plethora of approaches targeting different aspects of the genotype to phenotype landscape. First, several experiments are ongoing that are aimed at confirming several of our computational studies. Second, we are working on elucidating the molecular basis of epistatic interactions (for example: Ivankov et al, Cur Opinion Struc Biol, 2014). Third, we are continuing our efforts to bridge the gap between the micro and the macroevolutionary levels (among already published works: Meer et al. Nature, 2010). Finally, understanding the genotype to phenotype connection has potential in improving the prediction of impact of specific mutations (i.e. Kondrashov, Hum Mol Genet, 2005), a prospect we are keen in exploring for human proteins (Kretz et al., PNAS, 2015).

Other research

In parallel to addressing the issue of the genotype to phenotype connection, I have been studying the function, selection and evolution of genes and genomes in a diversity of different contexts. We have studied the evolution and selection of non-coding DNA sequences (Wolf et al., TiG, 2000; Castillo-Davis et al., Nat Genetics, 2001; Donaldson et al., BMC Evol Biol, 2008), including alternative splicing (Kondrashov and Koonin, Hum Mol Genet, 2001; Kondrashov and Koonin, TiG, 2003). Our work on gene duplications focused on the short-term impacts of potential increased dosage following a gene duplication (Kondrashov et al., Genome Biology, 2002; Kondrashov and Koonin, TiG, 2004; Pougach et al., Nat Commun, 2014; Howe et al., Open Biology, 2016) and its impact on their fixation (Kondrashov and Kondrashov, J Theor Biol, 2006; Kondrashov, Proc Biol Sci, 2012). Finally, in our work we frequently investigate selection pressure acting on standing variability in various populations (Sunyaev et al,. Hum Mol Genet, 2003; Bazykin et al., Nature, 2004; Yampolsky et al., Hum Mol Genet, 2005; Kondrashov et al., J Theor Biol, 2006; Babenko et al., Biology Direct, 2006; Schmidt et al., POLS Genetics, 2008; Povolotskaya et al., Biology Direct, 2012; Seplyarskiy et al., MBE, 2014).

ONGOING RESEARCH AND FUTURE PLANS

The past several years in my laboratory have been dynamic. We doubled in size since the end of 2013, at the same time considerably expanding our capabilities of integrating experimental and translational components to our research. The last couple of years have brought great change to our lab with the move from CRG, Barcelona to IST, Austria, leading to an almost complete replacement in lab composition. Nevertheless, our interest continue to be very broad, from issues in molecular evolution and population genetics, to systems biology and molecular biology with a biomedical aspect. At present, we are pursuing the following venues of research, among others.

Cell biology, human disease and epistasis
We are attempting to characterize on the molecular level several disease mutations that are present in healthy, wild-type individuals of other species. For such mutations that are easier to study, we are attempting to understand the molecular basis why a mutation that causes disease in humans presents a wild-type phenotype in other species. The principle idea is that if we understand what compensates for the disease effects in other species it may be easier to reconstruct the conditions that permit the presence of the disease mutation without deleterious effects that can lead to novel treatments. At present, we are working on several such examples.

Mouse genetics, Parkinson's disease and compensatory evolution
For one instance of a disease mutation that causes Parkinson's disease in humans but is present in wild-type individuals of other species we have moved our work *in vivo*. We have tested a compensation of the disease mutation in cell culture and have created knock-in mice in which the introduced mutation disrupts the compensatory interaction between the disease mutation and the compensatory site. We see early signs that these mice to develop symptoms similar to that of Parkinson's Disease, validating our prediction of the compensatory interaction and creating a Parkinson's Disease mouse model that recapitulates the evolutionary history of the human lineage. As a side note I would like to add that moving from bioinformatics straight to mouse genetics has been one of the bravest (or dumbest, depending on the outcome of the experiments) and hardest things I have done in my research career.

Genomics
We are continuing asking various questions in genomics using computational tools, frequently supplementing them with small experimental tasks. If we lack a bacterial genome for an adequate outgroup we sequence it, if we are uncertain about the quality of assembly of a specific region of a genome we can confirm the accuracy by PCR or Sanger sequencing, etc. We are studying the evolution of lnc-RNAs, recent evolution of duplicated genes and parallel protein evolution, among other individual projects. Some of our studies are supplemented with development of appropriate theoretical models necessary for the description of our results. Finally, we are spearheading several genome sequencing projects, including, among others, the genome of a critically endangered species.

Intra population epistasis
Although our research on the high prevalence of epistasis in molecular evolution remains controversial we believe that there is cause to quantify how prevalent are epistatic interactions within standing variation. To this end, we are in the middle of a computational project attempting such a quantification in the human population and an experimental project with the same aim in yeast.

Experimental evolution
We have recently started a large-scale project in collaboration with physicists and engineers to construct a device for high level of automation of selection experiments. We are following the morbidostat model, but attempting to make the devices much cheaper to allow us to work on selection experiments in a high-throughput manner. My current interest is to develop human cell experimental evolution among the more common microbe work.

TEACHING AND OUTREACH

General philosophy of teaching

The foundation for my teaching philosophy was forged in the course of my own education in my science-driven family and at the liberal arts school that I attended for my undergraduate degree, Simon's Rock College of Bard. Drawing from my experience, I participated in, and organized, many high-school programs that allowed me to experiment and hone my skills and approaches and to find my own pedagogical voice. My teaching philosophy transcends all levels of teaching, from high school to graduate students in my lab.

I believe in a hands-on, authentic educational experience that is used as the principle educational kernel, with classroom and lecture instruction used as auxiliary tools to create an integrative learning environment. Indeed, plenty of research in education provides evidence that an authentic research learning experience, a method of teaching reminiscent of an apprenticeship model, based on real, hands-on research, is an effective method of teaching. Participating in authentic research leads to a more effective and broader learning (van Eijck and Roth, PLoS Biol, 2007; Kim, J Sci Ed Tech, 2011; Miller et al., Bioscience, 2013) with a more positive retrospective outlook on the learning experience (Dijkstra and Goedhart, Res Sci Tech Ed, 2011). Interestingly, although my teaching experience at all levels has been almost exclusively oriented towards talented students, the philosophy of authentic experience is thought to be equally appropriate for talented and typical students (Harwood and McMahon, J Res Sci Teaching 1997; Stake and Mares, J Res Sci Teaching, 2001).

There is evidence that the authentic research learning model may be particularly suitable for providing a positive outcome in girls. First, there is data to suggest that girls benefit more from an authentic hands-on research experience (Rand and Gibb, J Ed Gifted, 1989; Potter and Rosser, J Res Sci Teaching, 1992; Bartholomew, J Career Dev, 1995; Burkam et al., Am Ed Res J, 1997; Jovanovic and King, Am Ed Res J, 1998; Dijkstra and Goedhart, Res Sci Tech Ed, 2011). Second, girls are more likely to be influenced by the interaction with a faculty and interpersonal relationships (Stake and Granger, J Ed Psych, 1978; Cerinsek et al., Int J Sci Ed, 2006), by peer interaction in the course of advanced learning (Riegle-Crumb et al., Soc Ed, 2006) and by engagement in problem solving (Harskamp et al., Ed Res, 2008), all of which are staple features of an authentic research experience. Finally, creating a supportive environment conducive to boosting self-confidence may have a stronger positive effect on girls (Koch, J Res Sci Teaching,1998; Meyer, J Res Sci Teaching, 1998; Stake and Mares, J Res Sci Teaching, 2011).
The authentic research learning model, being quite different from the typical classroom instruction, comes with its own set of challenges and specifics. Crucially, the authentic research model is more depended on the right mentorship, attention and peer support (Burgin et al., Res Sci Ed, 2012), which necessitates greater faculty involvement and more attention to the social aspects of the learning environment. Indeed, the importance of social factors and appropriate mentorship and peer group support for a positive outlook on science learning and a STEM career is widely recognized (Buday et al., Sex Roles, 2012; Robnett et al., J Res Adolescence, 2013; Wang and Degol, Dev Rev, 2013). Some data show that social support and encouragement is more important for positive science attitude then social status variables (Stake, J Apl Soc Psy, 2006). The social support is specifically important for supporting an already existing interest (Ben-Eliyahu et al., Appl Dev Sci, 2014), which may specifically apply to talented students.

In developing my teaching methods and philosophy, I strive to engage the students into real research given the constraints of each experience. Indeed, the degree of involvement of the students in the research activity positively correlates with successful outcomes (Roth et al., Am Bio Teacher, 2009). Furthermore, I believe that it is vital to provide the freedom of choice to the students, coupled by professional advice and supply of relevant information. Research suggest that an authentic research project that supplements a pre-existing interest provides more impact compared to a situation when the topic of the project is novel to the student (Burgin et al., Res Sci Ed, 2012). Therefore, the freedom to choose the research topic may provide important advantage to the learning process. How the authentic research model is implemented greatly depends on the level of achievement of the students and the academic stage of the student. Below, I discuss how I implement this philosophy to different academic levels.

Graduate level

The engagement of the graduate students in research is the basic idea of all graduate programs. Without laboring too long on the rather obvious topic I would like to stress three things that I strive to do with my graduate students that provide a learning environment beyond a good research project. First, I believe that the role of a good laboratory is to produce great scientists as much as it is to produce great science. To develop the critical thinking skills required of a good scientists I provide my students with as much intellectual, and actual, freedom as they need or want. My students are free to experiment, to fail, to choose their own research direction, even if their funding comes from a grant project on a specific topic. The intellectual freedom is liberating, and serves as a portal the door to intellectual creativity. This often translates to my students and postdocs to publish without having me as a co-author of their work. Second, I work hard to create a collaborative and supportive environment for all the people in the lab. I encourage people to interact, especially, to the exclusion of my direct participation. I believe that competition best serves the purpose of motivation when it is externalized and depersonalized, and that collaborative environments provide the right social basis for the free exchange and active development of students' ideas. Finally, I believe that graduate students thrive best when their freedom is supplemented by the necessary logistic and intellectual support. I provide the support in the form of the necessary budget for their work, in the availability of my own time and, when possible, intellectual contribution and in the attention to their progress and wellbeing. I also teach an evolutionary theory course to the lab, which grounds the work of most of the lab and often provides a starting point for the work of my students.

School of Molecular and Theoretical Biology

Over the years, my extensive experience in working with younger students evolved into an extraordinary science outreach program that has been active since 2012. Initially started in Russia through the support of the Dynasty Foundation, my program evolved into an renowned international organization that accepts applications from around the world (see Figure below), attracts research faculty from the best research institutions and provides a model of STEM engagement with younger students. At the core of the school is the integration of selected high school students into real research projects led by invited labs from around the world. The philosophy of educated choice is implemented in providing the students a chance to rote in different labs. They receive support by having a personal adviser that helps them choose a research project appropriate for them. Here are the highlights of our achievements:

1) Over 400 students coming from over a dozen different countries graduated from our program over 7 years of operation.
2) Our alumni go on to study at the best universities of the country from which they are from.
3) More than 50% of our alumni pursue a PhD, MA or equivalent degree, an astonishingly high rate for a high-school program.
4) We have international recognition, among which is a grant from HHMI.
5) Our faculty come from the best research institutions, such as Harvard University, University of Cambridge, and others.

Figure: Geographical distribution of applications to the School of Molecular and Theoretical Biology from 2012 to 2019.

More information about the vision and principles of SMTB, including the research, can be found here: http://molbioschool.org/en/ and www.facebook.com/molbioschool. A broad description of the project can be found in the Howard Hughes Medical Institute bulletin: http://www.hhmi.org/bulletin/winter-2015/immersion-lab