OMIC ENGINE

Newsletter.

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#synbioGR

National Hellenic Research Infrastructure on Synthetic Biology.

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Synthetic microbial ecology: the more the merrier

by Dimitrios G. Karpouzas

Editorial.

Synthetic microbial ecology is the baby born by the coming together of synthetic biology and microbial ecology. It deals with the construction, optimization and application of synthetic microbial communities which could be used for the optimization of biotechnology-driven production systems or for testing ecological theories in the microbial world. Synthetic microbial communities could be constructed based on (a) natural, not engineered, microorganisms or (b) engineered microbial members.

The interest on synthetic microbial communities of non-engineered members increased dramatically over the last few years facilitated by the introduction of powerful omic tools. Metagenomic and comparative genomic analyses suggested an evolutionary drift in bacterial genomes towards auxotrophic lifestyles on energetically costly amino acids and cofactors like B12 (Mee et al., 2014; Shelton et al., 2019), shaping microbial communities in various environments and the human gut (Zengler and Zaramela 2018). These auxotrophies promote strong cooperative interactions between microbes verifying the key functional role of microbial consortia in natural environments.

Synthetic microbial communities are assembled based on bottom-up approaches whereby individual microorganisms are isolated, characterized for their genomic and functional features, they are grown together, and their collective function is followed. Alternatively, natural microbial communities performing a desirable function, (i.e. pollutant biodegradation) isolated from nature, are characterized using metagenomic approaches, their individual members are isolated in pure cultures and they are functionally characterized. Individual microbes exhibiting undesirable features (i.e. antibiotic resistance) that might threaten the stability of the community are rejected, and the synthetic microbial community is reassembled in an optimized form (De Roy et al., 2014).

The reduced complexity, increased controllability and replicability of synthetic microbial communities offer an ideal tool for validating classic or new concepts in microbial ecology like (i) the black queen hypothesis (Morris et al., 2012), (ii) the key role of diversity in microbial community resilience to abiotic stressors (Wittebolle et al., 2009), (iii) the effect of predator richness on prey diversity and ecosystem functioning (Saleem et al., 2012) (iv) the spatial localization of functionally complementary microorganisms in complex environmental settings (Daims et al., 2006).

Synthetic microbial communities have been also used for optimization of biotechnology-driven industrial processes like (i) the recycling of waste products, with the most prominent success story coming from the European Space Agency which designed MELiSSA. This is a biogenerative life support system for the complete recycling of gas, liquid and solid wastes into nitrogen forms that could be exploited by plants and cyanobacteria for food production (Clauwaert et al., 2017), (ii) the production of bioethanol by constructed microbial consortia composed of *Zymomonas mobilis* and *Candida tropicalis,* that exploit the full extent of sugars produced by the enzymatically hydrolysed lignocellulosic biomass, leading to maximum ethanol yields (Patle and Lal 2007) (iii) bioremediation where synthetic

Editorial.

microbial consortia, based on an *Arthrobacter* atrazine-degrading strain and different satellite bacteria selected through metabolic modeling, showed optimum performance in atrazine soil bioremediation compared to monoculture inocula (Xu et al., 2019) (iv) curation of gut-diseases currently relying on fecal transplantation which entail the risk of counter infections by pathogens present in feces. The use of a synthetic microbial community consisting of 33 microbes led to the eradication *C. difficile* infections (Petrof et al., 2013).

Recent advances in synthetic biology allowed the construction of synthetic communities composed of engineered microbes. Engineering a biosynthetic or detoxification pathway in a single cell is often hampered by technical difficulties and metabolic burden imposed to the engineered microbial cell (Wu et al., 2016). In addition, monoculture engineered inocula are more prone to environmental perturbations increasing the possibility of failure in environmental applications. These limitations have promoted the construction of synthetic microbial consortia composed of microbes engineered to serve a specific biosynthetic or detoxification function. This could be achieved through engineering different parts of a multi-modular biosynthetic or detoxification pathway in the different members of the consortium and optimization of signaling, communication and transportation of metabolic intermediates between consortium members (McCarthy and Ledesma-Amaro 2019). To date the application of synthetic consortia composed of engineered microbes is limited to contained applications like (a) biodegradation of complex substrates (b) bioproduction of medicines and biofuels (c) functionalized biomaterials and (d) biosensing.

Synthetic microbial communities could be used in various branches of the agro-food sector in Greece like (i) wineries through the isolation, characterization and assemblage of consortia composed of microorganisms from the microbiome of local vine varieties. Such consortia could be used as starting inocula in vinification for the production of high-quality wines with enhanced local identity (ii) fruit-packaging plants, seed-producing companies, and livestock farms that produce wastewaters with high pesticide or veterinary drugs load. The utilization of synthetic microbial consortia as inocula in dedicated wastewater treatment systems is a viable solution for the reduction of the environmental footprint of such agro-food processing industries.

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Highlights from iGEM 2020 in Greece

iGEM.

2020 has been undoubtedly a very challenging year that affected our lives in multiple levels. iGEM Competition could not remain unaffected. For the first time ever, the Giant Jamboree took place online on 13 – 22 November 2020. 9 days were dedicated in the advances of Synthetic Biology, the amazing effort of 249 teams from all over the globe as well as collaboration and contribution.

The Greek teams managed to develop innovative research projects that can be applied in disease diagnosis and therapy as well as sustainable innovation in industry. The 2020 projects are Morphæ by iGEM Athens, Hippocrates by iGEM Patras and Amalthea by iGEM Thessaly.

A few days before the Virtual Giant Jamboree, we had the pleasure to welcome the Greek iGEM teams, on the first OMIC Webinar. The teams presented their projects and then we discussed their plans for the future. In parallel, Konstantinos Mathiopoulos, OMIC-Engine's coordinator, shared not only his vision regarding Synthetic Biology in Greece but his experience during iGEM 2019, as well. Finally, Athina Milona, European Ambassador of iGEM and iGEM Thessaly 2019 Alumni, presented the plans of the Virtual Giant Jamboree and expressed her warmest wishes for the 2020 teams. Re-watch the first OMIC Webinar, here.

Aiming to promote accessibility in science and society for all, for the first time ever, iGEM teams created exceptional promotion and presentation videos, freely available on iGEM Video Universe. During the Virtual Giant Jamboree, the teams presented their project in posters and judging sessions, while they had the opportunity to watch a plethora of keynote talks and take part in interactive activities shaping the future of Synthetic Biology.

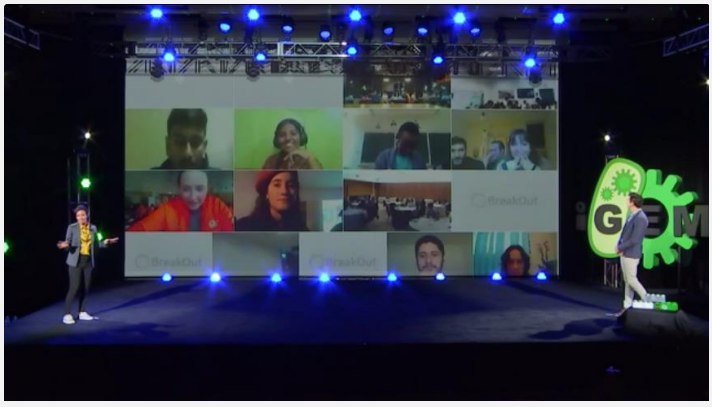
Virtual Giant Jamboree, Photo from Abobe, iGEM Foundation

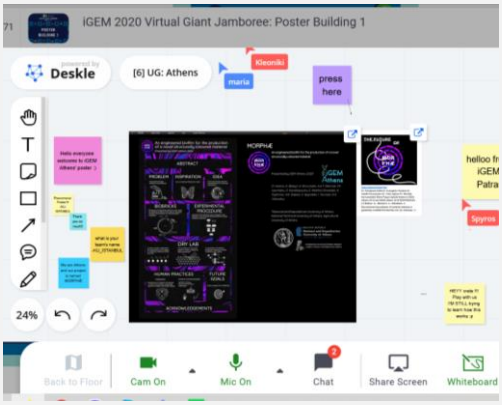
The Greek teams managed to earn a Gold Medal (Thessaly), two Silver Medals (Athens, Patras) and the Best Project Promotion Video community award (Athens). Below we are sharing their experience during the iGEM 2020 journey.

iGEM.

As iGEM Patras is mentioning "one word that could describe this year's competition, is uncertainty". The teams had to drastically change their plans, trying to adapt to the newly formed routine. Nevertheless, the members of iGEM Athens, were not discouraged, on the contrary, they pushed their limits harder. iGEM Thessaly states that "despite, online meetings are not the same as the physical ones, we are really grateful for working efficiently as a team, and for us that is our biggest achievement". On the same ground, iGEM Athens stated that "during this experience, we developed a new research project on our terms, discovered the interesting world of Synthetic Biology and we had the opportunity to learn a plethora of different techniques. Collaborations as well as friendships that were developed through the competition, will remain unforgettable for our team".

"What does iGEM mean to your team", was one of our questions and iGEM Patras mentioned that "iGEM is not just a simple competition. It is an amazing opportunity to make your dream project come true". In parallel, through iGEM, members from team Thessaly managed to discover themselves, their limits as well as the values of interdisciplinary collaboration. iGEM Athens shared with us that "iGEM was a unique opportunity aiming to discover the appropriate tools to express our ideas, while in parallel gave us the chance to propose innovative solutions to crucial societal challenges".



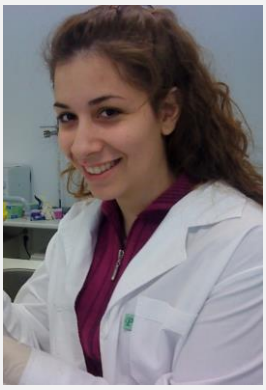


iGEM teams are the best ambassadors for the future of Synthetic Biology. In our question "How do you envision the future of iGEM and SynBio in Greece", all teams hope that more and more Greek participations will enrol in the competition during the upcoming years. iGEM Patras, hopes that High Schools could also participate in the competition, while iGEM Thessaly supports that the intensive collaboration between Research and Innovation initiatives and iGEM teams will bridge the gap between Synthetic Biology research and industry. On the other side of the spectrum, members of iGEM Athens firmly believe that the collaboration between iGEM teams and Greek Academic Institutions, should be established, aiming to make research, more accessible to undergraduate and postgraduate students. On that ground, Synthetic Biology will meet an enormous progress beyond the competition's limits.

We would really like to thank and congratulate all the teams for their achievements and we really hope that iGEM could be established here in Greece. Through this effort, we aim to promote the principles of interdisciplinarity and collaboration in Synthetic Biology research.

Interviews.

Interviewing OMIC-Engine Researchers



Maria Tokamani holds a PhD degree in Molecular Biology and Signalling (Dept. of Molecular Biology and Genetics, School of Health Sciences, Democritus University of Thrace, 2018) and a MSc in Research Methodology in Biomedicine, Biostatistics and Clinical Bioinformatics (Department of Biomathematics, School of Medicine, University of Thessaly, 2019). Her PhD thesis was funded by the EU-funded project CancerTFs (THALIS), focusing on the role of miRs in NFκB / E2F interaction. She was recruited by OMIC-Engine as a post-doctoral researcher to study the AMF community structure using HTS technology.

Contact Maria

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Maria, describe briefly your research work.

In a few words, my work focuses on the study of diversity and structure of AMF communities as affected by a variety of agricultural management parameters. AMF, also known as arbuscular mycorrhizal fungi, are root-associated symbionts in more than 80% of all plants and they inhabit a wide range of soils. Numerous studies have shown the importance of AMF in plant productivity. However, our knowledge regarding the effect of agricultural management and cultivation treatment on the structure of the AMF community is very limited. Armed with the analytical power of NGS technology, we study the AMF diversity in the soil of corn plants root system under several conditions and treatments. Our aim is to identify the optimal combination of AMF and agricultural management in order to maximize production and save resources.

Which opportunities did your secondment offer you in terms of training, networking and personal growth?

The opportunity to work in OMIC-Engine infrastructure was one of the best next-steps I could follow for my personal growth. Through this project, I challenged myself, I enhanced my laboratory and management skills, and developed new computational ones, and all that in a very friendly work environment, in Dr Sandaltzopoulos and Dr Grigoriou labs. Also, I was introduced in a new field of research, environmental biology, in which molecular techniques can offer answers and a fresh point of view. Last but most important, OMIC-Engine, as a multi-institutional collaboration, offers the chance to build a strong network of the most experienced people in the field. I met prospective mentors and partners, and gained access to the necessary resources that will foster my career development.

Interviews.

What do you think will be the impact in your future career?

Four critical parameters for career development are dedication, passion, skills and networking. Passion and dedication originate from the individual. However, one also needs opportunities to develop skills and to build a network. OMIC-Engine offered me the chance to acquire training and experience of the cutting-edge technology of NGS. This secondment gave me the opportunity to catch up with the new era of metagenomic and environmental research. On the other hand, OMIC-Engine helped me build and maintain a strong network within the infrastructure, granting ample opportunities to advance my career. It gave me collaborative skills and creativity, inspired new ways of thinking, and increased my odds of learning something new.

Has this secondment experience matched your expectations so far?

To be honest, my expectations were not very bold, but I did have expectations from myself. I expect myself to achieve the maximum possible and qualitatively excellent result. In my PhD thesis, I focused on human research, but the past two years I have entered in the completely different world of environmental research and agricultural development, which was completely unknown to me. After many months of effort and studying, enthusiasm and passion were born regarding the applications of our findings in everyday life. Therefore, if I had a single expectation from this study, it would be satisfaction, and I full-heartedly say that this has been adequately fulfilled! There is no as awesome a feeling as discovering something after months of laboratory work!

Three words that sum up your experience within the OMIC-Engine infrastructure.

Challenging... Innovative... Satisfactory...

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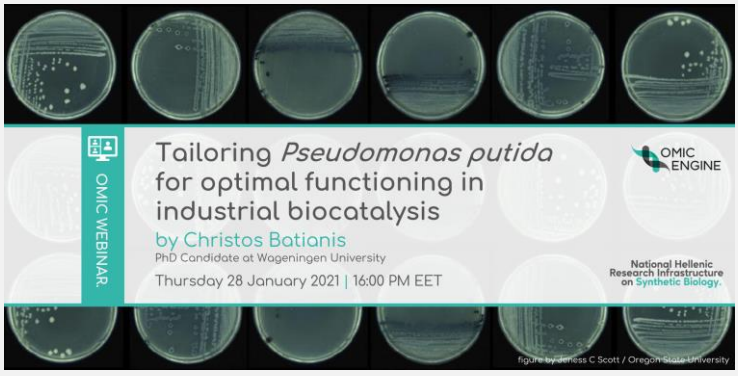
Outreach.

OMIC Webinars

Back in November we launched a new series of online events!

In our first Webinar we dove into the world of the iGEM Competition and welcomed the 2020 Greek iGEM teams from Athens, Thessaly and Patras.

Re-watch the Webinar



OMIC Webinar #2

by Christos Batianis

In our second OMIC Webinar we welcomed Christos Batianis, PhD Candidate at the Laboratory of Systems and Synthetic Biology of the Wageningen University in the Netherlands. During the speech, we had the opportunity to discuss the principles and current challenges of metabolic engineering, focusing on how organisms can be engineered for industrial level production of specific chemicals.

Re-watch the Webinar

Subscribe to our YouTube channel.

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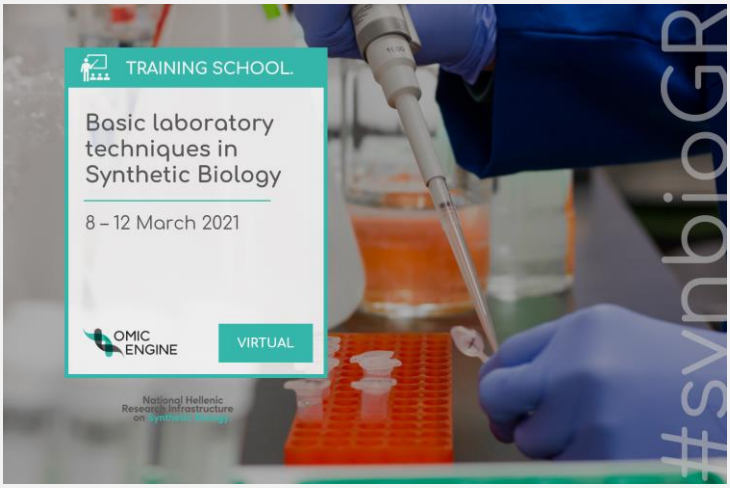
Education.



Training School

On the second week of March we are organising a Virtual Training School on "Basic laboratory techniques in Synthetic Biology".

Learn more

During this free online course, through the combination of theory and practicals, participants will have the opportunity to dive into the basic methods used in Synthetic Biology research as well as discover their applications on the field of agriculture. This educational course will focus on covering the core principles of cloning strategies, exploitation of CRIPSR/Cas9 technology as well as protein expression and purification. Finally, participants will be introduced in metagenomics and its usage in environmental samples.

Publications.

Check out our recent publications in peer-reviewed journals

Garagounis C., Beritza K., Georgopoulou M.-E., Sonawane P., Haralampidis K., Goossens A., Aharoni A., Papadopoulou K.K., "A hairy-root transformation protocol for *Trigonella foenum-graecum L.* as a tool for metabolic engineering and specialised metabolite pathway elucidation", Plant Physiology et Biochemistry. https://doi.org/10.1016/j.plaphy.2020.06.011

Vasilopoulos V., Pitou M., Fekas I., Papi R., Ouranidis A., Pavlidou E., Patsalas P., Choli-Papadopoulou T., (2020) "Graphene-Wrapped Copper Nanoparticles: An Antimicrobial and Biocompatible Nanomaterial with Valuable Properties for Medical Uses", ACS Omega. https://doi.org/10.1021/acsomega.0c00834

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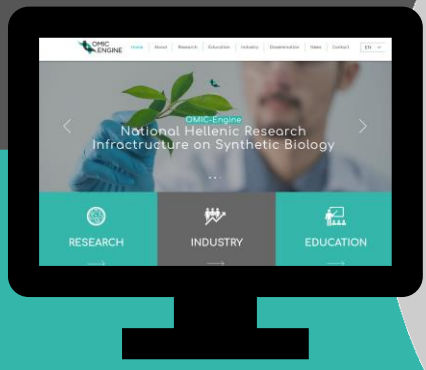
News.

Check out our new website!

www.omicengine.com



- More news
- Training opportunities
- Job positions
- Upcoming events
- New publications
- New services

National Hellenic Research Infrastructure on Synthetic Biology.

New Projects.

FOODBIOMES - Infrastructure of Microbiome Applications in Food Systems

Coordinator: Associate Prof. Y. Kourkoutas | ikourkou@mbg.duth.gr

FOODBIOMES aims at the utilization of microbiome applications in food systems to enhance their functional action, the production of new products with beneficial effects and superior quality, the documentation of food authenticity, the improvement of traditional production and processing techniques and the generation of new knowledge on the effect of innovative ingredients on the microbiome and human health. In this vein, FOODBIOMES will focus on the isolation of health-promoting microorganisms and bioactive components for the production of novel functional food ingredients that will be further tested in nutritional interventions in both animal models and in human volunteers. FOODBIOMES aims to become a Centre of excellence for research, education and innovation, connecting local actors with scientific Institutions at international and European level, also playing an important role in training and upgrading local human resources and industry, strengthening, at the same time, the economy of the remote and island Regions of Eastern Macedonia & Thrace, Epirus, North Aegean and Ionian Islands.

Exploitation of the microbial terroir of the "Pavlidis Winery" for the promotion of the distinct quality characteristics of the local wines – PavlidisTerroir.

Coordinator for MBG-DUTH: Prof. M. Grigoriou | mgrigor@mbg.duth.gr

Sensory quality plays a key role in the introduction of a wine product in the market, as it constitutes probably the main factor for distinction among other similar-type products, thus providing added value, in addition to a tool for active promotion. However, in industrial wine fermentation, the use of commercially available starter cultures has, to a large extend, deprived of the produced wines, the special organoleptic properties associated with indigenous microorganisms which are found on the grapes and reflect diverse environmental conditions, as well as management of the vineyard. PavlidisTerroir will combine molecular methodologies with classical microbiology approaches to identify, isolate and characterize indigenous yeasts from Pavlidis vineyards that will be tested for the production of novel wine products with distinctive, regional sensory characteristics.

Agro4+ - Holistic approach to Agriculture 4.0 for young farmers

Coordinator for MBG-DUTH: Prof. M. Grigoriou | mgrigor@mbg.duth.gr

Agro4+ aspires to be a major pillar of smart farming through the development of applications and cutting-edge services strengthening, thus, the economy and connecting it with research and innovation at regional level, in East Macedonia-Thrace, but also at National, European and International level. Using analytical approaches and modern applications of molecular biology and combining them with intangible, digital electronic approaches, Agro4+ will develop automated processes at the level of production and management of vineyards of East Macedonia-Thrace.

New Projects.

Within Agro4+ the collaborating laboratories of the Department of Molecular Biology & Genetics of Democritus University of Thrace, will utilize technologies developed within the National Infrastructure OMIC-Engine, to build on a series of molecular applications and diagnostic services related to food authentication, identification and/or certification of varieties and products and characterization of disease-related or resistance biomarkers.

ARISTO: The European Industry - Academia Network for Revlsing and Advancing the Assessment of the Soil Microbial TOxicity of Pesticides

Coordinator: Dimitrios G. Karpouzas | dkarpouzas@bio.uth.gr

ARISTO is an International Training Network (ITN) funded by the European Union's Horizon 2020 research and innovation programme under Marie Skłodowska-Curie grant agreement. Pesticides are major environmental pollutants. For this reason, the European Commission has imposed a stringent pesticide regulatory scheme for pesticides authorisation, where risk assessment for aquatic organisms and terrestrial macro-organisms is well defined. In contrast the assessment of the toxicity of pesticides on soil microorganisms is lagging behind, still relying on an outdated protocol which fails to identify effects on key microbial functions and on microbial diversity, which can now be accurately determined through advanced and standardized methods introduced in soil microbiology in the last 10 years. EFSA identified soil microorganisms as an attribute to monitor during pesticides environmental risk assessment and stressed the need for novel tests to assess the toxicity of pesticides on soil microorganisms. The ARISTO project will fulfil this scientific and regulatory gap through a unique doctoral program, based on the strong interaction of academia and industry, aiming to train the next generation of Microbial Ecotoxicologists. These will produce benchmarking knowledge supporting the development of advanced tools and procedures, based on the response of key microbial indicator groups, for the comprehensive assessment of the toxicity of pesticides on soil microorganisms. ARISTO offers doctorate fellows a challenging training program build along 5 research objectives: (1) to develop pioneering *in vitro* tests, as a first conservative step, to assess the toxicity of pesticides on distinct ammonia-oxidizing microorganisms and arbuscular mycorrhizal fungi (2) to develop advanced lab and field tests to assess the toxicity of pesticides on natural soil assemblages of AOM and AMF, as a more realistic toxicity assessment step; (3) to develop an ecosystem-level toxicity assessment looking at pesticide effects at microbial networks and across different trophic levels along the soil food web (predator - prey); (4) to develop novel tools to determine the soil microbial toxicity of pesticide mixtures, and bio-pesticides; (5) to develop and validate advanced *in silico* tools for prioritizing pesticide transformation products with potential toxicity to soil microbes.

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OMIC-Engine is implemented under the Action "Reinforcement of the Research and Innovation Infrastructure" funded by the Operational Programme "Competitiveness, Entrepreneurship and Innovation" (NSRF 2014-2020) and co-financed by Greece and the European Union (EU Regional Development Fund)

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