



Colloque 12-13-14 Octobre 2015

Institut des Systèmes Complexes Paris Île-de-France
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Approches théoriques et modélisation de la diversité biologique et résilience dynamique des systèmes complexes organisés multi-échelles : du système immunitaire aux macro-écosystèmes.

La relation entre biodiversité, variabilité, adaptabilité et résilience des systèmes vivants, soumis aux perturbations imprédictibles caractéristiques des systèmes complexes, quelles que soient leurs échelles, doit être questionnée, même en l'absence de mécanismes causalistes identifiables.

La rencontre interdisciplinaires entre biologistes, immunologistes, écologues, philosophes, mathématiciens, physiciens, informaticiens permettra l'étude des concepts de diversité et de variabilité dans le vivant adaptatif et de leurs rôles dans la résilience des systèmes vivants multi-échelles et organisés.

Le système immunitaire adaptatif en cognition de l'environnement moléculaire des êtres vivants a co-évolué pour permettre la tolérance ou destruction de tissus et du microbiote et présente une biodiversité cellulaire et moléculaire exceptionnelle. Ces systèmes représentent des modèles d'étude de l'organisation et variation de systèmes dynamiques multi-échelles tout comme les écosystèmes macroscopiques.

Il s'agira donc à travers les échelles des systèmes étudiés d'établir les modalités de synergie entre biodiversité et résilience ou robustesse.

Organisateurs

Véronique Thomas-Vaslin
Maël Montévil

Comité scientifique

Frédéric Jacquemart
Giuseppe Longo

Approches théoriques et modélisation de la diversité biologique et résilience dynamique des systèmes complexes organisés multi-échelles : du système immunitaire aux macro-écosystèmes.

12 octobre 2015

9:00	Frédéric Jacquemart	A la recherche de la source de sens
10:00	Nicolas Bouleau	Faire entrer les craintes dans le travail scientifique : réduction d'un être-question
11:00 café		
11:30	Alain Le Méhauté, Philippe Riot	'Relation entre résilience et approche catégorique de la conjecture Riemann'.
12:30 buffet		
14:00	Sophie Martin/isabelle Alvarez	« Illustrations de mesures de résilience et de robustesse dans le cadre de systèmes dynamiques contrôlés »
15:00	Maël Montevil	Biological organization and variation
16:00 café		
16:30	Giuseppe Longo	How Future Depends on Past Histories in Systems of Life
17:30	Discussion générale	

13 octobre 2015

9:00	Philippe Seksik	Microbiote and resilience
10:00	Véronique Thomas-Vaslin	Lymphocyte repertoire diversity and resilience: effects of perturbations a aging on the immune system
11:00 café		
11:30 short communications	Nicolas Derian	Inter-individual variability in gene expression
	Wahiba Chaara	Diversity and variability of lymphocyte repertoires
	Barbara Bravi	Biology: from Noise to Functional Randomness
12:30 buffet		
14:00	Table ronde 1	Resistance and resilience of complex ecologic systems
15:00	Guillaume Achaz	"What processes generate the observed genetic diversity ?"
16:00 café		
16:30	Jane Lecomte, François Sarrazin	Dépasser l'anthropocentrisme de nos regards sur la biodiversité: un saut évolutif?
17:30	Hugues Bersini	« What makes a complex system vulnerable ? »
18:30	Discussion générale	

14 octobre 2015

9:00	Victor Lefèvre	La stabilité des écosystèmes est-elle le fruit de mécanismes actifs régulation ?
10:00	Claire de Mazancourt, Jean-François Arnoldi,	Biodiversity and invariability: from populations to ecosystems.
11:00 café		
11:30	Pierre Collet	Evolution, évolution artificielle et diversité
12:30	Table ronde 2	« Mécanismes de synergie entre biodiversité et résilience ou robustesse »

Objectives of the meeting

Concepts and multi-scale exploration of biological diversity:

Living and diversified organisms integrate **macroscopic whole** communities and ecosystems (biosphere, eco-systems, social and cultural networks) as well as **microscopic** complex systems from polygenomic origins (cells, lineages, receptors, molecules, microbes...). Following organisation principles, **complex systems** are always multi-scale, self-assembling, adaptive dynamic and cognitive networks of diverse interacting structures with inter-relationships in time and space through processes and cascades of events, capable of sensing patterns with degenerative properties and memory. These multi-scale spatio-temporal networks are organized, dynamical, variable and highly diversified systems and sub-systems, reacting to **perturbations** and thus evolving through **unpredictable possible choices, adaptations and selection**. We are confronted to alarming signals from ecological crises on various scales, such as climate change, pollution, chemicals, biotechnologies, diseases. Various levels of the living are affected which is exemplified by the alteration of species biodiversity but also of food, increase in inflammatory, auto-immune allergies and cancer diseases related to immune systems and microbiote dysfunction. It is time to question the origin, function and evolution of biodiversity at various scales in the behaviour of systems and their resilience.

The relationship between biodiversity, variability and resilience of living systems, submitted to unpredictable perturbations of complex systems, should be questioned independently of the scale of the systems, even if causals mechanisms could not be identified. The resilience and robustness of complex systems to perturbations is related to the historicity and dynamics of evolutionary systems. This questions the role of diversity and aging in resilience processes after perturbations of complex systems, where reductionist and linear causal approaches are insufficient. Interdisciplinary interactions and discussions between researchers involved in biology, ecology, evolutionary ecology, immune system, philosopher, mathematicians, physicists and computer scientists should help to structure thoughts and deepen reflexions on the co-evolution of the diversity in biology from ecosystems, species, to immune systems, through the notions of biological organization, evolutionary and ontogenetic historicity, aging, and resilience from microscopic to macroscopic levels.

Multi-scale living systems evolve and age in a context of finitude, heterogeneity and variation, leading to indecidability and incompleteness. The aim of the colloquium is to trigger a multidisciplinary reflexion on the organisation, evolution, variation of living systems and the potential role of diversity on resilience after perturbations and aging. The level of organisms that are cognitive organisation where measurements are currently done could help in this reflexion. In each organism, while the nervous system insures the cognition and perception of "self" and external environment at macroscopic scales, defining ego and consciousness, the adaptive immune system is a cognitive, dynamic and anamnestic system, sensing the quality and quantity of microscopic patterns. This "immunoception" perceives antigenic diversity and allows defining the temporal identity of the organism within micro/macroscopic environment that is permanently changing. In metazoan organisms the cognitive immune system presents an exceptional diversity at the level of cells and molecules and represent a prototype model of diversity. In particular in Gnathostomes the somatic diversified immuno-receptor repertoires of B and T lymphocytes constitute an adaptive evolving memory system in direct cognition with the diversity of antigens, microbes and molecules derived from food, issued from plants and animal co-evolution and where dynamic tolerance should be maintained to insure the life of every organism.

In the first part philosophical notions and the meaning of terms "biodiversity" and "resilience" their relation to dualism, categories, "être question" and historicity will be discussed in relation to variation and diversity in evolving living systems, leading to the notions of organisation and their characteristics.

In the second part, the effects of perturbations, aging of systems, disorganization and their resilience will be discussed in particular in relation to biodiversity. Examples in various micro-to macro domain from physics, ecology to microbiotes and immune systems will be used to guide the discussion.

This colloquium should allow the emergence of new interdisciplinary collaborations and reflexions between biologists, ecologists, immunologists, physicians, physicists, mathematicians and philosopher that are rarely in contact. Analysing the consequences of perturbations and the resilience (or not) of our multi-scale complex environment is an urgent reflexion scientist should have together.

<p>Frédéric Jacquemart : Docteur en médecine, spécialiste de biologie médicale, docteur es sciences es immunologie, président du GIET, co-pilote de la mission biotechnologies de FNE, ancien membre du Haut Conseil des Biotechnologies (HCB).</p>	<p>A la recherche de la source de sens- Les termes du discours émergent et prennent sens dans le cadre d'un contexte culturel « déjà-là ». La source de sens est généralement subie comme un a priori hors de tout regard. Les termes de biodiversité, de résilience, qui font les objets principaux de cette rencontre auraient-ils un sens par eux-mêmes, un sens absolu ? La question « qui parle » s'avère être essentielle. Nous nous efforcerons d'introduire l'idée d'une source de sens émergente, délocalisée dans le temps et dans l'espace, propre au moins à une discussion de ces a priori.</p>
<p>Nicolas Bouleau : Chercheur émérite, mathématicien et philosophe, ancien directeur de recherches et professeur à l'École des Ponts ParisTech, chercheur associé au CIRED (Centre International de Recherche sur l'Environnement et le Développement)</p>	<p>Faire entrer les craintes dans le travail scientifique : réduction d'un être-question : Si on réfléchit à l'éventuel, les outils du positivisme sont insuffisants. Il y a lieu de prendre en compte des craintes (ou espoirs) en tant qu'êtres supposés. Le travail scientifique sur un être-question consiste à mettre à l'épreuve progressivement les propriétés de cet être supposé pour éventuellement le récuser comme inconsistant, ou au contraire le garder comme un souci durable. La disparition des mammifères marins, les effets des faibles rayonnements, les perturbateurs endocriniens, sont des êtres-questions, également le calorique, l'éther, le boson de Higgs, le prion, l'ont été pendant le temps de leur clarification et le sont encore pour certaines de leurs propriétés. Exemples historiques et actuels. Un être-question touche toujours à des orientations politiques, souvent il naît dans la société civile, mais l'étude de sa cohérence est un travail scientifique, d'autant plus difficile d'ailleurs qu'il s'effectue nécessairement en interaction avec une inquiétude sociale.</p>
<p>Alain Le Méhauté*, Philippe Riot, Institut Franco Québécois Paris 41 rue Jacob 75006 Département de Physique, Université Fédérale de Kazan, Tatarstan Russie.</p>	<p>'Relation entre résilience et approche catégorique de la conjecture de Riemann': Une étude détaillée de la conjecture de Riemann à la lumière de la théorie des catégories confirme tout à la fois l'universalité de la fonction de Riemann et son auto similarité. Cette dernière propriété confère à toute dynamique analytique contrôlée par des équations différentielles fractionnaires (liées aux propriétés précédentes via les groupes hyperboliques) une stabilité dont l'exceptionnelle efficacité et adaptabilité tiennent à une dualité macro-dynamique. On montrera comment les symétries associées aux liens alors particuliers entre macro-micro entraînent la résilience de systèmes complexes et comment celle-ci peut être détruite lorsque la dynamique devient purement stochastique.</p>

<p>Sophie Martin http://sophie.martin.perso.free.fr/</p> <p>Isabelle Alvarez http://www.lip6.fr/actualite/personnes-fiche.php?ident=P4</p>	<p>Illustrations de mesures de résilience et de robustesse dans le cadre de systèmes dynamiques contrôlés</p> <p>Concepts of robustness and resilience are related to the ability of a system to maintain or restore properties despite disruptions caused by perturbations. From models of socio-ecological systems including their dynamics and the properties at stake, values of robustness and resilience should provide information on the impact of a possible disturbance on the system ability to maintain certain properties: the maximal perturbation intensity a system can support now and in the future without loosing these properties is a matter of robustness, while given sets of anticipated disturbances resilience is concerned with the possibility of restoration and its cost.</p> <p>We propose tools to evaluate robustness and resilience when models are made of controlled dynamical systems. Robustness and resilience can then be combined to identify (within the model hypothesis) dangerous areas which are very sensitive to perturbations.</p>
<p><u>Giuseppe LONGO</u>, mathématique et informatique, <u>Centre Cavaillès</u> (République des Savoirs, UMR 3608), <u>CNRS, Collège de France & Ecole Normale Supérieure</u>, Paris (équipe: "Complexité et information morphologiques").</p> <p>Transitions théoriques mathématiques/physique/biologie ; phylogénèse vs. ontogenèse; temps biologique et transitions critiques ; aléatoire et l'incomplétude descriptives en mathématique, physique et biologie ; enablement.</p>	<p>How Future Depends on Past Histories in Systems of Life¹</p> <p>The dependence on history of both current and future dynamics of life is a common intuition in biology and in humanities. This talk hints to a rigorous analysis of "path dependence", which may be found also in physics, in terms of invariants and invariance preserving transformations. The idea is that the (relatively) invariant traces of past ecosystemic transformations contribute to the "determination" of present and future state of affairs and introduce by this a peculiar form of unpredictability (or randomness) in biology, at the core of novelty creation. This applies a fortiori to cognitive and historical human dynamics.</p> <p>¹Partly supported by the IEA-Nantes project "Lois des dieux, des hommes et de la nature": http://www.di.ens.fr/users/longo/CIM/ProjetLongo2014-17.pdf</p>
<p><u>Mael Monteveli</u> : Chercheur en biologie théorique, post-doctorant au laboratoire Matière et Systèmes Complexes (Paris Diderot), et associé à l'IHPST (Institut d'Histoire et de Philosophie des Sciences et des Techniques), Etudie les principes d'organisation, d'historicité, de variation et d'adaptabilité dans le vivant : aspects philosophiques et mathématiques permettant d'analyser des transitions critiques et instabilités- organisation, variation</p>	<p>Biological organization and variation</p> <p>We argue that a theory of biological systems should rely on organization and variation as fundamental theoretical principles. Biological systems are organized natural systems that undergo functional variation. In this presentation we will provide a specific characterization of each principle while emphasizing their mutual relations. Organization provides the relevant kind of complexity for functional variation to occur; and, in turn, variation enables the maintenance of organization over time, notably at the evolutionary scale.</p>

<p>Pr. Philippe Seksik Directeur de l'U1157 INSERM. Sorbonne Universités-UPMC Univ Paris 06, INSERM ERL 1157, AP-HP, Hôpital Saint Antoine, CNRS UMR 7203 LBM, CHU Saint-Antoine- Paris PU-PH de Gastroentérologie Hôpital St-Antoine, Service de Gastroentérologie et Nutrition, F- 75012, Paris philippe.seksik@sat.aphp.fr http://www.labos.upmc.fr/lbm/eq4/lbm-eq4.html</p>	<p>Microbiote and resilience : The human gut contains 10^{14} bacteria and many other micro-organisms such as Archaea, viruses and fungi. This gut microbiota has co-evolved with host determinants through symbiotic and co-dependent relationships. Bacteria, which represent 10 times the number of human cells, form the most depicted part of this black box owing new tools. Re-evaluating the gut microbiota showed how this entity participates to gut physiology and beyond this to human health. Studying and handling this real 'hidden organ' remains a challenge for clinicians. Besides its biodiversity, gut microbiota major characteristics are stability over time and resilience after perturbation. We will examine how ecology helps to define resilience in this setting. We will explore mechanisms and consequences of this particular characteristic when taking into account gut microbiome in medical science.</p>
<p>Véronique Thomas-Vaslin : Docteur en Immunologie, Chercheur au CNRS (CNRS FRE3632 UMRS UPMC INSERM, Labex Transimmunom): Immunologie intégrative, modélisation de la dynamique et diversité du système immunitaire https://www.i3-immuno.fr/en/#People/VTv</p> <p>Porteur du réseau ImmunoComplexiT http://www.immunocomplexit.net/</p>	<p>« Lymphocyte repertoire diversity and resilience: effects of perturbations and aging on the immune system » : The generation of somatic diversity and selection of lymphocytes in time and space in high vertebrates is an example of an evolutive selective processes occurring in a microscopic ecosystem connected to the antigenic environment. Observing the organization of the immune system from mice suggests a progressive connection and integration of lymphocytes during the ontogeny, allowing for the maintenance of the integrity of the poly-genomic organism. However, disorganisation occurs through aging, related to multi-scale alterations, from adipocyte accumulation and energy dissipative reduction to structural tissues and cell disorganization, quantified by an increase of perturbations, inter-individual variability and a decrease in immuno-receptor diversity. Computer modelling of perturbations shows that the immune system of young individuals is diversified and resilient to transient perturbations. However, similar perturbations in old mice accelerate aging and reduce the repertoire diversity with unpredictable lymphocyte clonal expansions, reducing the potential immunocompetence of the organism. This questions the relation between diversity, organisation and resilience of live systems.</p>

<p>Nicolas Derian : PhD student UPMC (CNRS FRE3632 UMRS UPMC INSERM).</p>	<p>Inter-individual variability in gene expression. The primary roles of the immune system is to recognize pathogens and react accordingly to the nature of the pathogen. The immune system contains a vast collection of cell populations having specific roles in the immune process. It has been shown that at the level of cell populations, looking at the transcriptome (the collection of products of gene expression process) across many individuals lead to an important inter-individual variability for the genes specifically involved in the immune system regulation. The inter-individual variability is then important to insure a large panel of recognition sensibilities leading to the adequate answer against the pathogen in at least some individuals within the population, insuring the survival of the specie. When measuring the inter-individual variability in the immune-related cell populations, it is sensible to stimuli, large in healthy state, it globally decreases in patient with infections. Looking at the inter-individual variability of the transcriptome of immune-related cell might lead to new insights in the biological processes involved in the immune response.</p>
<p>Wahiba Chaara : PhD student UPMC (CNRS FRE3632 UMRS UPMC INSERM),</p>	<p>Diversity and variability of lymphocyte repertoires The immune system is a complex and dynamic system characterized by a great number of heterogeneous entities and evolving during the life of the organism. The lymphocytes, including T-lymphocyte, are key actors in this system because they allow specific recognition of antigens in the body and therefore the induction of adaptive immune responses, influenced by the environment. Each T-lymphocyte expresses on its surface a unique receptor, called TCR, which ensures the specificity of antigen recognition. Thus, the TCR repertoire of a T-cell population at a given time determines the repertoire of antigens it can recognize and thus its capacity to develop an adaptative response. The TCR repertoire diversity emerges from series of somatic gene rearrangements occurring during the T-lymphocyte thymic differentiation. However, while the potential number of TCR being generated by this process amounts to 10^{15}, the actual number of T-lymphocytes in the human body for example is well below (10^{12}). Characterizing the T-cell population diversity through their TCR repertoire is thus crucial to understand the evolution of an individual immune system during its development, aging or in case of pathology.</p>

Barbara Bravi, Marie Curie Early Stage Researcher and PhD candidate at King's College London (department of Mathematics). My current research topics are statistical physics approximations and mathematical models for metabolic and regulatory networks in biology.

Biology: from Noise to Functional Randomness

In biology, phenotypes' variability stems from stochastic gene expression as well as from extrinsic fluctuations that are largely based on the contingency of developmental paths and on ecosystemic changes. Both forms of randomness constructively contribute to biological robustness, as resilience, far away from conventional computation frameworks, where elaboration and transmission of information are robust when they resist to "noise". We discuss common tools for the analysis of unpredictability within some mathematical formalisms, from the Langevin approach to the Fokker-Planck equation for diffusion, to limit theorems of probability theory related to the Law of Large Numbers. In biology, though, randomness acquires a peculiar status as it is inherent to the variability, adaptivity and diversity of life, as crucial components of its structural stability. Stochastic gene expression is introduced as striking example that already provides hints towards a novel, hopefully more proper, definition of biological randomness. Finally we argue that the notion of "extrinsic noise" allows one to grasp the importance of history and contexts in the structure of determination already at the molecular level.

Guillaume Achaz : UMR7205 (ISYEB), équipe Atelier de Bioinformatique, MNHN, Paris UMR 7241 (CIRB),
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"What processes generate the observed genetic diversity ?" Since the advent of the neutral theory of molecular evolution, the amazing genetic diversity one can observe within groups of mating individuals (ie. a species) is typically interpreted in the light of a single reference model. The so-called standard neutral model was proposed at a time where genetic data were hardly accessible. Although there are several arguments in favor of this model, it may well be the case that the use of a single reference model obscures our ability to apprehend the world as it is. Indeed as any model is doomed to be false, it would more adequate to consider not one, but several models that are grounded on the structure of genetic diversity we observed today. I will striking illustrate this claim by few chosen biological examples.

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Dépasser l'anthropocentrisme de nos regards sur la biodiversité: un saut évolutif? L'érosion actuelle de la biodiversité tarde à être freinée malgré les nombreuses initiatives en ce sens, dont certaines s'appuient de plus en plus sur la notion de services apportés par la biodiversité au bien être humain. L'anthropocentrisme semble alors être un horizon indépassable, au moins d'un point de vue pragmatique, pour répondre à cet enjeu. Cependant, si les interactions entre les humains et le reste de la biodiversité – les non humains – sont issues de trajectoires sociales et culturelles, elles sont aussi issues de nos trajectoires évolutives conjointes qui mériteraient d'être considérées pour mieux comprendre les inerties actuelles dans nos modes de perceptions et d'actions sur la biodiversité. Nous introduirons cinq scénarios des trajectoires humains/non humains qui dépendent de différentes valeurs intrinsèques ou instrumentales apportées au reste du vivant. Notre grille de lecture qui vise à considérer sciences humaines et approches évolutives nous apparait susceptible de générer de nouvelles perspectives de recherche, de recommandations d'action de conservation et de prise en compte des contraintes et enjeux de leur mise en œuvre.

<p>Hugues Bersini : Professor in Université Libre de Bruxelles and Co-Director of the IRIDIA laboratory http://iridia.ulb.ac.be/bersini/</p>	<p>« What makes a complex system vulnerable ? » Needless to say, the immune system is both complex and vulnerable. Why makes a simple system switches to a complex one is: the non-linearity of the interactions, the non-homogeneity of the interaction topology (some biological nodes are much more connected than others) and, above all, the gradual substitution of a linear causality by a circular one (in the presence of many positive and negative feedback loops). This latter reinforces the behavioral autonomy of these systems (as compared with the importance given to external impacts) and gives rise to the most intricate dynamical regimes such as multi-stability, cycles or chaos. Those well-known insights coming from physics and computer sciences allow shedding new lights on these systems vulnerability: the self-organization of a homeostatic/viable regime, the possibility to autonomously getting closer to bifurcation frontiers and the elimination of strategic nodes. The talk will remind those classical physical facts and how, for more than 30 years, they considerably influence how my inspirers (Coutinho, Varela, Stewart) and myself perceive immune system.</p>
<p>Victor Lefèvre : Doctorant en philosophie de l'écologie, Institut d'Histoire et Philosophie des Sciences (IHPST/Paris 1).</p>	<p>Explaining the stability of living beings: from organisms to ecosystems and back again Ecosystems and organisms are dissipative systems which must maintain themselves at every moment against the tendency to reach thermodynamic equilibrium and disturbances. Organisms manage this double challenge due to their organizational closure and their regulatory mechanisms. Is the stability of ecosystems explainable analogously? And conversely, can the models of theoretical ecology help to explain the stability of organisms?</p>
<p>Jean-François Arnoldi, PhD (Mathematics) Postdoctoral researcher Claire de Mazancourt, CR1 CNRS Centre for Biodiversity Theory and Modeling. Webpage: http://www.cbtm-moulis.com/m-198-jean-francois-arnoldi.html</p>	<p>Biodiversity and invariability: from populations to ecosystems. Stability is a notion of central interest in ecology. Different definitions and interpretations of stability exist, depending, amongst other things, on the level of ecological organization. In the context of interacting species there are two major levels of organization: the population and the ecosystem level. The first one focuses on the dynamical behavior of a set of species, while the ecosystem level describes global properties of these communities that can be conserved through community change. Classical stability theory based on the rate of return to equilibrium is a population-level stability measure that cannot address the stability of ecosystem level properties such as total biomass. We present a new theory, based of temporal invariability, which is flexible across levels of organization. It relates to the abstract notion of structural stability. It matches empirical measurements and corroborates the empirically observed stabilizing effect of biodiversity at the ecosystem level. It sheds new light on the mechanisms through which diversity stabilizes ecosystems.</p>
<p>Pierre Collet Professeur à l'Université de Strasbourg. Evolution artificielle, optimisation stochastique et des mécanismes inspirés de la nature, Coordonne (avec Cyril Bertelle) le Complex Systems Digital Campus, UniTwin de l'UNESCO présidé par Paul Bourgine, réunissant plus de 120 universités dans 28 pays.</p>	<p>Evolution, évolution artificielle et diversité L'évolution est l'une des grandes lois de la nature. Elle régit aussi bien le vivant que le non-vivant, le matériel et l'immatériel, les idées et la société. L'intérêt de l'évolution artificielle est qu'en implémentant des mécanismes évolutionnaires dans les ordinateurs, on peut jouer avec les concepts sous-jacents et en voir les effets sur des problèmes jouets. Ainsi, l'une des premières choses que l'on remarque est qu'une population qui a convergé (dont tous les individus sont devenus semblables) ne se re-diversifie plus. L'impact de cette observation est très grand si l'environnement dans lequel évolue la population étudiée est dynamique.</p>



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