The CEA and Covid-19
Resilience and responsiveness

Resilience and responsiveness: retrospective of an unusual year

The pandemic affecting France for a year now has led public and private stakeholders to take action in line with their possibilities and skills.

The CEA's status in the field of research and innovation in France, its proximity with State public safety issues and its unique working environment have enabled it to react quickly across the board.

Historically, the CEA has long had a foot in both camps - civil and defence - not to mention a strong base in fundamental research (especially biology) and a wealth of experience in developing technologies for transfers to its industry partners. It has therefore been able to rely on collaborations with its partners (research organisations, universities, hospital departments, companies and local authorities) in France and Europe alike, as well as on the responsiveness of its staff and the flexibility of its resources. The CEA's strong nuclear safety and industrial safety culture, together with its emergency preparedness have made it easier for its teams to take action under these exceptional circumstances, by placing all sensitive facilities (test reactors, clean rooms, etc.) in secure conditions and defining suitable operating schedules adapted to the restricted conditions.

Lockdown and the widespread implementation of 'working from home' have proved complex when research requires access to laboratory equipment or for activities dealing with highly sensitive information that cannot be taken outside secure premises. Faced with such situations, the teams managed to reconfigure their activities so they could continue supporting the state and industry partners by organising rotating schedules and implementing very strict rules to comply with Covid safety measures and data confidentiality. Key clients in industry have expressed their gratitude for our continuous services under such difficult circumstances, and the French Minister of the Armed Forces even thanked the CEA for its efforts in meeting its defence-related milestones. This is how the CEA has been able to provide a swift response in fields

directly related to the pandemic (new devices for protection, diagnosis, therapeutic research, vaccine prevention and approaches, and pandemic models) without sacrificing its main research programmes underway.
Knowledge and scientific communities have been mobilised beyond the field of health, particularly to support strategic value chains; this has been possible by relying on ongoing or short-term cooperation agreements, which have proven to be essential.

Nothing would have been possible without this cooperation with our partners who are simply too numerous to mention here. Rather than mention only a few to the detriment of the rest, we have chosen to cite no one; they will know who they are and recognise our gratitude.

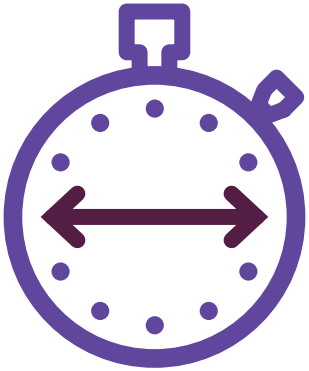
The Covid-19 pandemic has reminded us of three fundamental principles for maintaining a prosperous society: know-how when faced with risk, a capacity for resilience to recover in the aftermath, and absolute sovereignty during and after the difficulties.

The examples below offer a clear illustration of these points.

For a year now, investment in science has been significant and efforts have been sustained. The circumstances of the pandemic and society's needs have both evolved. A new way of working has been implemented. This is why we believed it was worth reflecting on this peculiar year that recently came to an end.

The purpose of this document is to situate the CEA's unique contribution within the country's efforts during this period and to highlight some of the experiences that will help us to better tackle similar events that may arise in the future. It also allows us to showcase our success stories in a time of uncertainty and instability.

François Jacq
CEA Chairman



Responding

... rapidly to help protect local populations

Driven by the urgency of the pandemic, the CEA quickly mobilised its teams and resources to first support the professionals working on the front line to fight the virus.
The few examples given herein highlight both the CEA's solidarity and its ability to rapidly redirect its efforts where needed.

Supporting patients and medical staff: development of emergency medical equipment

As early as March 2020, the CEA decided to share its face mask and hand sanitizer stocks from its medical units with local hospital and medical centres.
Faced with a shortage of personal protective equipment, the CEA also redeployed its additive production capability to design (in collaboration with hospitals) and produce safety components such as visors, temples for safety glasses, and "hands-free" door openers.
It also helped design the OCOV face masks that can be reused up to 100 times.
A total of 300,000 masks were made available to dentists and companies from a broad range of sectors that were all able to continue working.

The expertise gained under the NRBC-E defence programme (fight against nuclear, radiological, biological, chemical and explosive threats) enabled the CEA to help assess the filtration ability of alternative fabrics that could be suitable for protective masks. A test campaign was therefore carried out during the first lockdown to assess the performance of new types of masks.

There was also a risk of seeing a global shortage of ventilators, which is why the CEA launched another project in March 2020 to increase the ventilator capacity for Covid-19 patients.
Its teams developed a first system called Clear-M that optimised the ventilators used in emergency wards and patient transport vehicles.

Patented by the CEA who assigned the licence for this system free of charge, a second system called Clear-R was developed to optimise emergency equipment by enabling the robotic actuation of manual resuscitators.

Detecting Covid-19 virus particles in the air and diagnostic biomarkers

The CEA is currently developing a system to detect Covid-19 virus particles in the air in high-risk areas with the aim of protecting health professionals and their patients. The ARISE technology will also be designed to analyse the impact of different transmission methods and the survival rate of the virus in the air. Within the scope of a partnership with several hospitals, teams at the CEA developed a set of mathematical methods and software tools to process mass spectrometry data on exhaled air. Such technologies have made it possible to identify four diagnostic biomarkers in the exhaled air of patients exhibiting sever forms of Covid-19.

Rapid diagnosis of Covid-19: production of biological reagents

As early as the end of March, in collaboration with its industry and hospital partners, the CEA embarked on the production of biological reagents that can be used on test strips to provide a diagnosis in less than fifteen minutes. The CEA was also involved in the production of antibodies, currently in the process of being selected for the development of a fast antigen test making it possible to detect virus particles in nasal and saliva swabs.

Preclinical trials on hydroxychloroquine

Thanks to the equipment and expertise acquired with the platform dubbed IDMIT (infection disease models for innovative therapies), the CEA initiated an in vivo study as early as February 2020 on the effect of hydroxychloroquine (HCQ) as a prophylaxis for SARS-CoV-2. This study demonstrated the inefficacy of HCQ.

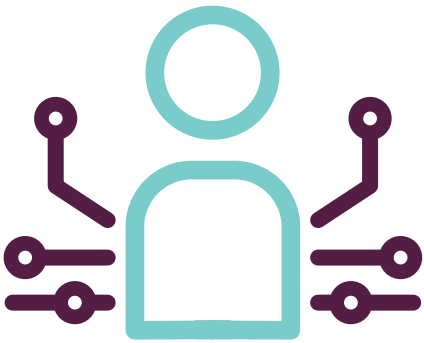
Different treatment protocols were tested, i.e. administered either as means of prevention, or immediately after contamination, and with the appearance of symptoms after five days, with or without azithromycin, and at varying doses.

This preclinical study will have helped to better understand the pathophysiological mechanisms of the SARS-CoV-2 virus and to collect accurate information on the bio-distribution of the HCQ molecule in the body.

Adapting

… how teams worked and facilities operated during these unusual conditions

The CEA's long-standing responsibility of managing sensitive facilities meant it was able to react quickly to the pandemic: plans to continue activities and secure its facilities are always prepared in advance and regularly reviewed. However, owing to the abruptness, severity and duration of the pandemic, the lockdown initiated in March 2020 has tested the resilience of staff and the organisation.



Adapting operations

For many facilities and platforms, shutdown requires tremendous rigour and exactitude in preparation, while start-up is preceded by lengthy verification procedures.
Other activities cannot be carried out remotely: this not only holds for laboratory operations, but also for those dealing with sensitive data concerning trade secrets or defence issues, thus imposing secure premises and equipment.
The procedures foreseen in the case of such events allowed the CEA to sidestep all potential incidents; despite the pandemic, the organisation was able to pursue not only its core programmes thanks to the commitment of its staff, but also its duties to the state and industry partners.

Strong engagement

The level of commitment and solidarity from staff across the board in all divisions and centres of the CEA deserves a special mention, whether in research or support (health, safety, IT, technical services, logistics, communications, human resources, finance, purchasing, legal affairs, etc.) Here are few examples.
The CEA 'clean rooms' in Grenoble are both research facilities and platforms deemed essential to its partners. Their shutdown in only just three days was considered extraordinary, but the real feat was resuming activities as soon as lockdown was lifted, returning to nominal operation as early as the end of May.

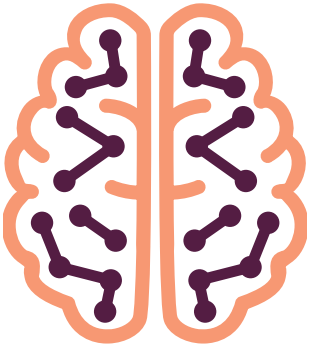
The start-up plan was elaborated in late April in close collaboration with its

priority partners and under the cautious eye of the industrial safety and occupational health professionals.
It is the exceptional mobilisation of CEA staff, together with the support of our contract partners, which stands out: right from the start, 240 volunteers came forward when only 60 were needed!
Top-priority operations were resumed almost immediately, such as the installation of a pilot line to develop a new silicon carbide substrate, which represented some high stakes in the power components sector.
Through everyone's strong involvement up to the end of the year, the impact of the pandemic was limited and our partners were very thankful for the support they received from the teams in Grenoble.

Nuclear safety remained the overriding priority

It is yet another matter entirely in the nuclear field as test reactors and hot laboratories represent a completely different set of safety issues that take top priority. The three main facilities at the CEA - located on the Marcoule, Saclay and Cadarache sites - were shut down and secured between 16 and 17 March 2020 with the assistance of researchers and operators.
Only a few long-term experiments were maintained according to a programme that had been reduced to the strict minimum to avoid losing years of work.

With help from contractors and site support services in radiation protection, effluent treatment, industrial safety, etc., facility staff were able to maintain regular surveillance activities during lockdown, sending updates to the French nuclear safety authority (ASN) on a weekly basis.
Work progressively returned to normal up to July 2020 to guarantee the safest possible conditions for its staff and the facilities.
Annual maintenance operations and nuclear material inventories considered top priority were followed up with inspections by Euratom.
Feedback from the first lockdown proved invaluable during the second round; it has helped better adjust the level of activities in facilities and avoid the arduous authorisation procedures with the ASN, which are required before resuming activities.



Exploiting

... digital means to face the pandemic and the challenges of tomorrow

Highly committed to the digital transformation, the CEA has set up and supports a veritable environment of high-performance computers in France; it invests in big data management, in artificial intelligence and in innovative software solutions. These digital means were not only put to the test during the pandemic, but also in the aftermath to help quickly resume activities.

Providing high-performance computing tools

Together with its French and European partners, the CEA was ready as early as April 2020 to provide the scientific community with the Joliot-Curie supercomputer *via* a specific call for projects devoted to research on Covid-19. Nine European projects have thus benefited from a total of 145 million hours of computing time, which was used in particular to study the virus's mechanisms of infection, transmission and replication. Two other French projects were allocated 10 and 15 million hours of computing time respectively; the first was to assess the risks of contamination as a function of various parameters (physical distance, face masks, etc.), while the second was to find inhibitors to fight the virus. All of this research has gained from the valuable technical support provided by CEA teams.

Spread of aerosol particles in public transport

Coordinated by the CEA, the NRBC-E programme exploits a number of numerical modelling tools and methods to assess the risk of exposure to contaminating and polluting particles in public spaces, whether well ventilated or more or less confined.
During the pandemic, the public authorities contacted the CEA as expert to study the risk associated with the spread of aerosol particles in public transport. The purpose of this study was to i) demonstrate the efficiency of wearing a face mask in public transport, ii)

to recommend any changes to make to ventilation systems, and iii) to define the best protective measures to help reduce the risk of contamination between public transport users.
The technologies generated under the NRBC-E programme are the subject of transfers to French industrial companies with the capability to market them. Twenty technology transfers have already taken place to date.

Digital twins for the French nuclear fleet

The robustness of the French power generation system is mainly due to the availability and operational flexibility of its fleet of nuclear reactors.
Having access to tools that simplify its maintenance and ensure high operational safety levels is therefore primordial.
The development of a platform devoted entirely to numerical simulation, capable of reproducing the condition of each nuclear power plant (their digital twin) in real time regardless of its age, will allow operators to better exploit its nuclear fleet, including during a pandemic. It should therefore be possible to optimise power generation by facilitating maintenance and by carefully managing the fleet upgrade programme (dubbed the Grand Carénage by EDF).
These digital twins can now be shared with partners and contractors; each power plant can be monitored in real time during its service life from operation through to dismantling.

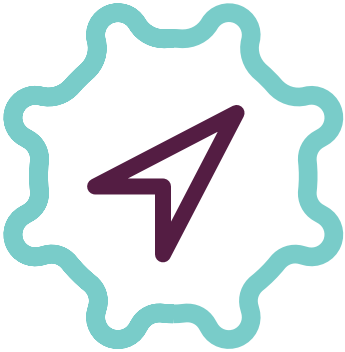
Helping

... to improve cybersecurity and to counter threats exacerbated by the pandemic

The pandemic has highlighted the importance of digital technology in society and thus the relevance of issues such as cybersecurity and privacy.
Long committed to improving cybersecurity, the CEA manages the European consortium called Sparta, which provides input for the European Commission's think-tanks working on its roadmap in this field.

The laboratories at the CEA continued research in this field throughout 2020, designing the first integrated circuit using the fully depleted silicon-on-insulator (FD-SOI) technology with improved security functions. This new technology should lead to the development of new building blocks for reliable hardware and software solutions with better energy efficiency ratings.
The software sector is not to be outdone, having developed a new model designed to analyse the security of assembler codes at the core of cryptographic and data processing components.

This major breakthrough for software security and critical applications (industrial communications, I&C systems) has been validated for Linux distribution; in the process, it has detected more than 500 non-conformity issues. In the much longer term, researchers are looking into post-quantum cryptography (PQC) to guarantee the security of communications when quantum computers (still largely in the future) will be capable of undermining our current cryptographic defences. By adding a random noise to information on the encryption key, the CEA has invented a novel method of guaranteeing the confidential exchange of data, even on networks whose reliably are largely unknown.



Sustaining

... efforts to meet the top priorities for France in a time of economic uncertainty

Encouraged by the public authorities to lead research in fields of major strategic and societal importance, the CEA has maintained strong ties with its partners in both the civil and nuclear industry. During this period of uncertainty, it has met the demands of the French government within the scope of actions destined to strengthen the country's resilience and stimulate its industry.

Maintaining investment in quantum technology

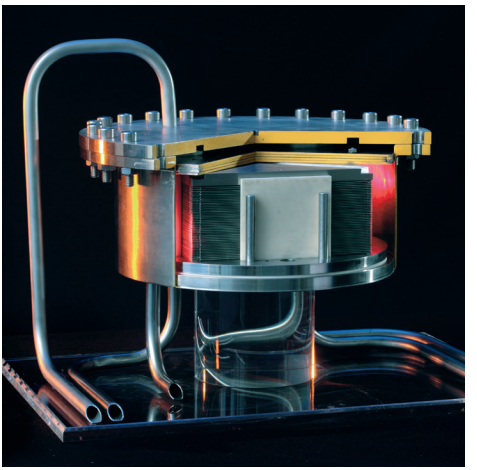
In the vast field of computing, the CEA chose to bank on quantum technology (sensors, information networks, computers) right from the start; its research now reflects the state-of-the-art, making France as a key player on the European and world stage. It has also consistently worked, in collaboration with other French research organisations, with the interministerial task force set up by the government in January 2020 to coordinate public actions for the development of quantum technology. This sustained involvement has led to its co-leadership of a priority research programme falling within the scope of the French 'Quantum Plan' announced by the French President in January 2021. This programme aims at developing quantum technologies to benefit its citizens in three areas, i.e. health, the environment and mobility.

Building a smarter energy future

Based on discussions initiated in autumn 2018, the CEA completed the reorganisation of its energy research divisions in February 2020. The teams have therefore been able to continue their research within an integrated approach to energy: production of low-carbon energy (nuclear and renewable), operation and optimisation of energy systems (storage, control and conversion), distribution on different scales (from local to nation-wide), reduced energy losses (energy efficiency, energy consumption management) and recycling of materials.

In this context, the CEA has continued its research within the scope of the project on innovative decarbonised nuclear energy systems (IDNES). This project aims at using nuclear energy to produce heat locally by means of cogeneration to provide hydrogen *via* electrolysis at high temperature or hot water at low temperature for household use.

Among the systems under investigation, small modular reactors (SMR) are good candidates for local power production as they are capable of providing for modest energy needs.
Along the same lines, the CEA and its industry partners continued characterising the different energy scenarios chosen for the French national energy and climate plan (known as the PPE), which plans to reduce the fraction of nuclear energy to 50% of the total energy mix by 2035. Four installed capacity scenarios have been chosen to describe the renewal of the French nuclear fleet and to assess the different fuel cycle options with their related material and waste flows. The preliminary results were presented to the public authorities in 2020 as scheduled.



Launching the first EXA-1 supercomputer module for the French Defence

As planned, the CEA started building the initial supercomputer called EXA-1 in October 2020. Capable of performing one million billion operations per second (1 petaflop per second), it exploits a new range of high-performance systems considered precursor worldwide and is the result of a CEA co-development project. It represents the first step towards integrating and validating the computer codes that will run on the first partition of the EXA-1 supercomputer, which once commissioned (planned for late 2021), will improve the accuracy of simulations needed to meet the performance requirements for the French deterrent force.

Protecting

... fundamental research by giving it the time it needs

The CEA has a long history of being able to rapidly propose solutions that better society in one way or another. This is because of the close proximity between its researchers focused on technical innovations and those exploring the more fundamental mechanisms of nature. The examples cited illustrate just how much this fundamental research needs time and cutting-edge equipment for ideas to mature and make knowledge available in times of crisis.

SARS-CoV-2: discovery of a very unusual mode of transmission

To develop vaccines and treatments against Covid-19, it is first necessary to understand how the virus behaves in the human body. In general, viruses are armed with an arsenal of proteins acting much like a set of keys, which allow them to unlock the cell barriers. Very early in 2020, the protein known as ACE-2 was identified as an entry receptor for the virus, leading to the development of the vaccines that are now available.

Researchers at the CEA discovered that SARS-CoV-2 binds to other receptors on the surface of immune cells to spread throughout the body. In high numbers in the respiratory mucous membranes and lung tissue, these immune cells are not infected by the virus but act as host where they carry the virus to target cells that have the ACE-2 protein. Researchers also demonstrated that this new mode of transmission could be blocked by glycomimetic molecules. These molecules had already been studied by the CEA for their ability to inhibit pathogens, particularly HIV. This opens the door to novel treatments to limit the transmission and proliferation of the virus in the body.

Veritable viral factories at work

Researchers at the CEA proved *in vivo* that the measles virus develops membraneless liquid-like organelles on its peripheral regions like droplets of oil in water. In this configuration, the virus protects itself in an isolated cellular compartment (viral

factory) where the RNA molecules become concentrated and allow the virus to replicate. The purpose of studying these veritable fleeting 'viral factories' is to find new therapeutic targets that provide just as many possibilities for new drugs. These droplet-like particles also provide new knowledge that can be used to develop bio-production processes, which offer promising solutions in numerous applications, whether in the health, pharmacology, industry or energy sector.

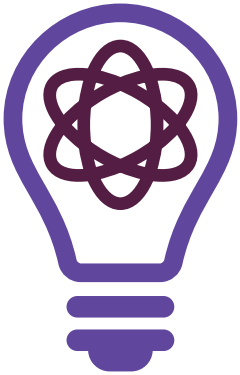
Observing the impact of the pandemic on global CO_2 emissions

An international team (including CEA researchers) highlighted the effect of lockdown measures due to the pandemic on global CO_2 emissions, which dropped by 9% between January and June 2020 compared with that over same period the previous year. Based on the collection and automatic processing of data of CO_2-emitting activities (e.g. movement of people and goods, gas and electricity consumption levels, industry production rates, etc.), their research has provided a valuable tool for monitoring carbon emissions almost in real time. It can gauge the impact of population behavioural changes (effect of weekend or holiday departures) and economic policies, as well as anticipating future changes so they can be pre-empted. The Carbon Monitor website, open to the public since June 2020, illustrates the distribution and variations in global carbon emissions in the atmosphere, oceans and terrestrial biosphere for eleven different countries.

Simulating future epidemics in a hotter world

Diseases spread by a vector, whether mosquitoes or gnats, regularly provoke health crises. They are triggered by multiple and sometimes unexpected causes, e.g. the fact that some vectors are able to survive long distances in planes or containers. Nevertheless, would it have been possible to predict the Zika epidemic in Brazil in 2015-2016, the outbreak of bluetongue virus in France in 2007-2008, or the outbreak of the Rift Valley fever in Kenya and Tanzania in 2006-2007 ?

The innovative coupling of climatology and epidemiology in numerical simulation has produced the Epiclim project, which has already detected a rise in the risk of malaria on the East African plateaus and its slight decrease in the plains of West Africa. It can also test trend break scenarios using new precipitation and temperature distribution curves, together with their impact on the emergence of new diseases, or the resurgence of existing diseases due to their growing resistance to insecticides and drugs. These results will be exploited to better prepare public health systems and to anticipate any new risks by adapting the behaviour of populations.



Accelerating
... innovation

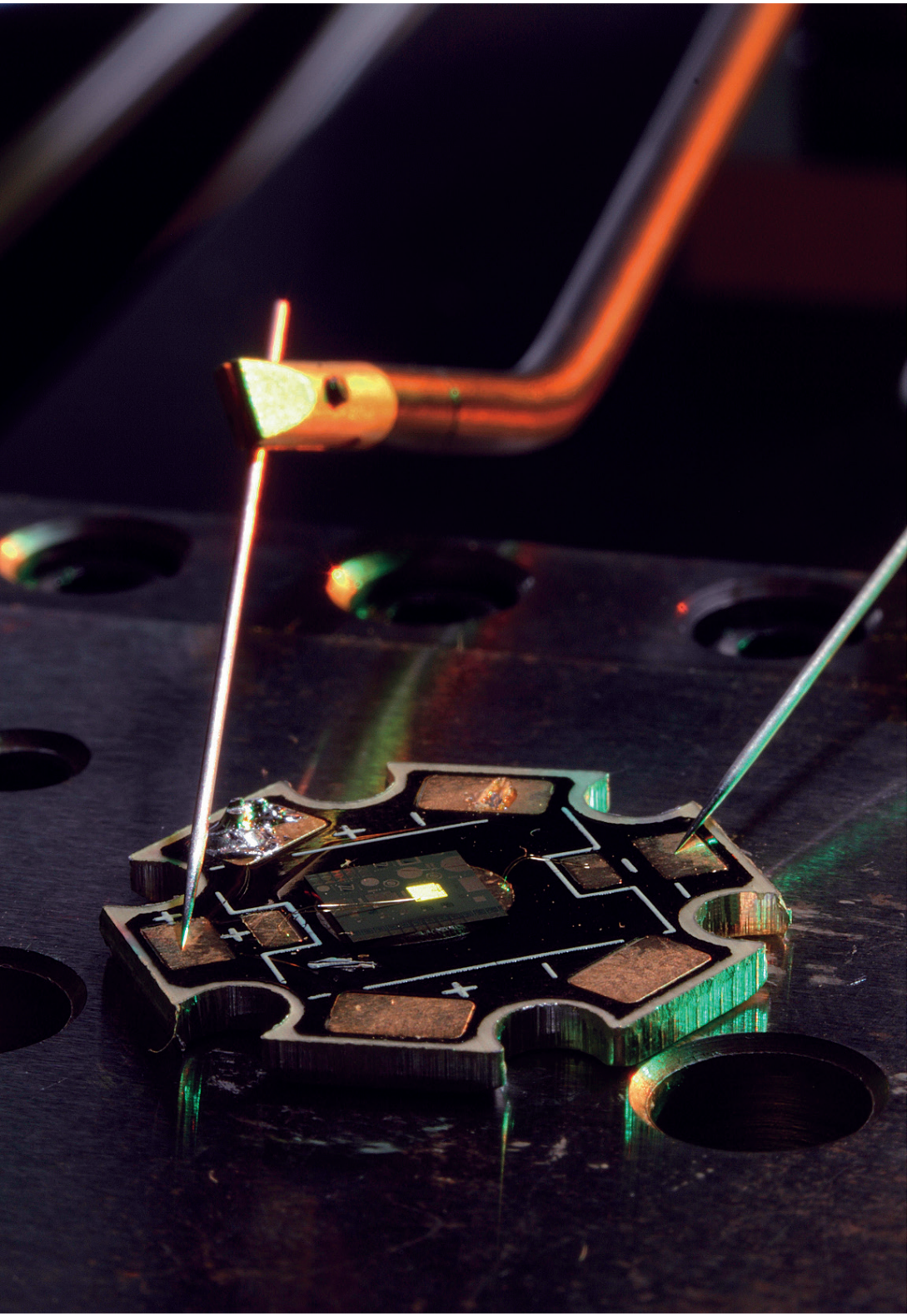
Taking advantage of the French economic recovery plan and the focus on hydrogen as an energy vector, the CEA continued its research pushing to develop the large-scale production of hydrogen in France under the Genvia project, which brings together industry and institutional stakeholders.

The Genvia project will drive the CEA's disruptive innovation, i.e. hydrogen production by high-temperature electrolysis, through to industrial maturity.

This technology is based on exceptional know-how and more than fifteen years of CEA research on both ceramic materials and on cell-stacks and systems associated with the materials.

Despite the pandemic, CEA-initiated start-ups either continued to grow or increased in number in 2020. Significant funds were raised, such as those needed to market an innovative 3D LED technology that was originally developed by the CEA to light up future smartphone screens, connected watches and augmented-reality glasses. Thanks to the flexibility of working conditions between home and onsite, the project was able to meet its milestones when it delivered, in due time, two demonstrators and manufactured the first nanowire chips. At the same time, this start-up announced the construction of the first factory near Grenoble, which is expected to generate around 600 jobs over four years.

Last of all, the CEA launched an initiative in June to double the number of start-ups created per year by staff originally from their laboratories. The idea is to encourage the development of innovative CEA technologies through flexible start-up structures. It does not seem that the pandemic has deflated the morale of future CEA entrepreneurs, as ten proposals were chosen after a first short-list in July: each applicant will benefit from training before their project is formalised, aiming for final validation in spring 2021. The programme sets out to support the creation of between 15 and 20 new start-ups per year.



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