

# N.N. BURDENKO VORONEZH STATE MEDICAL UNIVERSITY

# The reverse translation from English to DNA: the way how to encrypt messages in the genome

# ABCDEFGH

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SYNTHETIC BIOLOGY, SYNTHETIC CHROMOSOME, JCVI-syn1.0 clone sMmYCp235-1, MOLECULAR BIOLOGY, MOLECULAR GENETICS, BIOTECHNOLOGY, GENE, GENOME, BIOINFORMATICS, LINGUISTICS, ENGLISH LANGUAGE

# THE FIRST EVER CREATED SPECIES, CONTROLLED BY A SYNTHETIC GENOME



02.07.2010

ROCKWILL, MARYLAND, USA

INSTITUTE OF CRAIG VENTER



COVER of the SCIENCE journal: Electron micrograph of synthetic cells *Mycoplasma mycoides* JCVI-syn1.0 (magnification ~25,000×)

THE YEAR 2010 WAS SIGNIFICANT FOR BIOLOGY IN THE LIGHT OF COMPLETE ARTIFICIAL SYNTHESIS OF GENOME AND ITS [Gibson D. G., Glass J. I., ITRANSPILANITATION al cell controlled by a chemically synthesized genome. Science. 2010;329:52–56. doi: 10.1126/science.1190719.]



A RESEARCH GROUP, LED BY THREE PROMINENT SCIENTISTS TRANSPLANTED DE NOVO SYNTHESIZED CHROMOSOME OF MYCOPLASMA MYCOIDES INTO MYCOPLASMA CAPRICOLUM

NÖRE

*Hamilton Othanel Smith,* Nobel prize laureate. Prominent for investigations of restriction enzymes. His studies revolutionized the methods of molecular biology and biotechnology

*Clyde A. Hutchison III,* prominent for investigations in sphere of site-directed mutagenesis. Participated in the determination of a complete genome sequence of phage  $\Phi$ X174. Made a contribution to the polymerase chain reaction discovery

*John Craig Venter,* prominent for Human Genome Project and initial studies in synthetic biology

# THE CONCEPTION OF EXPERIMENTAL WORK



## DESIGN OF THE SYNTHETIC CHROMOSOME



SYNTHETIC CHROMOSOME CONTAINS 6 EXTRA REGIONS: 4 WATERMARKS WITH DECODED MESSAGES IN ENGLISH LANGUAGE, TETRACYCLINE RESISTANCE GENE (tetM) AND BETA-GALACTOSIDASE GENE (LacZ) In order to verify the success of the experimental work, the donor genome was edited by inserting the nucleotide sequence of **4** watermarks into different loci of the genome, **antibiotic (tetracycline) resistance gene (tetM) and beta-galactosidase (lacZ) gene**. Thus, the efficiency of transplantation could be evaluated using three approaches:

1.Control sequencing of the synthetic genome and identification of watermarks

<sup>2.</sup>Testing viability of bacterial culture, treating their growth medium with antibiotic.

<sup>3.</sup>Turning the colony bright blue in the presence of an organic compound X-gal, metabolizing by a product of lacZ gene.

# 1. CONTROL SEQUENCING OF THE SYNTHETIC GENOME AND IDENTIFICATION OF WATERMARKS



# 2. TESTING VIABILITY OF BACTERIAL CULTURE, TREATING THEIR GROWTH MEDIUM WITH ANTIBIOTIC



3. TURNING THE COLONY BRIGHT BLUE IN THE PRESENCE OF AN ORGANIC COMPOUND X-GAL, METABOLIZING BY A PRODUCT OF lacZ GENE



X-gal, metabolized by lacZ gene product (beta-galactosidase)





INTACT CELLS (lacZ-negative) DO NOT METABOLIZE X-gal, THE COLONY DOES NOT TURN BLUE



These three approaches confirmed <u>success</u> in transplantation, proclaiming that the <u>first</u> ever species was created by <u>human</u>. The linguistic interest of this great scientific breakthrough lies in <u>watermarks</u>, which were inserted into the donor genome. Each additional sequence encodes a message in English.

### THE AIM OF THE STUDY:

<sup>o</sup>To biologically and linguistically analyze the adapt of English alphabet to a genetic code

<sup>o</sup>Mapping the <u>exact</u> localization of 4 watermarks in synthetic genome (<u>WMs loci have never been published</u>)

Deciphering encoded data (complete nucleotide sequence of the watermarks has never been published; decoded data is partially available)

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# MATERIALS AND METHODS

- 1. Analysis of C. Venter's book "Life at the speed of light" in order to get cryptography between English alphabet and a specific trinucleotide code, used to encipher it.
- 2. Building the tagging sequences (TSs) for pairwise alignment in order to identify watermarks in the synthetic chromosome. TSs were created without punctuation marks, except commas and spaces as .txt files and converted in FASTA format by MEGA-X (Version: 10.1.7) tool.
- 3. Dividing the sequence of synthetic chromosome in 5 fragments (Fs) in order to simplify and speed up the pairwise sequence alignment, using **DNASTAR Lasergene 17.01.1 (2020) MegAlign Pro**.
- 4. PSA (Pairwise Sequence Alignment) of Fs and TSs, completed by **DNASTAR Lasergene 17.01.1 (2020) MegAlign Pro** with **MAUVE** algorithm.
- 5. An extra PSA was completed by **DNASTAR Lasergene 17.01.1 (2020) MegAlign Pro**, using the **Smith-Waterman** DNA alignment algorithm [Matrix: "NUC44"; Gap penalty: 10; Gap extension penalty: 1].
- 6. Deciphering the watermarks codon by codon, moving to the 5'-end and 3'-end.
- 7. Overview of decoded watermarks.

### 1. ANALYSIS OF THE "LIFE AT THE SPEED OF LIGHT

The chapter **8** "Synthesis of the M. mycoides Genome" has a key for deciphering the nucleotide cryptography, used in watermarks. The series of characters, including complete English alphabet of 26 letters; newline; space; numbers (0-9); various punctuation marks, such as point, comma, hyphen etc; mathematical signs, such as plus, minus and some additional symbols were represented by the developed trinucleotide code.

THE CRYPTOGRAPHY BETWEEN WATERMARKS AND ENGLISH ALPHABET, PUNCTUATION MARKS AND ADDITIONAL CHARACTERS

- A is encoded by TAG trinucleotide; B AGT; C TTT; D ATT; E TAA; F – GGC; G – TAC; H – TCA; COMMA (,) – GTG; POINT (.) – CGA; SPACE (\_) – ATA; 1 – CTT; 2 – ACT; 3 – AAT; @ - TCG etc.
- Total number of encoded characters 64, <u>corresponding to the real</u> <u>number of DNA-codons</u>.
- There is a **total mismatch** between codification of the English alphabet and one-letter code of amino acids. The only exception is in position **12**: letter L of JCVI-syn1.0 alphabet corresponds to leucine (Leu, L). Mismatch example: letter G in JCVI-syn1.0 alphabet is encoded by TAC, which in the real genetic code means M (Met, methionine) etc.
- The table of cryptography was created to make building the tagging sequences more convenient. It also was used for further decoding.

# 2. BUILDING THE TAGGING SEQUENCES (TSs) FOR PAIRWISE ALIGNMENT

Identification of watermarks in the synthetic genome required building the sequences to complete pairwise alignment. Because of the fact the whole sequences of watermarks remained unpublished, 4 specific tagging sequences (TSs) were created in order to identify corresponding fragments of each watermark in the chromosome. The TSs were built according to the only available data from "The life at the speed of light". The chapter 8, "Synthesis of M. mycoides genome", fragmentally provides some insights of what was encoded in each watermark. Thus, among encrypted data in  $WM_1$  there is "Craig Venter Institute"; the quote from James Joyce: "To live, to err, to fall, to triumph, to recreate life out of life" in WM<sub>2</sub>; the quote of Robert Oppenheimer: "See things not as they are, but as they might be" in WM<sub>3</sub> and Richard Feynman's quote: "What I cannot build, I cannot understand" in WM<sub>4</sub>. Considering these insights from the chapter 8 we hypothesized that "Craig Venter Institute" and the quotes above are suitable to be such tagging sequences for PSA. Using the cryptographic features from Table 1 TSs were created with no punctuation marks, except comas and spaces as .txt files and converted in FASTA format.

> THE FILES CONVERTATION WAS COMPLETED BY MEGA-X (V:10.1.7)

# 3. DIVIDING THE SEQUENCE OF SYNTHETIC CHROMOSOME

Complete sequence of synthetic Mycoplasma mycoides JCVIsyn1.0 clone sMmYCp235-1 was found in NCBI Nucleotide database (**GenBank: CP002027.1**) and downloaded in FASTA. The sequence was divided in **5 fragments**, according to the schematic representation of watermarks in original paper "Creation of a bacterial cell controlled by a chemically synthesized genome". There are:

- • $F_0$  (1 $\rightarrow$ 200000 nucleotides)
- • $F_1$  (200001 $\rightarrow$ 400000)
- • $F_2$  (400001 $\rightarrow$ 600000)
- • $F_3$  (600001 $\rightarrow$ 800000)
- • $\mathbf{F}_4$  (800001 $\rightarrow$ 1078809)

This manipulation was completed in order to **simplify** and **speed up** the pairwise sequence alignment.







The sequence was fragmentated, using DNASTAR Lasergene 17.01.1 (2020) MegAlign Pro



# Fragmentation of the complete sequence of synthetic Mycoplasma mycoides JCVI-syn1.0 clone sMmYCp235-1



 $F_0$  (1→200000 nucleotides);  $F_1$  (200001→400000) ;  $F_2$  (400001→600000);  $F_3$  (600001→800000);  $F_4$  (800001→1078809)

4. PSA (MAUVE ALGORITHM); 5. CONTROL PSA (SMITH-WATERMAN ALGORITHM). COMPLETED BY DNASTAR Lasergene 17.01.1 (2020) MegAlign Pro 1. The first WM was identified via alignment of  $F_2$  and  $TS_1$ : CONTROL PSA WAS COMPLETED BY CLUSTAL



5'-TTTCTATAGCTGTACATATTGTAATGCTGATAACTAATACTGTGCGCT56F1WTAREGAT CCTGATAA-3'  $\rightarrow$  "Craig Venter Institute" (565527 $\rightarrow$ 565592).

2. WM<sub>2</sub> was found via alignment of  $F_3$  and  $TS_2$ :

5'-

TGACGTAACCTGTTGTAATGACGTTAACTACTATGACGTGGCTAGAACAACTGACGT TGACTACTGTCCCAAACATCATGACGTCTATAATTTCTATAATAGTGATAAAACCTGG <u>GCTAACG</u>TTCCTGACGTGGCAACCTGGGCTAA-3' → "<u>To live, to err, to fall, to triumph</u>, to recreate life out of life", James Joyce (726295→726492).

#### 3. WM3 was identified via TS<sub>3</sub>:

5'-

GCTTAATAAATATGATCACTGTGCTACGCTATATGCCGTTGAATATAGGCTATATGATC ATAACATATATAGCTATAAGTGATAAGTTCCTGAATATAGGCTATATGATCATAACAT ATACAACTGTACTCATGAATAAGTTAA-3'  $\rightarrow$  "See things not as they are, but as they might be", - the quote of Robert Oppenheimer ( $390264 \rightarrow 390407$ ).

4. The last watermark (WM4) was detected via  $TS_4$ :

5'-

GTCTCATAGTGAATACTGATATTTTAGTGCTGCCGTTGAATAAGTTCCCTGAACATTGT GATACTGATATTTTAGTGCTGCCGTTGAATATCCTGCATTTAACTAGCTTGATAGTGCA

# 6. DECIPHERING THE WATERMARKS CODON BY CODON, MOVING TO THE 5'-END AND 3'-END



After WMs were identified, their complete sequences were decoded, moving to the 5'-end and to the 3'-end until the beginning of a senseless nucleotide context (?,fgjhdnf?>smkl31:":F or something like that)

# **<u>RESULTS:</u>** 4 WMs IN JCVIsyn-1.0 WERE <u>IDENTIFIED</u> AND <u>DECIPHERED</u>

### WATERMARK 1

5'-

TTAACTAGCTAAGTTCGAATATTTCTATAGCTGTACATATTGTAATGCTGATAACTAA TACTGTGCGCTTGACTGTGATCCTGATAAATAACTTCTTCTGTAGGGTAGAGTTTTATT TAAGGCTACTCACTGGTTGCAAACCAATGCCGTACATTACTAGCTTGATCCTTGGTCG GTCATTGGGGGGATATCTCTTACTAATAGAGCGGCCTATCGCGTATTCTCGCCGGACCC CCCTCTCCCACACCAGCGGTGTAGCATCACCAAGAAAATGAGGGGAACGGATGAGG AACGAGTGGGGGGCTCATTGCTGATCATAATGACTGTTTATATACTAATGCCGTCAACT CATGACAAAACAGCCGGTCATGACAAAACAGCCGGTCATAATAGATTAGCCGGTGA CTGTGAAACTAAAGCTACTAATGCCGTCAATAAATATGATAATAGCAACGGCACTGA CTGTGAAACTAAAGCCGGCACTCATAATAGATTAGCCGGAGTCGTATTCATAGCCGG TAGATATCACTATAAGGCCCAGGATCATGATGAACACAGCACCACGTCGTCGTCCGA GTTTTTTGCTGCGACGTCTATACCACGGAAGCTGATCATAAATAGTTTTTTGCTGCG GCACTAGAGCCGGACAAGCACACTACGTTTGTAAATACATCGTTCCGAATTGTAAAT AATTTAATTTCGTATTTAAATTATGATCACTGGCTATAGTCTAGTGATAACTACAAT AGCTAGCAATAAGTCATATATAACAATAGCTGAACCTGTGCTACATATCCGCTATAC GGTAGATATCACTATAAGGCCCAGGACAATAGCTGAACTGACGTCAGCAACTACGTT TAGCTTGACTGTGGTCGGTTTTTTTGCTGCGACGTCTATACGGAAGCTCATAACTATAA GAGCGGCACTAGAGCCGGCACACAAGCCGGCACAGTCGTATTCATAGCCGGCACTC ATGACAAAACAGCGGCGCGCCTTAACTAGCT-3'.

oThe largest WM. It is localized in the region: 565506 → 566573
 oConsisting of 1068 nucleotides
 oEncoding 356 characters

# DECIPHERED WM1

Q2>EJ. CRAIG VENTER INSTITUTE 2009 [PARAGRAPH] ABCDEFGHIJKLMNOPQRSTUVWXYZ [PARAGRAPH] 0123456789#@)(-+\=/:<;>\$&}{\*]"[%!'., [PARAGRAPH] SYNTHETIC GENOMICS, INC. [PARAGRAPH] <!DOCTYPE HTML><HTML><HEAD><TITLE>GENOME TEAM</TITLE></HEAD><BODY><A HREF=<u>HTTP://WWW.JCVI.ORG/</u>">THE JCVI</A><P>PROVE YOU'VE DECODED THIS WATERMARK BY EMAILING US <A HREF=<u>MAILTO:MROOSTIZ@JCVI.ORG</u>">HERE!</A></P></BODY></HTML> >F5+ERS

# ENCODED DATA

- Involved organizations and year of origin: Craig Venter institute, Synthetic Genomics, 2009
- Contains the key for deciphering (the series of used characters)
- HTML-code for emailing after decoding the watermark

# WATERMARK 2

5'-TTAACTAGCTAACAACTGGCAGCATAAAACATATAGAACTACCTGCTATAAGTGAT ACAACTGTTTTCATAGTAAAACATACAACGTTGCTGATAGTACTCCTAAGTGATAGCTTA GTGCGTTTAGCATATATTGTAGGCTTCATAATAAGTGATATTTTAGCTACGTAACTAAATA AACTAGCTATGACTGTACTCCTAAGTGATATTTTCATCCTTTGCAATACAATAACTACTAC ATCAATAGTGCGTGATATGCCTGTGCTAGATATAGAACACATAACTACGTTTGCTGTTTTC AGTGATATGCTAGTTTCATCTATAGATATAGGCTGCTTAGATTCCCTACTAGCTATTTCTG TAGGTGATATACGTCCATTGCATAAGTTAATGCATTTAACTAGCTGTGATACTATAGCAT CCCCATTCCTAGTGCATATTTTCATCCTAGTGCTACGTGATATAATTGTACTAATGCCTGT AGATAATTTAATGCCTGGCTCGTTTGTAGGTGATAATTTAGTGCCTGTAAAACATATACCT GAGTGCTCGTTGCGTGATAGTTCGTTCATGCATATACAACTAGGCTGCTGTGATATGGTC GATATGACGTATATAACTACTAGTGATATGACGTATAGGCTAGAACAACGTGATATGAC GTATATGACTACTGTCCCAAACATCAGTGATATGACGTATACTATAATTTCTATAATAGT GATAAATAAACCTGGGCTAAATACGTTCCTGAATACGTGGCATAAACCTGGGCTAACGA **GGAATACCCATAGTTTAGCAATAAGCTATAGTTCGTCATTTTTAAGGCGCGCCTTAACTA GCT-3**′

o The smallest WM. It is localized in the region:
 725653 → 726558

Consisting of 909 nucleotides
 Encoding 303 characters

# DECIPHERED WM2

Q2>EMIKKEL ALGIRE, MICHAEL MONTAGUE, SANJAY VASHEE, CAROLE LARTIGUE, CHUCK MERRYMAN, NINA ALPEROVICH, NACYRA ASSAD-GARCIA, GWYN BENDERS, RAY-YUAN CHUANG, EVGENIA DENISOVA, DANIEL GIBSON, JOHN GLASS, ZHI-QING QI. [PARAGRAPH] "TO LIVE, TO ERR, TO FALL, TO TRIUMPH, TO RECREATE LIFE OUT OF LIFE." – JAMES JOYCEF5+ERS

# ENCODED DATA

- Names of the scientists, participated in the project (n=13)
- The quote from the James Joyce's
- "A Portrait of the Artist as a Young Man"



COVER OF THE BOOK

#### 5'-

TTAACTAGCTAATTTAACCATATTTAAATATCATCCTGATTTTCACTGGCTCGTTGCGTGA TATAGATTCTACTGTAGTGCTAGATAGTTCTGTACTAGGTGATACTATAGATTTCATAGAT AGCACTACTGGCTTCATGCTAGGCATCCCAATAGCTAGTGATAGTTTAGTGCATACAACG TCATGTGATACAACGTTGCTGGCTGTAGATACAACGTCGTATTCTGTAAGTGATACAATA GCTATTGCTGTGCATAGGCCTATAGTGGCTGTAACTAGTGATATCACGTAACAACCATAT AAGTTAGATTTAATGCCCCTGACTGAACGCTCGTTGCGTGATAGTTTAGGCTCGTTGCAT ACAACTGTGATTTTCATAAAACAACGTGATAATTTAGTGCTAGATAAGTTCCGCTTAGCA AGTGATAGTTTCCGCTTGACTGTGCATAGTTCGTTCATGCGCTCGTTGCGTGATAAACTAG AGTGATACTACGTAGTTAACTATGAATAGGCCTACTGTAAATTCAATAGTGCGTGATATT GAACTAGATTCTGCAACTGCTAATATGCCGTGCTGCACGTTTGGTGATAGTTTAGCATGC ATCACTGTGCTACGCTATATGCCGTTGAATATAGGCTATATGATCATAACATATATAGCT ATAAGTGATAAGTTCCTGAATATAGGCTATATGATCATAACATATACAACTGTACTCATG AATAAGTTAACGAGGA-3'

oLocalized in the region: 389493 → 390413
 oConsisting of 921 nucleotides
 oEncoding 307 characters

# DECIPHERED WM3

Q2>ECLYDE HUTCHISON, ADRIANE JIGA, RADHA KRISHNAKUMAR, JAN MOY, MONZIA MOODIE, MARVIN FRAZIER, HOLLY BADEN-TILSON, JASON MITCHELL, DANA BUSAM, JUSTIN JOHNSON, LAKSHMI DEVI VISWANATHAN, JESSICA HOSTETLER, ROBERT FRIEDMAN, VLADIMIR NOSKOV, JAYSHREE ZAVERI. [PARAGRAPH] "SEE THINGS NOT AS THEY ARE, BUT AS THEY MIGHT BE."

# ENCODED DATA

- Names of the scientists, participated in the project (n=15)
- Robert Oppenheimer's qoute

# WATERMARK 4

5'-TTAACTAGCTAATTTCATTGCTGATCACTGTAGATATAGTGCATTCTATAAGTCGCTCC CACAGGCTAGTGCTGCGCACGTTTTTCAGTGATATTATCCTAGTGCTACATAACATCAT AGTGCGTGATAAACCTGATACAATAGGTGATATCATAGCAACTGAACTGACGT AGCTCAACTGTGATCAGTGATATAGATTCTGATACTATAGCAACGTTGCGTGA TGACTGTAGTGCATATGATAGTACGTCTAACTAGCATAACTAGTGAT `ATAGCTGTACATATTGTAATGCTGATAACTAGTGATATAATCCAA TATGCTAACTAGTGATAAAA 'CAT ϓʹϲϫϫϫ "I'A A ( TCACTGAGTTCCATACATCGTCGTGCT CTGCTACGTGAT  $|| \Delta |$  $\Box A T$ TAACTAGTGATATGA CATAGATA GTGATAAT TCTGTAGTGC GATAC ΤА AAGTGATAAGTCTA CTGATT TACTAATGAATAGCTTGGTT TTGGCATA GCACTGGTGATAGCTTTTCGTTGATGAATAATTTCCCTAGCACTGTGCGTGATATGCTA TCTGTAGATAGGCTAAATTCGTCTACGTTTGTAGGTGATAGTTTAGTTGCTGTAAC CTGTGCCGTTGCTAAGCTGTGATATCATAGTGCTGCTAGATATGATAA TAATATTATC GCAAACTAATAGAGTCGAGGGGGGGGGGGTCTCATAGTGAATACTGATAT TAGTGCTGCC TGAATAAGT CTGAACATTGTGATACTGATATTTTAGTG °TGCCGT TGAATATCC TGCATTTAACTAGCTTGATAGTGCATTCGAGGAATACCCATACTACTGTTTTCATAGCT AATTATAGGCTAACATTGCCAATAGTGCGGCGCGCCTTAACTAGCT-3'

oLocalized in the region: 958641 → 959684
 oConsisting of 1044 nucleotides
 oEncoding 348 characters

# DECIPHERED WM4

Q2>ECYNTHIA ANDREWS-PFANNKOCH, QUANG PHAN, LI MA, HAMILTON SMITH, ADI RAMON, CHRISTIAN TAGWERKER, J CRAIG VENTER, EULA WILTURNER, LEI YOUNG, SHIBU YOOSEPH, PRABHA IYER, TIM STOCKWELL, DIANA RADUNE, BRIDGET SZCZYPINSKI, SCOTT DURKIN, NADIA FEDOROVA, JAVIER QUINONES, HANNA TEKLEAB. [PARAGRAPH] "WHAT I CANNOT BUILD, I CANNOT UNDERSTAND." – RICHARD FEYNMANF5+ERS

# ENCODED DATA

- Names of the scientists, participated in the project (n=18)
- Richard Feynman's qoute

# CONCLUSION

THIS STUDY REVEALED:
•EXACT LOCI OF WATERMARKS (WM1: 565506 → 566573; WM2: 725653 → 726558; WM3: 389493 → 390413; WM4: 958641 → 959684.
As far as we know, this data is absolutely exclusive and it has been never published before.
•COMPLETE NUCLEOTIDE SEQUENCE OF THE WMs

WATERMARKS WERE FULLY DECODED. THEY CONTAIN:
•THE KEY FOR DECIPHERING AND HTML CODE FOR EMAILING
•16 NAMES OF SCIENTIST, INVOLVED IN THE PROJECT
•4 QUOTATIONS
•TOTAL NUMBER OF NUCLEOTIDES, COMPOSING 4 WATERMARKS
= 3942

•THE LARGEST IS WM1 (1069 NTs), THE SMALLEST IS WM2 (909 NTs)





# ON THE 90<sup>TH</sup> ANNIVERSARY ON THE 10<sup>TH</sup> OF THE DEPARTMENT OF ANNIVERSARY OF FOREIGN LANGUAGES SYNTHETIC MYCOPLASMA THANK YOU FOR ATTENTION! ABCDEFGH

К 90-ЛЕТИЮ КАФЕДРЫ ИНОСТРАННЫХ ЯЗЫКОВ. ON THE 90<sup>TH</sup> ANNIVERSARY OF THE DEPARTMENT OF FOREIGN LANGUAGES. ZUM 90-JÄHRIGE JUBILÄUM DER FAKULTÄT FÜR FREMDSPRACHEN. DEBIDO AL 90 ANIVERSARIO DEL DEPARTAMENTO DE LENGUAS EXTRANJERAS. SUR LE 90E ANNIVERSAIRE DE LA FACULTÉ DES LANGUES ÉTRANGÈRES.