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Role	Signatures
Premier Research, Inc. [redacted]	Print Name: [redacted] Sign Name [redacted]
Annexon Biosciences [redacted]	Print Name: [redacted] Sign Name: [redacted]

Role	Signatures
Annexon Biosciences [redacted]	Print Name: [redacted] Sign Name: [redacted]
Annexon Biosciences [redacted]	Print Name: [redacted] Sign Name: [redacted]

Document History

Not applicable.

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List of Abbreviations

Abbreviation	Definition
AE	adverse event
AESI	adverse events special interest
AIHA	autoimmune hemolytic anemia
ATC	anatomical therapeutic chemical
BMI	body mass index
C1q	component of C1 complement complex
CI	confidence interval
CRF	case report form
[redacted]	[redacted]
CSR	clinical study report
CTCAE	common terminology criteria for adverse events
CV	coefficient of variation
DSUR	development safety update report
ECG	electrocardiogram
eCRF	Electronic case report form
EMA	european medicines agency
[redacted]	[redacted]
FAS	full analysis set

Abbreviation	Definition
FDA	food and drug administration
GCP	good clinical practice
HR	heart rate
ICF	Informed consent form
ICH	international conference on harmonization
IRR	Infusion-related reactions
LDH	lactate dehydrogenase
MedDRA	medical dictionary for regulatory activities
NCI	National Cancer Institute
Q1	first quartile
Q3	third quartile
PD	pharmacodynamic
PI	principal investigator
PK	pharmacokinetic
PKAP	pharmacokinetic analysis plan
PP	Per protocol
PT	Preferred term
SAE	serious adverse event
SAF	Safety population

Abbreviation	Definition
SAP	statistical analysis plan
SD	standard deviation
SOC	system organ class
TEAE	treatment-emergent adverse event
wAIHA	warm autoimmune hemolytic anemia
WHO-DD	world health organization drug dictionary

1. Overview

This statistical analysis plan (SAP) describes the planned analysis and reporting for Annexon Biosciences protocol number ANX005-wAIHA-02 (A Phase 2, Open-Label, Repeat Dose Study to Assess the Safety, Tolerability, Pharmacokinetics, Pharmacodynamics and Proof-of-Concept of Intravenous ANX005 in Subjects with Warm Autoimmune Hemolytic Anemia), dated 23-Mar-2022 (Version 3.0). Operational aspects related to collection and timing of planned clinical assessments are not repeated in this SAP unless relevant to the planned analysis.

The structure and content of this SAP provides sufficient detail to meet the requirements identified by the Food and Drug Administration (FDA), European Medicines Agency (EMA), and International Conference on Harmonization (ICH) of Technical Requirements for Registration of Pharmaceuticals for Human Use: Guidance on Statistical Principles in Clinical Trials (ICH, 1998). All work planned and reported for this SAP will follow internationally accepted guidelines, published by the American Statistical Association (ASA, 2018) and the Royal Statistical Society (RSS, 2014), for statistical practice.

The planned analyses identified in this SAP may be included in clinical study reports (CSRs), regulatory submissions, or future manuscripts. Also, post-hoc exploratory analyses not necessarily identified in this SAP may be performed to further examine study data. Any post-hoc or unplanned, exploratory analysis performed will be clearly identified as such in the final CSR.

The statistical plan described hereafter is an *a priori* plan. It will be approved before any descriptive analysis of data pertaining to Annexon Biosciences's study ANX005-wAIHA-02.

2. Study Objectives and Endpoints

2.1. Study Objectives

2.1.1. Primary Objective

The primary objectives are:

- To evaluate the safety and tolerability of two once-weekly intravenous infusions of 100 mg/kg ANX005 in patients with Warm Autoimmune Hemolytic Anemia (wAIHA).
- To evaluate the clinical effect of two once-weekly intravenous infusions of 100 mg/kg ANX005 in patients with wAIHA.

2.1.2. Secondary Objectives

The secondary objectives are:

- To evaluate the pharmacokinetic (PK) profile of ANX005 in patients with wAIHA.
- To evaluate the effect of ANX005 on classical complement pathway inhibition as measured by complement system related biomarkers in patients with wAIHA.

2.1.3. Exploratory Objectives

The exploratory objectives are:

[redacted]

2.2. Study Endpoints

2.2.1. Efficacy Endpoints

2.2.1.1. Primary Efficacy Endpoint

The primary efficacy endpoints of this study are:

- Change from baseline in hemoglobin over time up to Day 71.
- Maximum absolute change in hemoglobin from baseline.
- Change from baseline in biomarkers of hemolysis (reticulocyte count, haptoglobin, LDH, total and indirect bilirubin) over time up to Day 71.

2.2.1.2. Secondary Efficacy Endpoint(s)

The secondary efficacy endpoints of this study include the following:

- Inhibition of classical complement activity as measured by serum CH50 change from baseline over time up to Day 71.
- Change and percent change from baseline in serum C4 concentrations over time up to Day 71.
- Change and percent change from baseline in serum free C1q concentrations over time up to Day 71.

2.2.1.3. Exploratory Efficacy Endpoint(s)

The exploratory efficacy endpoints of this study include the following:

[redacted]

2.2.2. Safety Endpoints

The primary safety endpoint of this study includes the following:

- Number and percent of patients experiencing treatment-emergent adverse events (TEAEs).

2.2.3. Pharmacokinetic/Pharmacodynamic Variable(s)

The PK endpoints and the calculation of parameters for PK/PD analysis will be described in a separate PK analysis plan (PKAP).

3. Overall Study Design and Plan

3.1. Overall Design

This is an open-label, repeat-dose, Phase 2 study in adult male and female patients with wAIHA. One cohort of up to approximately 12 patients with wAIHA will be enrolled in this study. Patients will receive ANX005 at Day 1 and Day 8, and regular visits will be performed until end of study, at Day 71.

3.2. Sample Size and Power

The sample size for this study is not based on providing statistical power for hypothesis testing. However, for an adverse event (AE) with a true rate of 10%, a sample size of up to 12 patients provides up to 72% likelihood that the event will be observed during the study.

3.3. Study Population

The study population consists of male and female patients aged 18 and above, inclusive, at the time of consent with wAIHA with evidence of activation of the complement system.

Patients will be primarily recruited from a non-interventional study (ANX-wAIHA-01), designed to establish the level of complement activation in a wide range of patients with wAIHA.

3.4. Treatments Administered

All patients will receive first dose of 100 mg/kg dose of ANX005 at Day 1 and second dose at Day 8.

3.5. Schedule of Events

Please see the protocol for a detailed schedule of events.

4. Statistical Analysis and Reporting

4.1. General Introduction

Data processing, tabulation of descriptive statistics, and graphical representations described in this SAP will primarily use SAS (release 9.4 or higher) or later. If the use of other software is warranted, the final statistical methodology report will detail what software was used for what purposes.

Continuous (quantitative) variable summaries will include the number of subjects (n) with non-missing values, mean, standard deviation (SD), median, first and third quartiles (Q1, Q3), minimum, and maximum. Summaries may include 95% confidence intervals (CIs) if appropriate. PK summaries will include coefficient of variation (CV%) and the geometric mean.

Categorical (qualitative) variable summaries will include the frequency and percentage of subjects who are in the particular category or each possible value. In general, the denominator for the percentage calculation will be based upon the total number of subjects in the study population, unless otherwise specified.

The minimum and maximum will be reported with the same degree of precision (ie, the same number of decimal places) as the observed data. Measures of location (mean and median) will be reported to 1 degree of precision more than the observed data and measures of spread (SD) will be reported to 2 degrees of precision more than the observed data.

Percentages will be presented to 1 decimal place, unless otherwise specified. General exceptions to this rule are values of 100% which will be displayed without any decimal places and zero counts which will not display percentages.

All the analysis described in this SAP are descriptive. No inferential statistics will be performed. All participant data will be listed.

4.2. Interim Analysis

No interim analyses are planned.

4.3. Final Analysis

The final analysis of all data will be based on data from the complete study and will be performed after all subjects have completed the study (End-of-Study visit on Day 71 or early termination) and all data from the study are in the database and the database is locked.

5. Analysis Populations

The following analysis populations are planned for this study:

- **Full Analysis Set (FAS):** The FAS population includes all subjects who sign an Informed Consent Form (ICF) and meet all eligibility criteria as assessed by the investigator
- **Safety Population (SAF):** The Safety Population includes all subjects who receive any amount of ANX005.
- **Pharmacokinetic Population (PK):** The PK Population includes all subjects in the Safety Population who have evaluable ANX005 concentration data
- **Pharmacodynamic Population (PD):** The PD Population includes all subjects who received at least 1 completed infusion of ANX005 and have at least one post infusion PD assessment.
- **Per Protocol Population (PP):** The PP Population includes all subjects who completed all infusions of ANX005 and do not have major protocol violations. Major protocol violations may include, but are not limited to, violations of eligibility criteria, receipt of incorrect dose of ANX005, use of prohibited medications, and non-compliance with study assessments.

The PP set will be used for clinical and functional assessments and biomarker endpoints. Assignment of subjects to populations, including PP, will be confirmed at a data review meeting to be held before the study database is locked.

6. General Issues for Statistical Analysis

6.1. Statistical Definitions and Algorithms

6.1.1. Baseline

The last non-missing observation recorded before the first dose of ANX005 will be used as the baseline observation for all calculations of change from baseline. For [redacted], baseline is defined as last non-missing observation before or on Day 1.

6.1.2. Study Day

Study Day 1 is date of the first dosing date (normally Day 1 visit). For dates before study day 1, study day= reference day – day 1 visit. For dates after study day 1, study day = reference day – day 1 visit + 1.

6.1.3. Rescreening Data

Subjects who do not meet all inclusion and exclusion criteria at Week -6 may rescreen twice over the 6-week screening period for eligibility criteria, using rescreening kits, if there is cause to believe that the patient will be eligible upon rescreen. Patients who are rescreened will retain their original patient identification number.

6.1.4. Handling of Dropouts or Missing Data

Any subject who withdraws from the study will not be replaced.

Imputation of missing data will be performed only for adverse events and medications onset dates (for example to determine if an adverse event is a TEAE or a medication is prior or concomitant) following rules in Section 6.1.10. No imputation of efficacy data will be done.

6.1.5. Analysis Visit Windows

By-visit summaries will be generally based on electronic case report form (eCRF)-defined nominal visits. The only exception will be in case a scheduled measurement is not available, and the unscheduled measurement falls within the analysis visit windows as described in Table 2. If multiple visits (including unscheduled visits) share the same visit window, the latest visit will be used.

Table 1: Analysis Visit Windows

Analysis Visit	Target Day[a]	Lower Limit	Upper Limit
Week -2	-14	-17	-11
Day 1	1	1	1
Day 2	2	2	2
Day 4	4	4	4
Week 1 (Day 8)	8	8	8
Week 2 (Day 15)	15	13	17
Week 3 (Day 22)	22	20	24
Week 4 (Day 29)	29	27	31
Week 5 (Day 36)	36	34	38
Week 6 (Day 43)	43	40	46
Week 7 (Day 50)	50	47	53
Week 8 (Day 57)	57	54	60
Week 10 (Day 71)	71	68	74

[a]Target day refers to Study Day 1 (date of first infusion).

Data collected during unscheduled visits and not assigned to a nominal visit will be listed and included in the overall AE summary table.

6.1.6. [redacted]

[redacted]

6.1.7. TEAEs

Any adverse event with an onset date/time after the first infusion date/time of ANX005 until the end of the study will be considered as TEAE.

6.1.8. Prior and concomitant medications

Medications that started before the first infusion of study drug will be considered prior medications whether or not they were stopped before. Any medications continuing or starting after the first infusion of study drug will be considered to be concomitant. If a medication starts before and continues after the first infusion of study drug it will be considered both prior and concomitant.

6.1.9. Derived Variables

- Body Mass Index (BMI) = Weight in kg / (Height in cm/100)^2
- Time since first wAIHA diagnostic (years) = (Date of ICF – date of first wAIHA diagnostic)/365.25
- Actual drug volume (ml): Sum of all the volumes administered (from different rates and bags) in a visit
- Total Actual Dose (mg): Actual drug volume * (total planned dose /total planned volume)
- Change from baseline = value at current time point – value at baseline.
- Percent change from baseline = $\left(\frac{value\ at\ current\ time\ point - value\ at\ baseline}{value\ at\ baseline}\right) * 100\%$

6.1.10. Data Adjustments/Handling/Conventions

All collected data will be presented in listings. Data not subject to analysis according to this plan will not appear in any tables or graphs but will be included only in the data listings.

Medical history will be coded using the Medical Dictionary for Regulatory Activities (MedDRA) (v24.1 or an updated version at the time of the database lock). Prior and concomitant medications will be coded using World Health Organization Drug Dictionary (WHODD v.B3G September 2021 or an updated version at the time of the database lock).

If partial dates occur, the convention for replacing missing dates for the purpose of statistical analysis is as follows: if just day is missing then the day assigned is the first day of the month or the date of first dose (if in the same month), whichever is later; if just month is missing then the

month assigned is the month of the first dose, unless that results in a date before the first dose in which case the month after the first dose is used; and if both month and day are missing then the month assigned is the month of the first dose and the day assigned is either the first day of the month or the first dose date, whichever is later.

If partial times occur, the convention is as follows: if the missing time occurs on the day of the first dose and both the hour and minute are missing then the time assigned is the time of the first dose, otherwise if both the hour and minute are missing and the date is not the date of first dose the time assigned is 12:00; if the date is the same as the date of the first dose and only hour is missing the hour assigned is 12 or the hour of first dose, whichever is later, and if the date is the same as the date of first dose and only the minute is missing the minute assigned is 30 or the minute of first dose, whichever is later. Otherwise the hour assigned is 12 if the hour is missing and the date is not the same as the date of first dose and the minute assigned is 30 is the the date is not the same as the date of first dose.

These conventions will be applied only to prior/concomitant medication and adverse event onset dates and times with the following precaution: if the missing date and time reflect the date and time of onset of an adverse event, the modified date and time will be constructed to match the first documented date/time post drug administration while preserving the order in which the AE was reported in the eCRF.

7. Study Patients/Subjects and Demographics

7.1. Disposition of Patients/Subjects and Withdrawals

Disposition will include tabulations of the number of patients screened and screen failures will be summarized for all patients present in the database. Patients completing the treatment (defined as those with infusions at Day 1 and Day 8 and not reporting any AE with “Drug Withdrawn” as action in the CRF), patients completing the study, tabulated reasons for discontinuation from the study and number of subjects in each analysis population will also be summarized.

7.2. Protocol Violations and Deviations

Number and percentage of subjects in FAS Population with at least one important/non important protocol deviation will be summarized. All details of the protocol deviations will be listed.

7.3. Demographics and Other Baseline Characteristics

Summary statistics for age, gender, childbearing potential, race, ethnicity, height, weight, BMI (see Section 6.1.99), number of patients with a historical diagnosis of wAIHA, number of patients with mixed AIHA, and number of patients with history of arterial blood clots and history of venous blood clots will be presented.

Another summary for wAIHA Medical History including the variables collected in eCRF and time since first wAIHA diagnostic (see Section 6.1.99) will be produced.

For not predefined medical histories, they will be grouped by MedDRA system organ class (SOC) and preferred term (PT), coded using MedDRA v 22.1.

For the continuous variables, the number of non-missing values and the mean, standard deviation, minimum, median and maximum will be tabulated.

For the categorical variables, the counts and proportions of each value will be tabulated.

These analyses will be conducted for the Safety Populations. Demographic summary will be repeated for FAS, and for PP Population but specifically in the following subsets: patients with a historical diagnosis of wAIHA, patients with mixed autoimmune hemolytic anemia (AIHA) and a pooled analysis of the total population (wAIHA and mixed AIHA) will also be performed.

7.4. Exposure and Compliance

Summary statistics for total planned and actual dose (mg), total planned and actual drug volume (ml), planned and actual infusion rate (ml/hr), number of bags will be tabulated by visit. Additionally, the number of doses and number of dosage (defined as the number of different infusions needed to administer the doses) will be tabulated in an overall summary. For actual dose and actual drug volume derivations Section 6.1.99. This analysis will be performed in the Safety Population

8. Efficacy Analysis

8.1. Primary Efficacy Analysis

The primary efficacy endpoints are the change from baseline of hemoglobin and hemolysis biomarkers (reticulocyte count, haptoglobin, lactate dehydrogenase [LDH], total and indirect bilirubin) over time up to Day 71. Descriptive by-visit summaries, including change from baseline and percent change from baseline will be performed for these parameters in the SAF Population. Additionally, maximum absolute change from baseline will be tabulated for the SAF Population.

8.1.1. Sensitivity Analyses of the Primary Efficacy Endpoint

All the analysis described above will be repeated for the PD and PP Population. Every analysis performed in the PP set will be done for the following subsets: patients with a historical diagnosis of wAIHA, patients with mixed autoimmune hemolytic anemia (AIHA) and a pooled analysis of the total population (wAIHA and mixed AIHA) will also be performed.

8.2. Secondary Efficacy Analysis

Descriptive by-visit summaries of serum CH50, C4 and free C1q including change from baseline will be performed. For C4 and free C1q percent change from baseline will be provided as well. These analyses will be performed for the Safety Population and repeated on the PD Population and PP.

8.3. Exploratory Efficacy Analysis

[redacted]

9. Safety and Tolerability Analysis

Safety will be evaluated from reported adverse events (AEs), changes in clinical laboratory values, changes in vital signs, physical examination, and electrocardiogram (ECG results).

All safety analyses will be performed on the Safety population.

9.1. Adverse Events

All AEs, treatment emergent AEs (TEAEs), and serious adverse events (SAEs) will be coded using the MedDRA v24.1.

The number and percent of subjects reporting TEAEs, grouped by MedDRA system organ class (SOC) and preferred term (PT), will be tabulated. In the case of multiple occurrences of the same TEAE within the same subject, each subject will only be counted once for each PT. The summary

will be presented in descending order of frequency of SOC and then PT within SOC based on overall patients. This analysis will be repeated for:

- TEAEs with a severity of grade 3 or higher according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) by SOC and PT.
- TEAEs by SOC, PT and highest grade of severity.
- Treatment related TEAEs by SOC and PT.
- Treatment related TEAEs with a severity of grade 3 or higher by SOC and PT.
- Treatment related TEAEs by SOC, PT and highest grade of severity.

In the summaries showing severity the event with the maximum severity will be reported. Severity is reported as per NCI CTCAE v 5.0. If a particular event is missing the severity and/or relationship, then the strongest possible severity or relationship will be assumed for analysis (severity = Grade 5, relationship = related).

In the AE data listings, all AEs will be displayed. AEs that are not treatment-emergent will be flagged.

9.1.1. Adverse Events Leading to Withdrawal

A summary with number and percent of subjects with TEAEs leading to treatment withdrawal, by SOC and PT will be prepared for the Safety Population. This will be repeated for TEAEs leading to study discontinuation.

A data listing of TEAEs leading to withdrawal of study drug will also be provided, displaying details of the event(s) captured on the eCRF.

9.1.2. Deaths and Serious Adverse Events

Any deaths that occur during the study will be summarized and listed.

Treatment-emergent serious adverse events will be listed and also tabulated by system organ class and preferred term.

9.1.3. Other Significant Adverse Events

Adverse events of Special Interest (AESIs), captured in the eCRF, are defined as hypersensitivity (eg, rash, angioedema, anaphylaxis, serum sickness reaction), infusion-related reaction (IRRs), evidence of an infection with encapsulated bacteria, or development of a systemic autoimmune disorder.

Incidence of Treatment Emergent AESI will be summarized by frequencies and percentages by SOC and PT and the analysis will be repeated for treatment-related AESIs.
Incidences of treatment emergent immune reactions (with number of patients and percentages) will also be summarized by SOC and PT.

9.2. Clinical Laboratory Evaluations

Samples for hematology, chemistry, and urinalysis will be collected at Screening, Day 1, Day 2, Day 4, Week 1 to Week 8 and Week 10.

Laboratory test results (serum chemistry, hematology and urine analysis) will be summarized descriptively by time point with both observed values and change from baseline values. For subjects who discontinued the study, the assessments performed at the early termination visit will be presented separately.

Laboratory values that are outside the normal range will also be flagged in the data listings, along with corresponding normal ranges. Any out-of-range values that are identified by the investigator as being clinically significant will also be shown in a data listing.

Serum pregnancy test, coagulation and anti-nuclear antibody results will be listed.

9.3. Vital Signs

Vital signs will be collected at Screening, Day 4, Week 1 to Week 8 and Week 10. Additionally at infusions days (Day 1 and Week 1), they will be collected at the following timepoints: 15, 45, 75, 105, 135 minutes after onset.

Descriptive summaries by time point of actual values and changes from baseline will be calculated for upright seated systolic blood pressure, upright seated diastolic blood pressure, heart rate (HR), respiratory rate, and oral body temperature.

9.4. Electrocardiograms

Electrocardiograms will be collected at Screening, Day 1, Week 1 and Week 10.

Descriptive summaries will be presented for ECG measures of ventricular HR, PR interval, RR interval, QRS interval, QT interval, QT_C interval (both correction methods), P wave and T wave. These summaries will be presented by time point.

9.5. Further Safety Evaluations

Physical examination data will be listed.

Number and percentage of patients with anti-ANX005 antibodies (a positive test result) by visit and at least once during the study will be tabulated. Additionally anti-ANX005 antibody results will be listed.

9.6. Concomitant Medication

Concomitant and prior medications will be summarized descriptively using counts and percentages.

Frequencies and percentages will be summarized descriptively by Anatomical Therapeutic Chemical (ATC) classification Level 4 and Preferred Name. The summary will be presented in descending order of frequency of ATC and then Preferred Name within ATC based on overall patients.

Both prior and concomitant medications (defined in Section 6.1.8) will be listed.

10. Changes from Planned Analysis

There are no changes from Planned Analysis

11. Other Planned Analysis

11.1. Pharmacodynamic Analysis

All PD parameters not analysed in the efficacy analysis will be descriptively summarized by visit and timepoint. All PD data will also be listed. All analysis will be on the PD Population and repeated on the PP Population (by patients with a historical diagnosis of wAIHA, patients with mixed AIHA and total population).

12. References

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FACIT Org (n.d.). FACIT Fatigue Scoring Downloads. https://www.facit.org/measures-scoring-downloads/facit-fatigue-scoring-downloads

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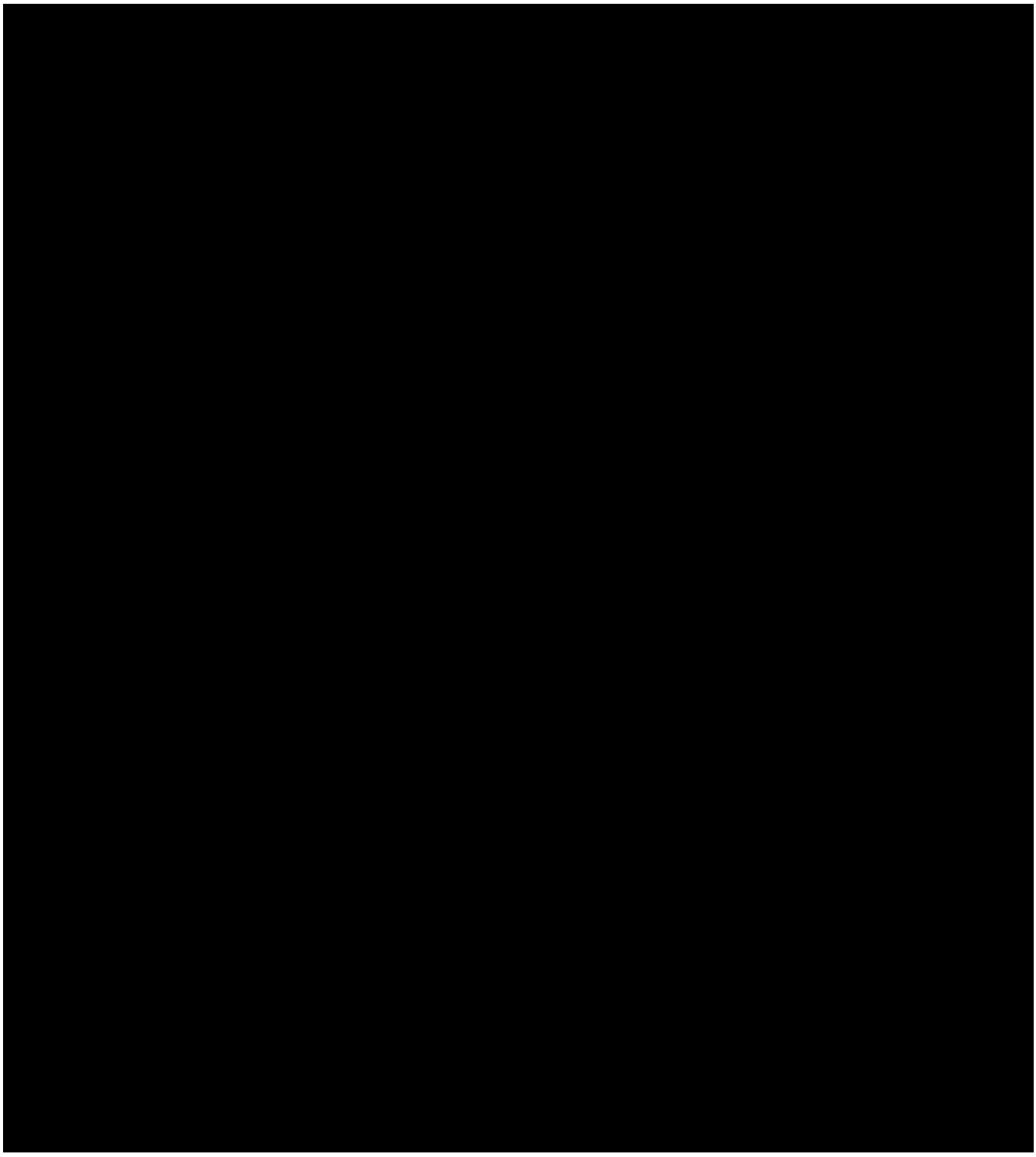
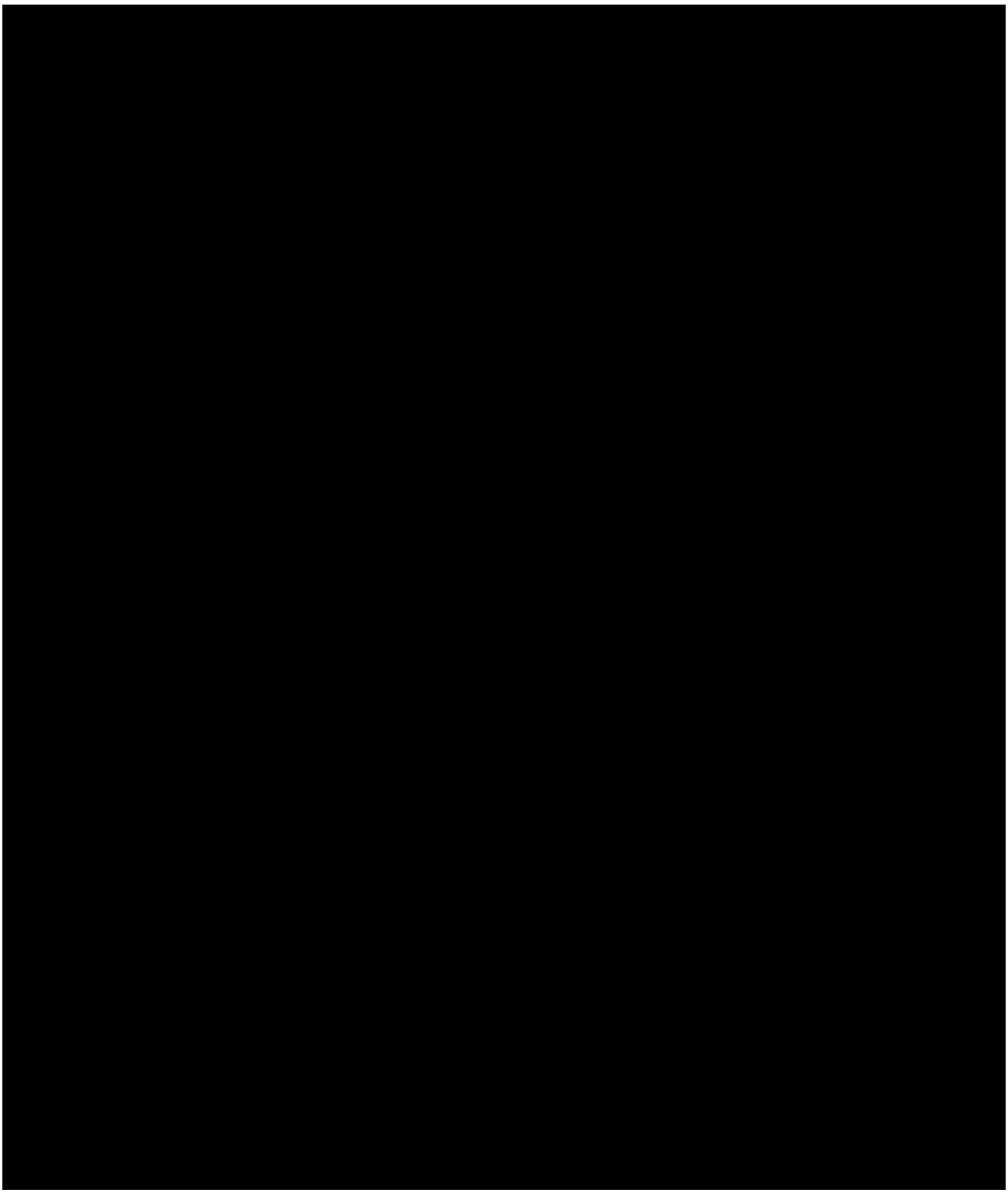
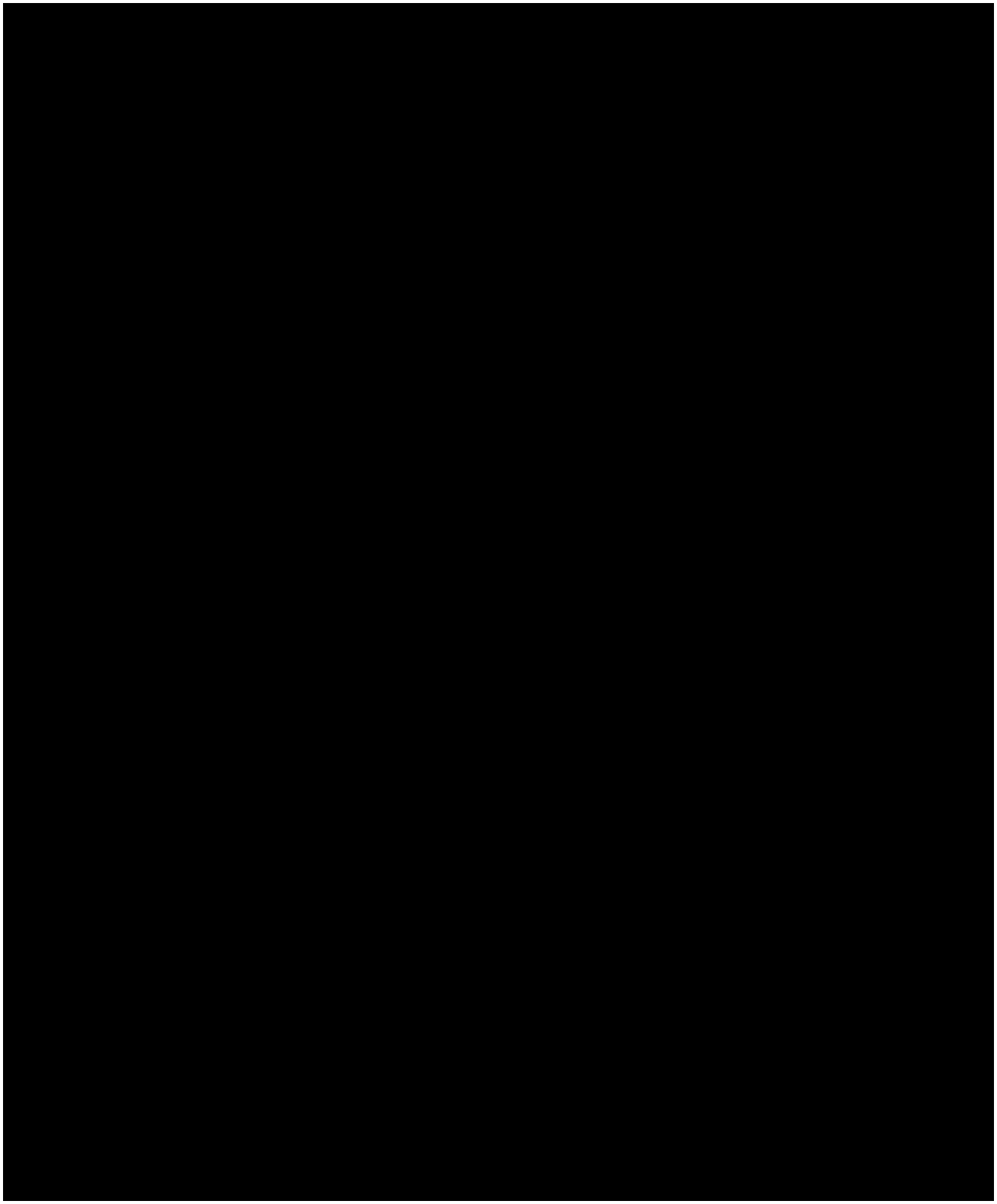
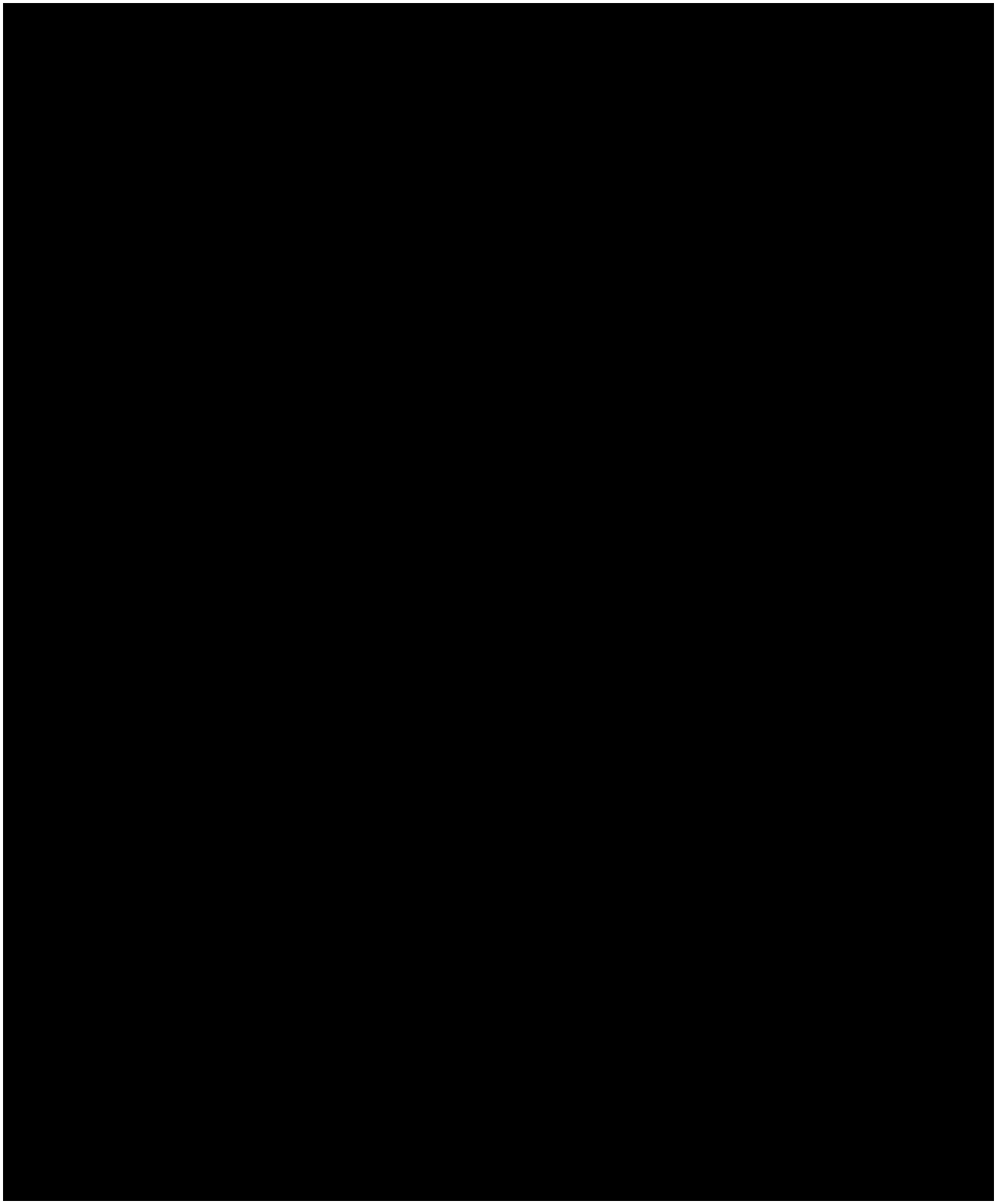
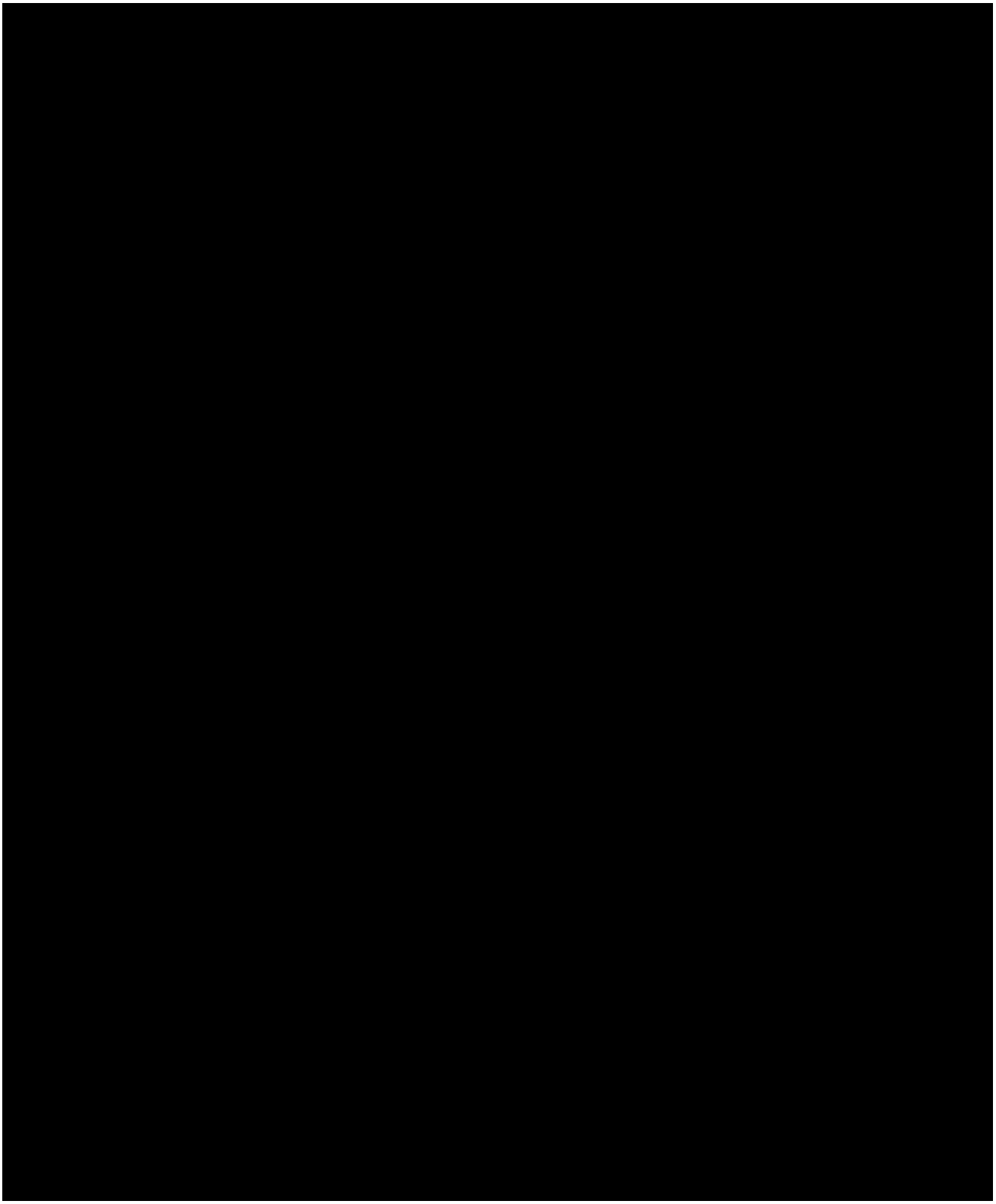
13. Tables, Listings, and Figures

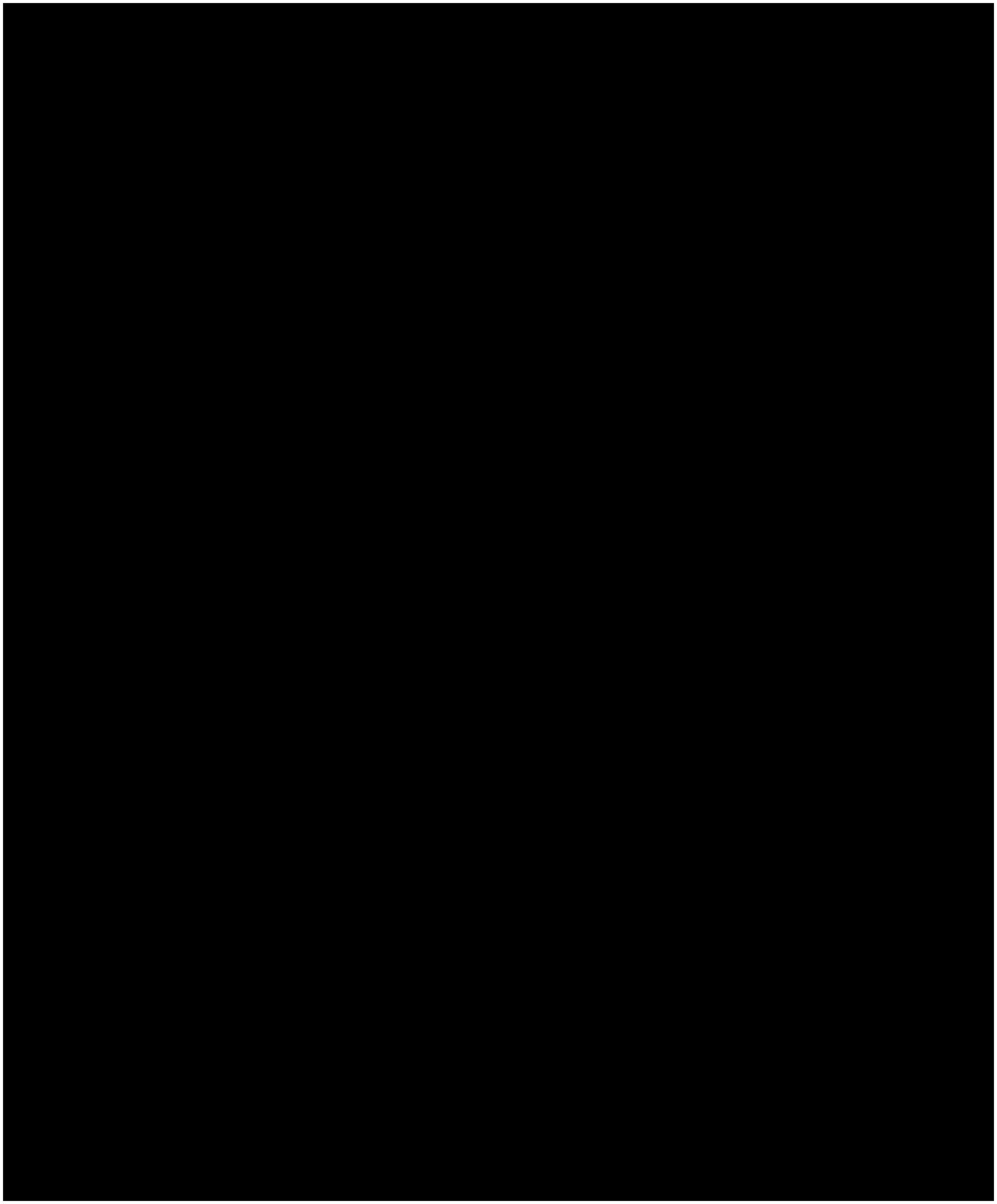


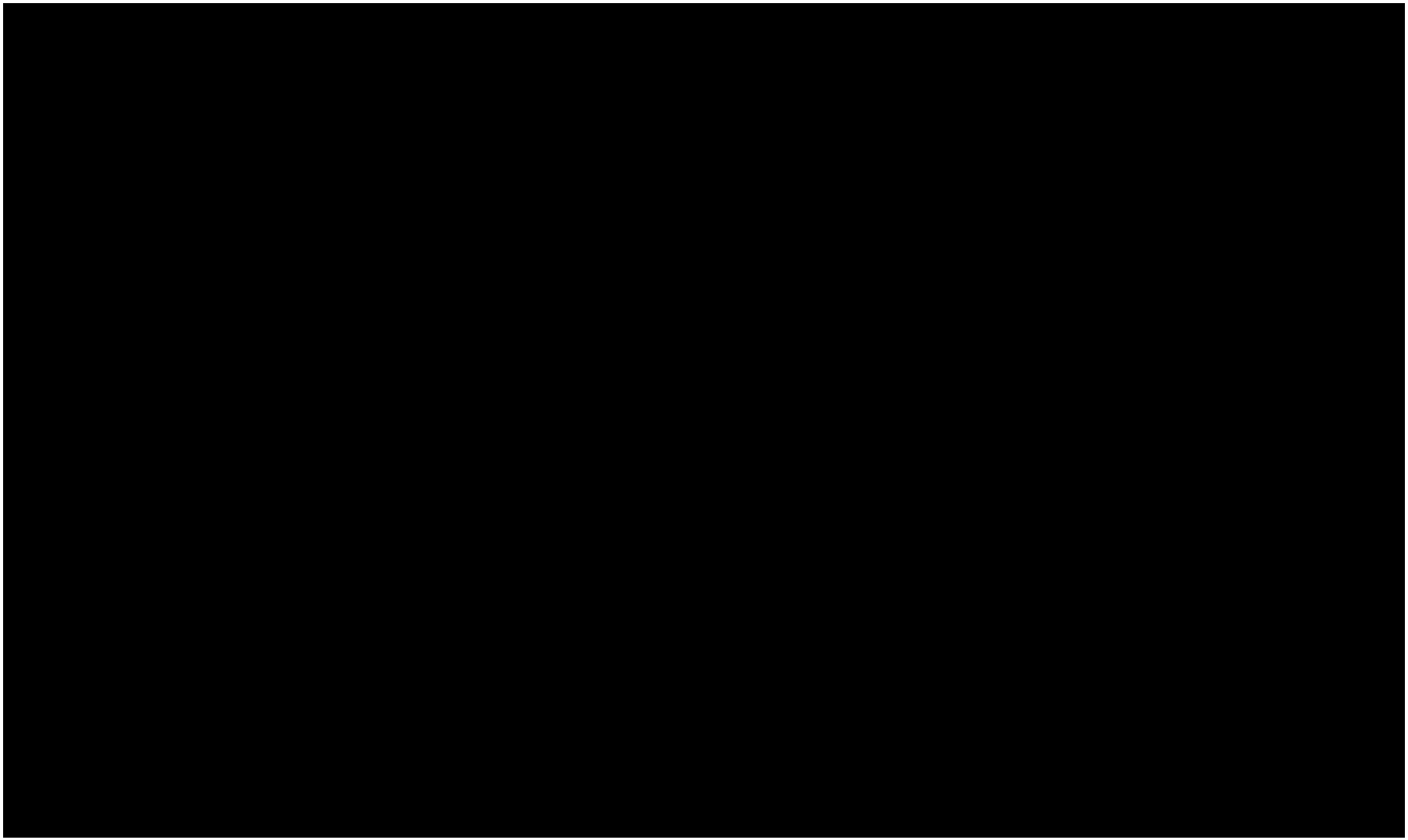


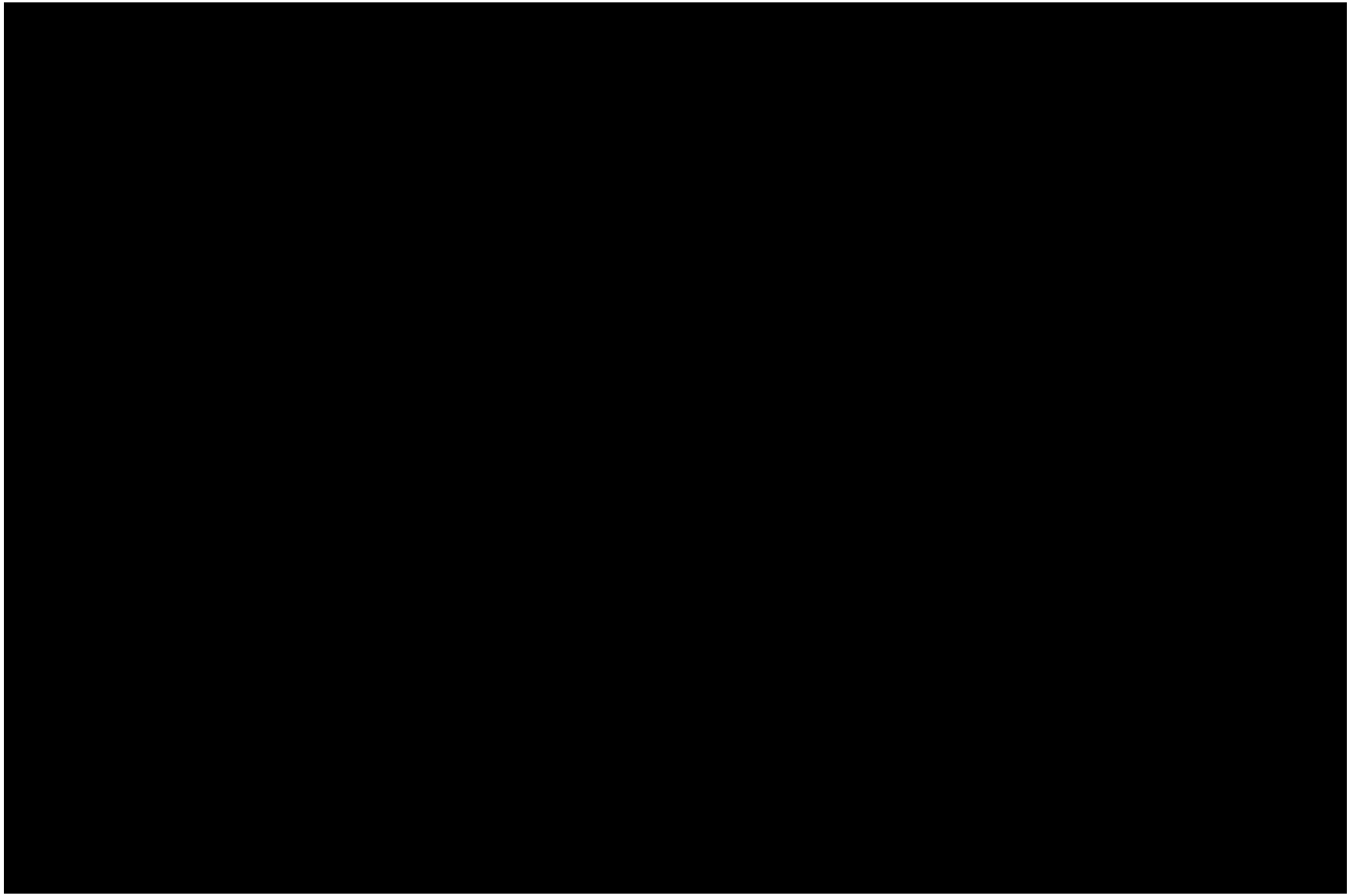


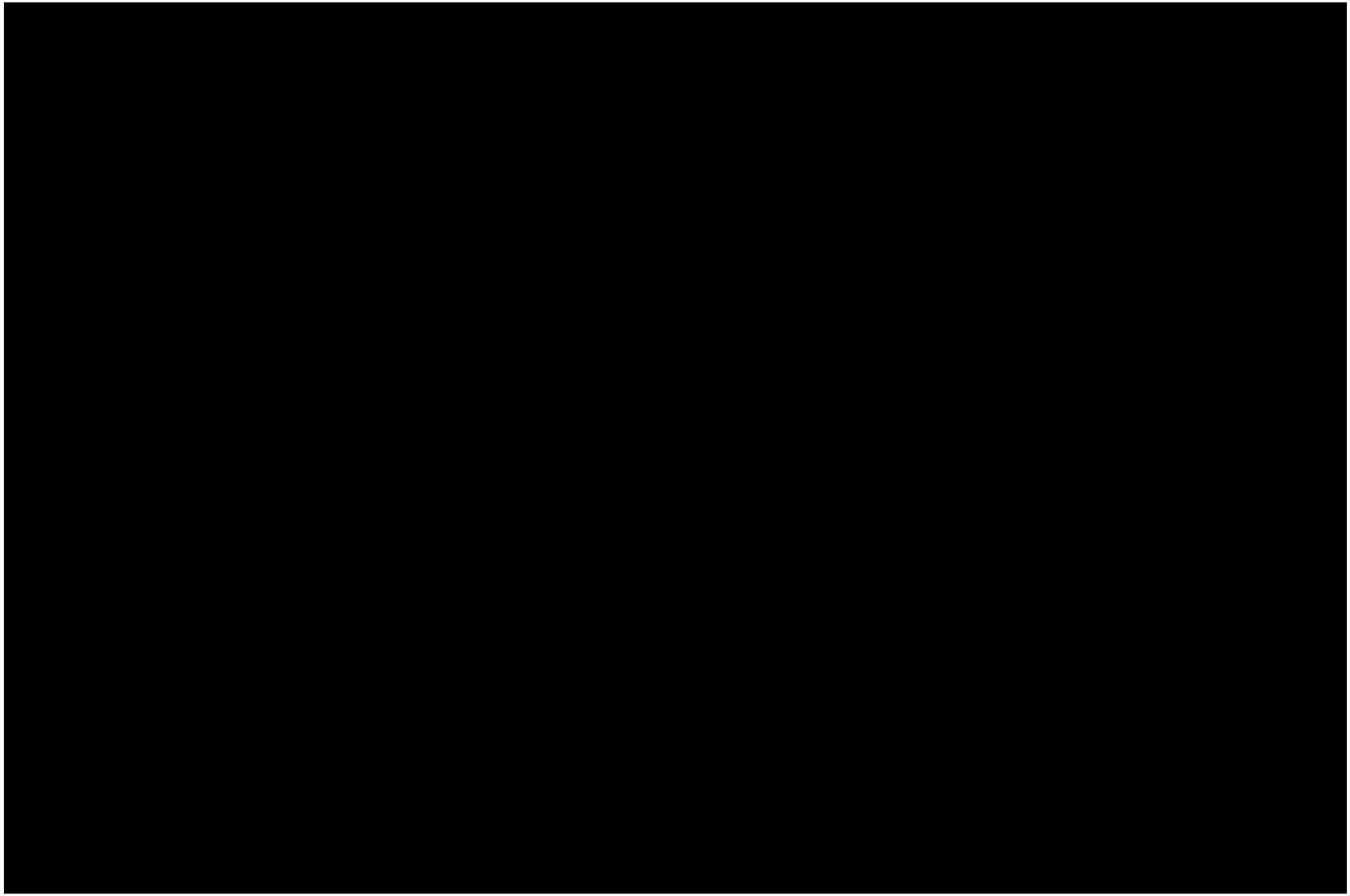


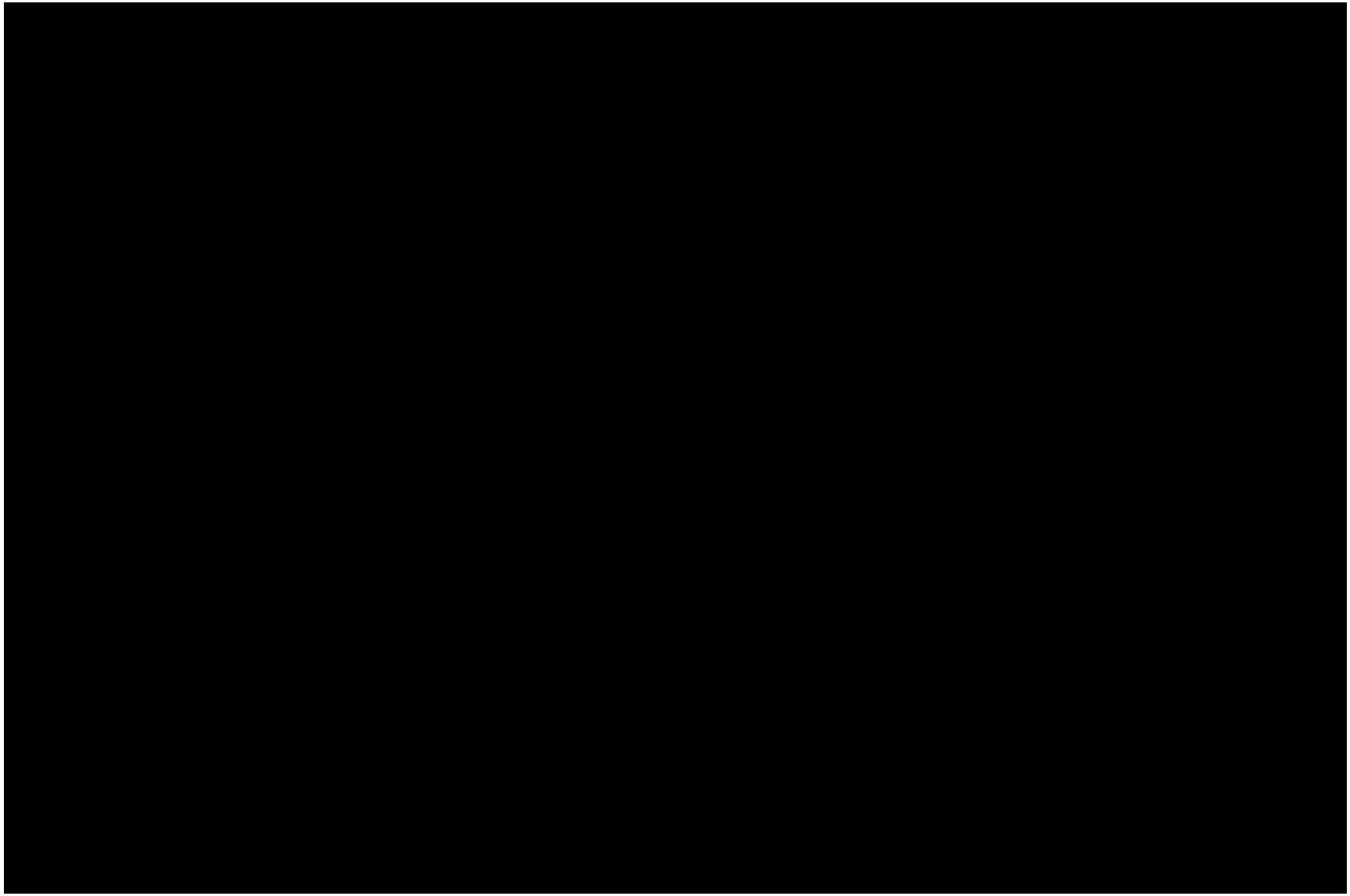


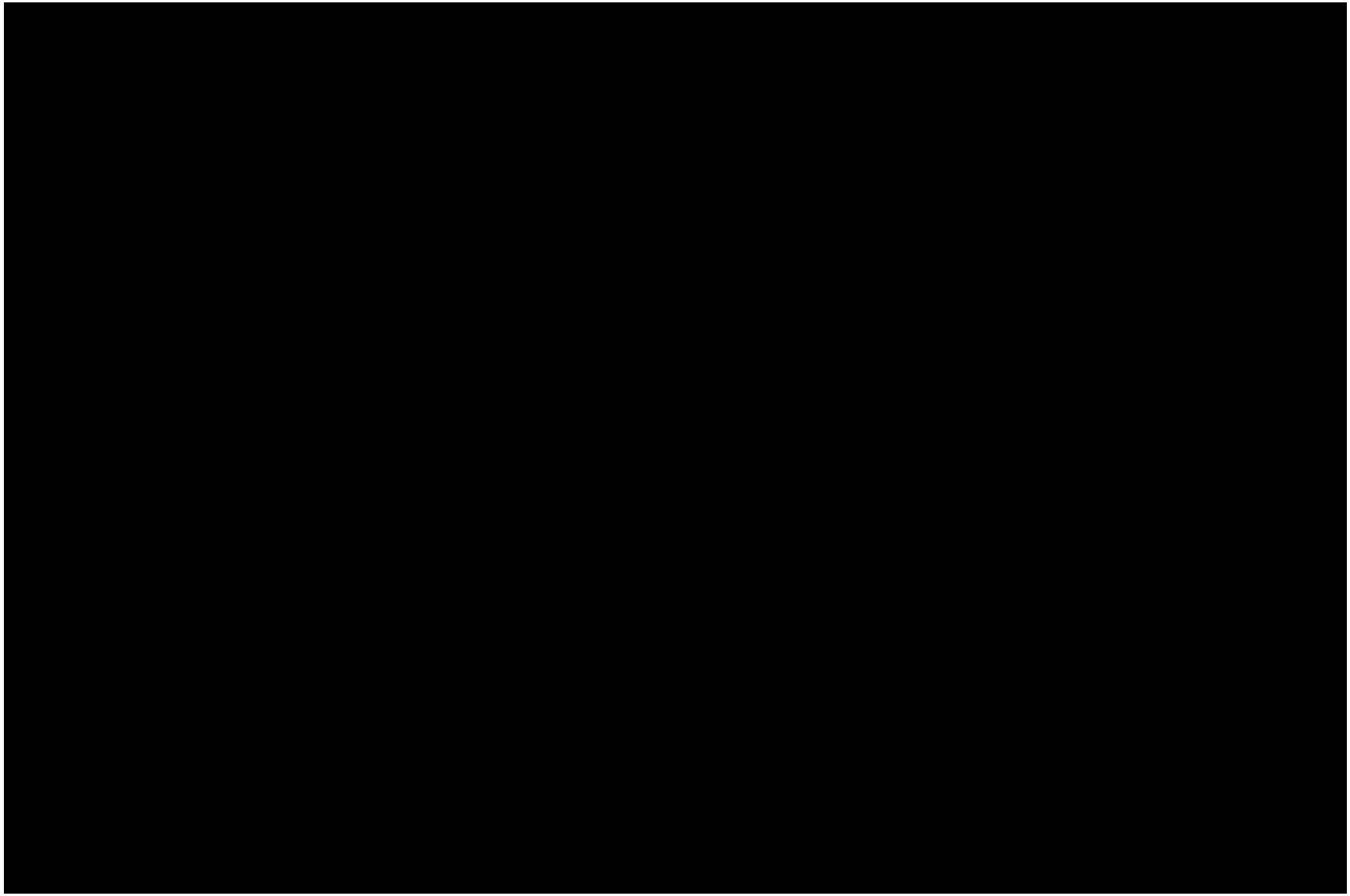


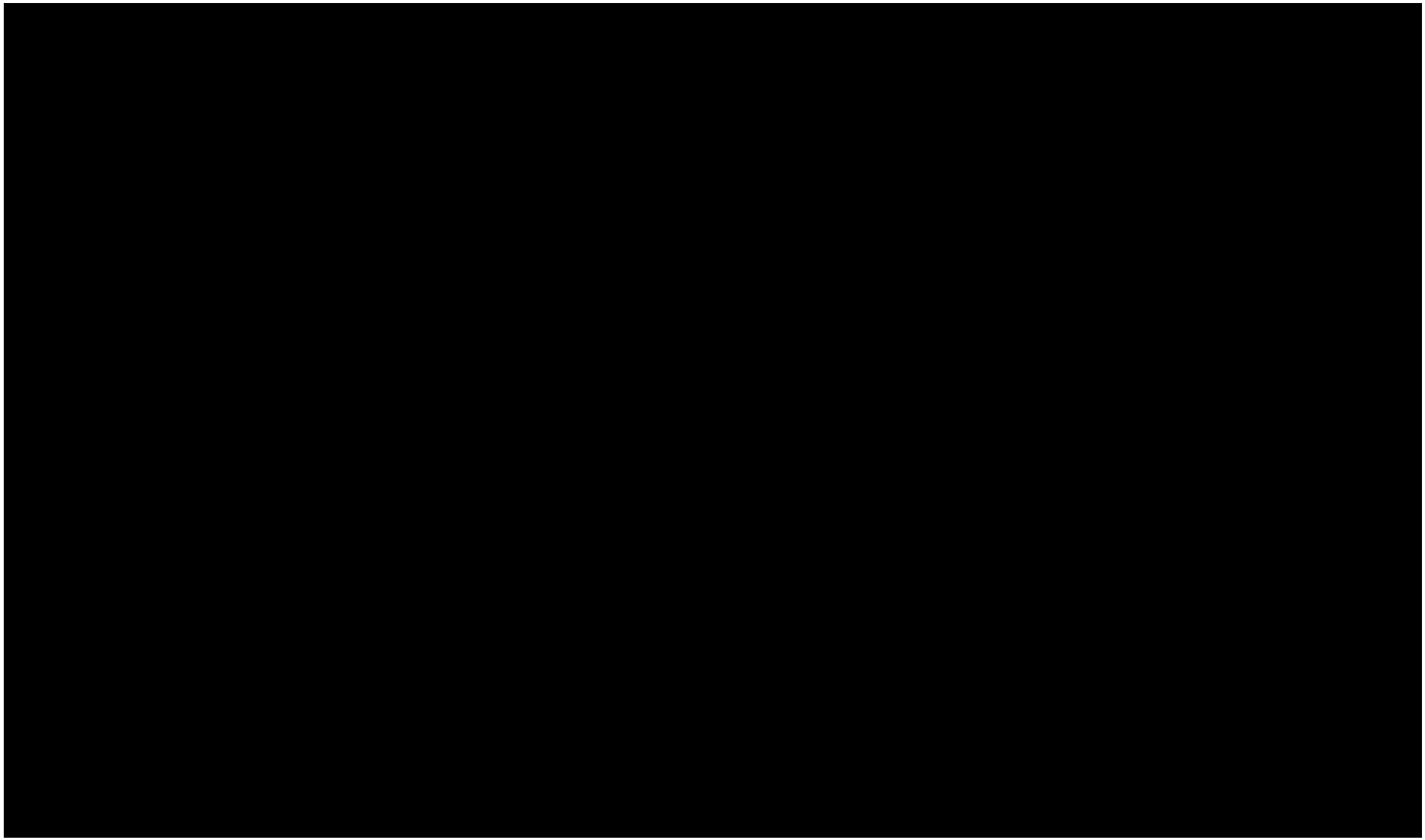


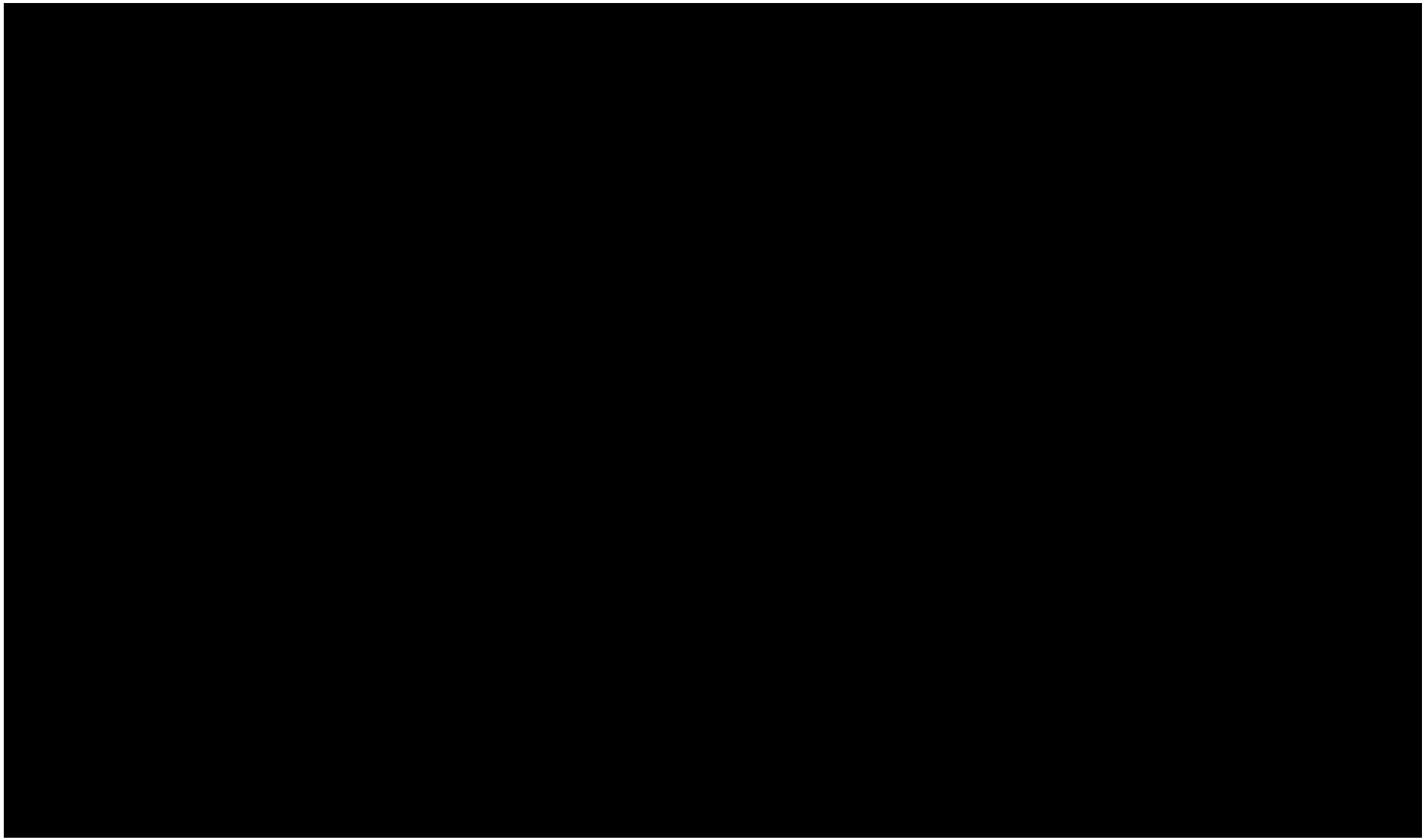


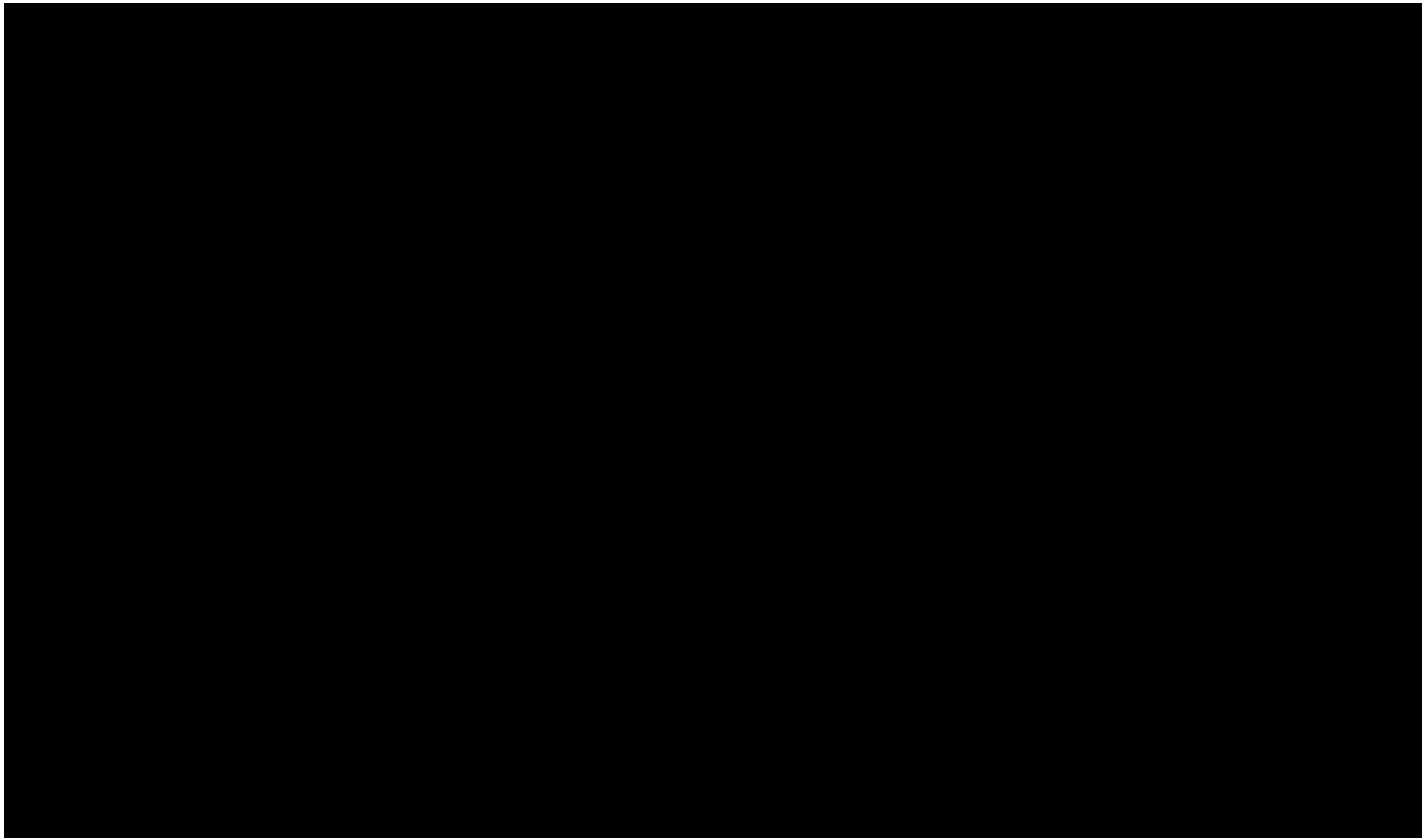


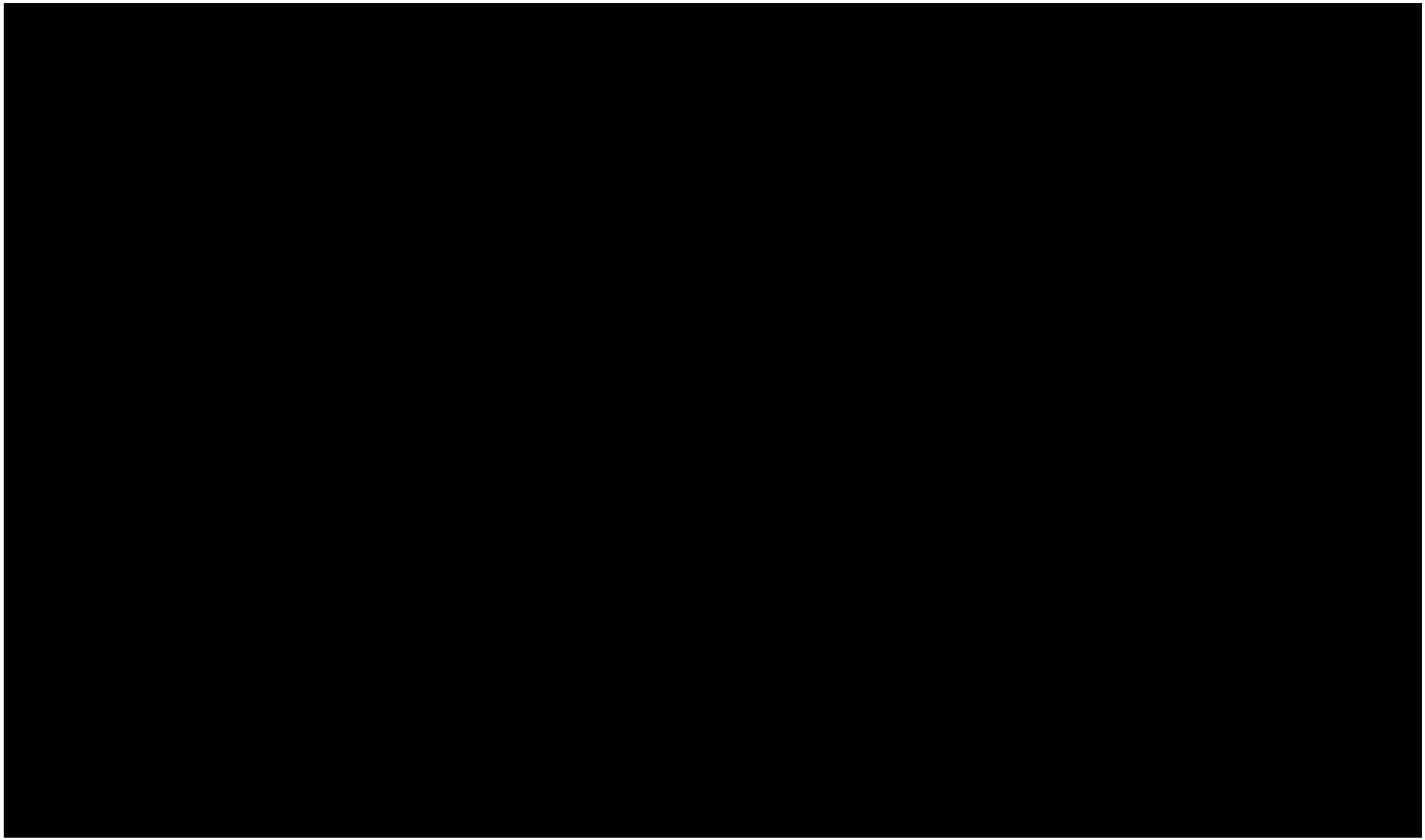


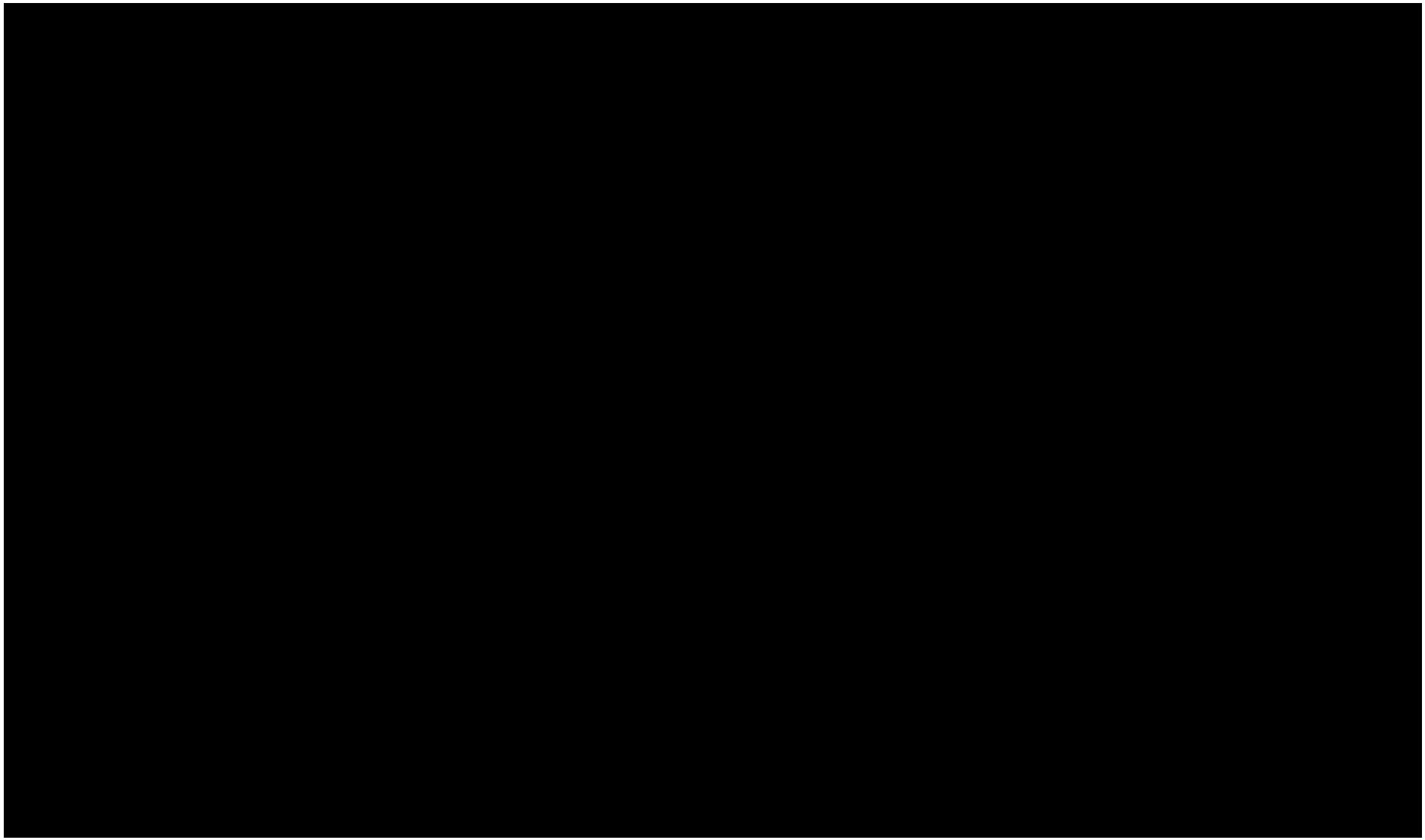


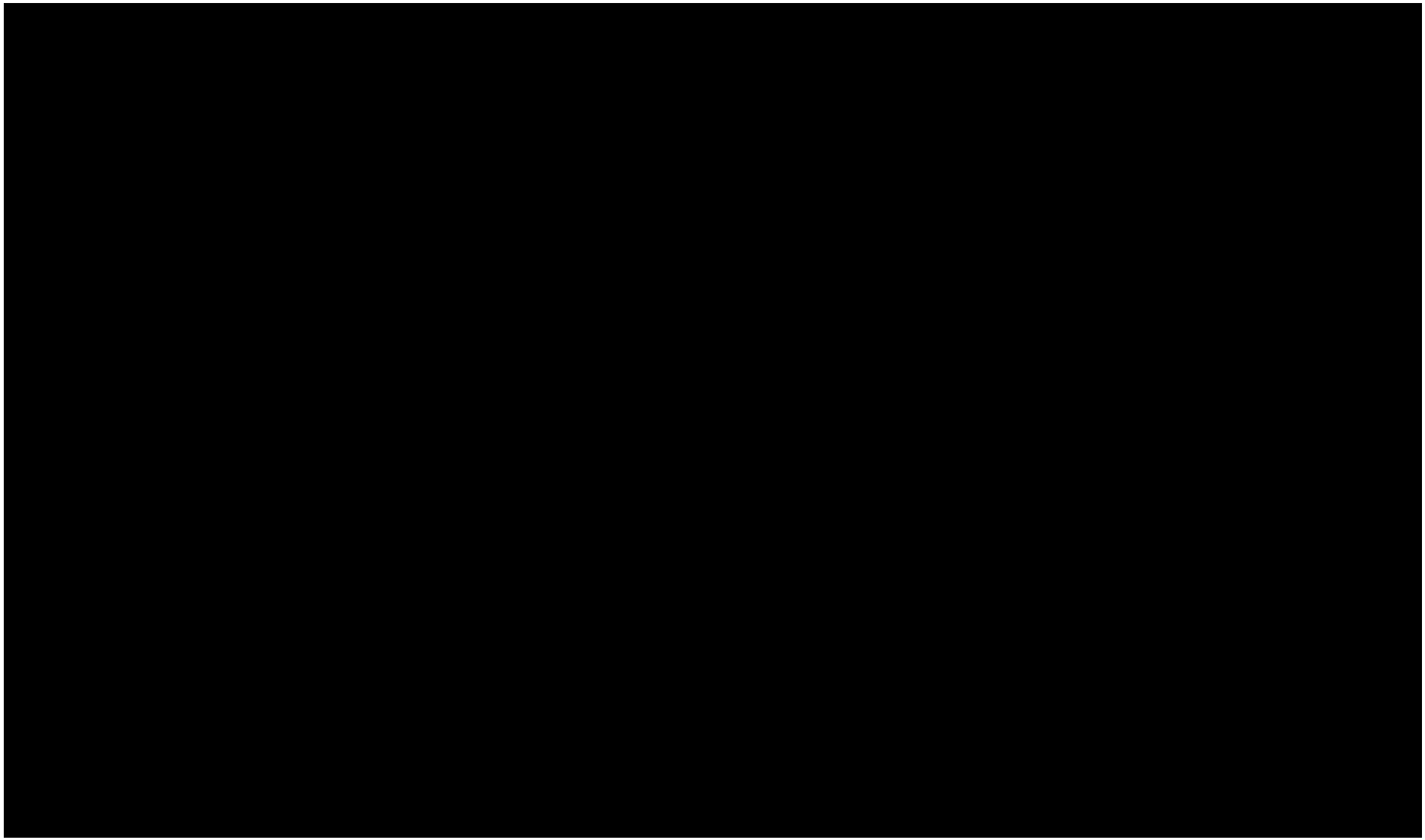


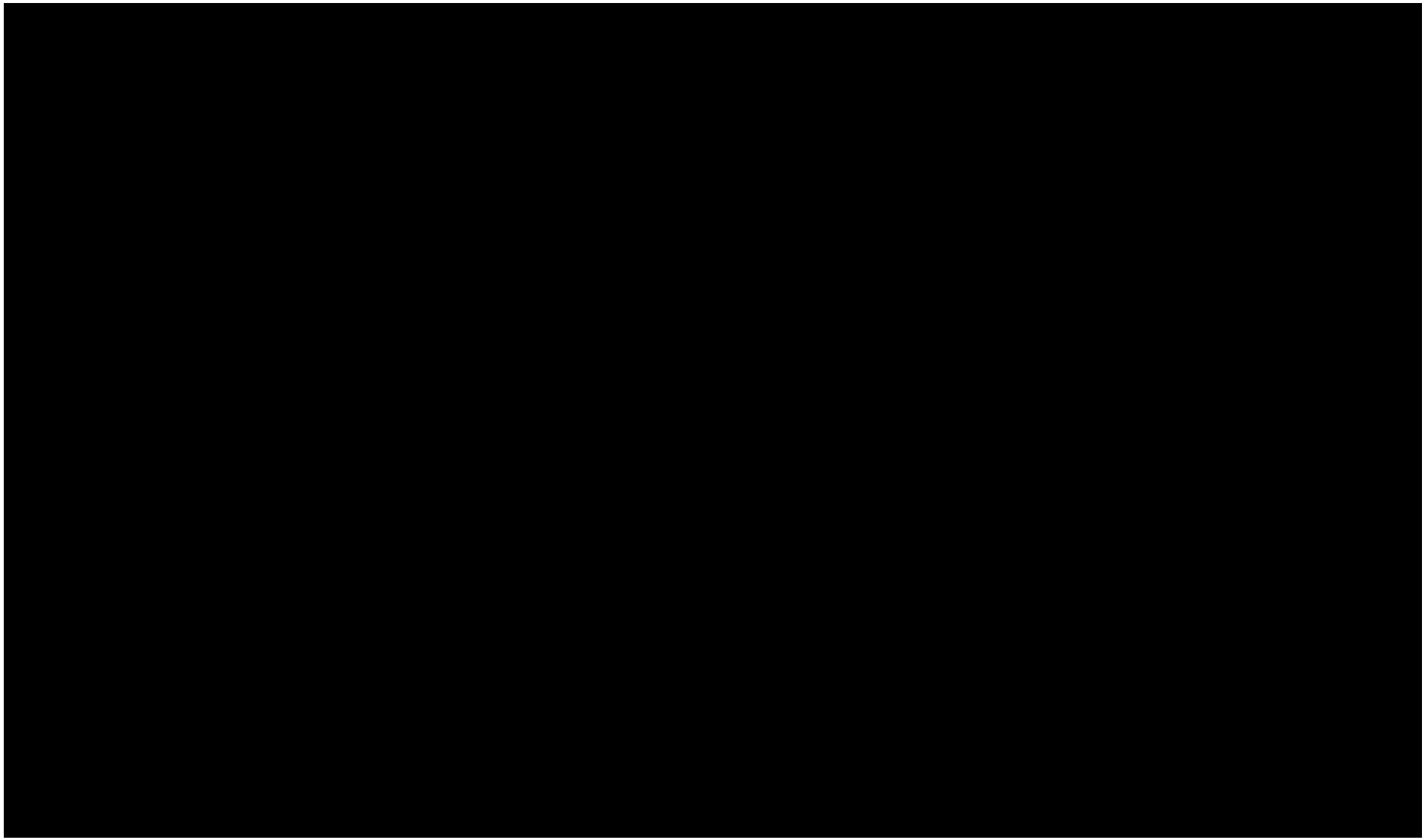


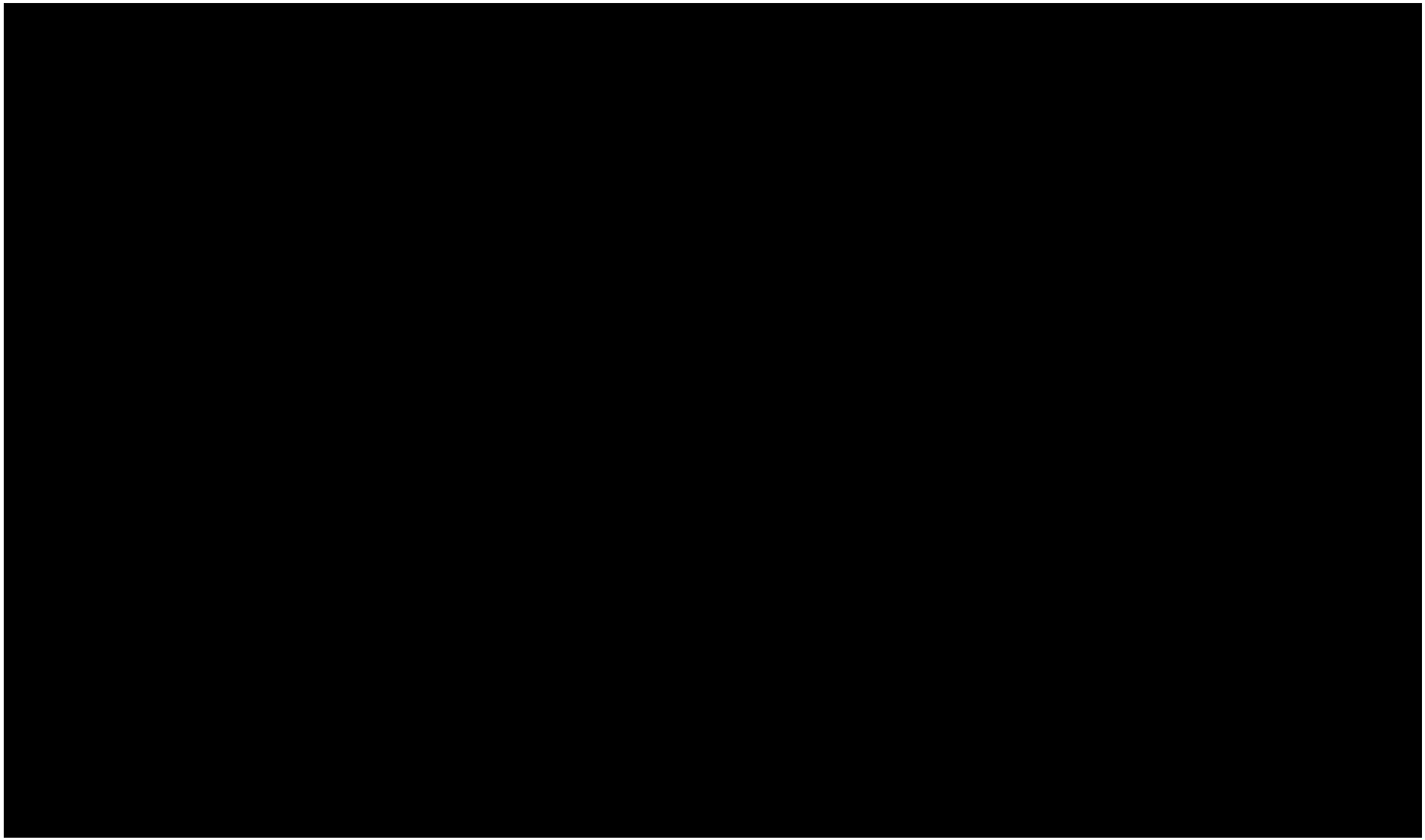


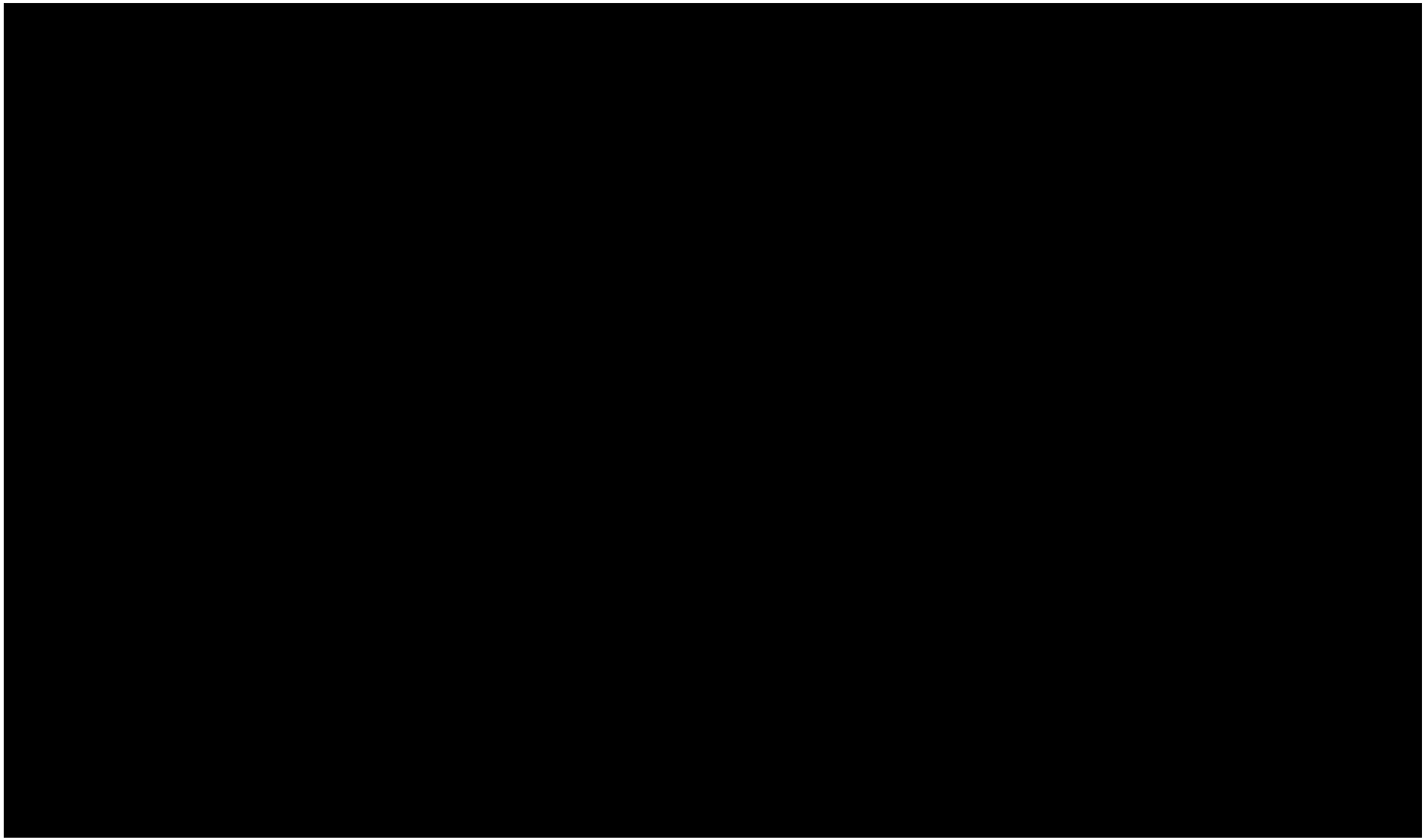


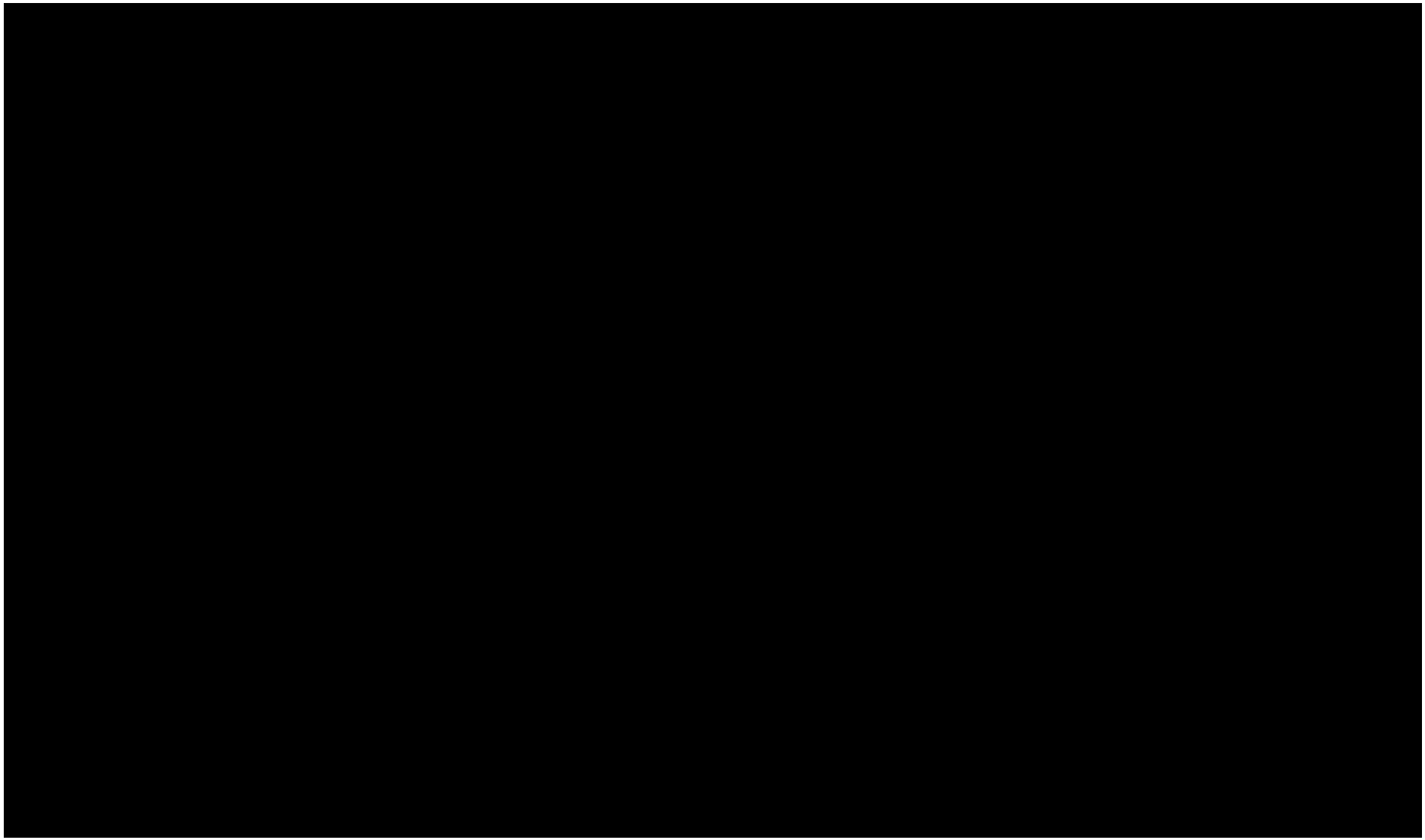


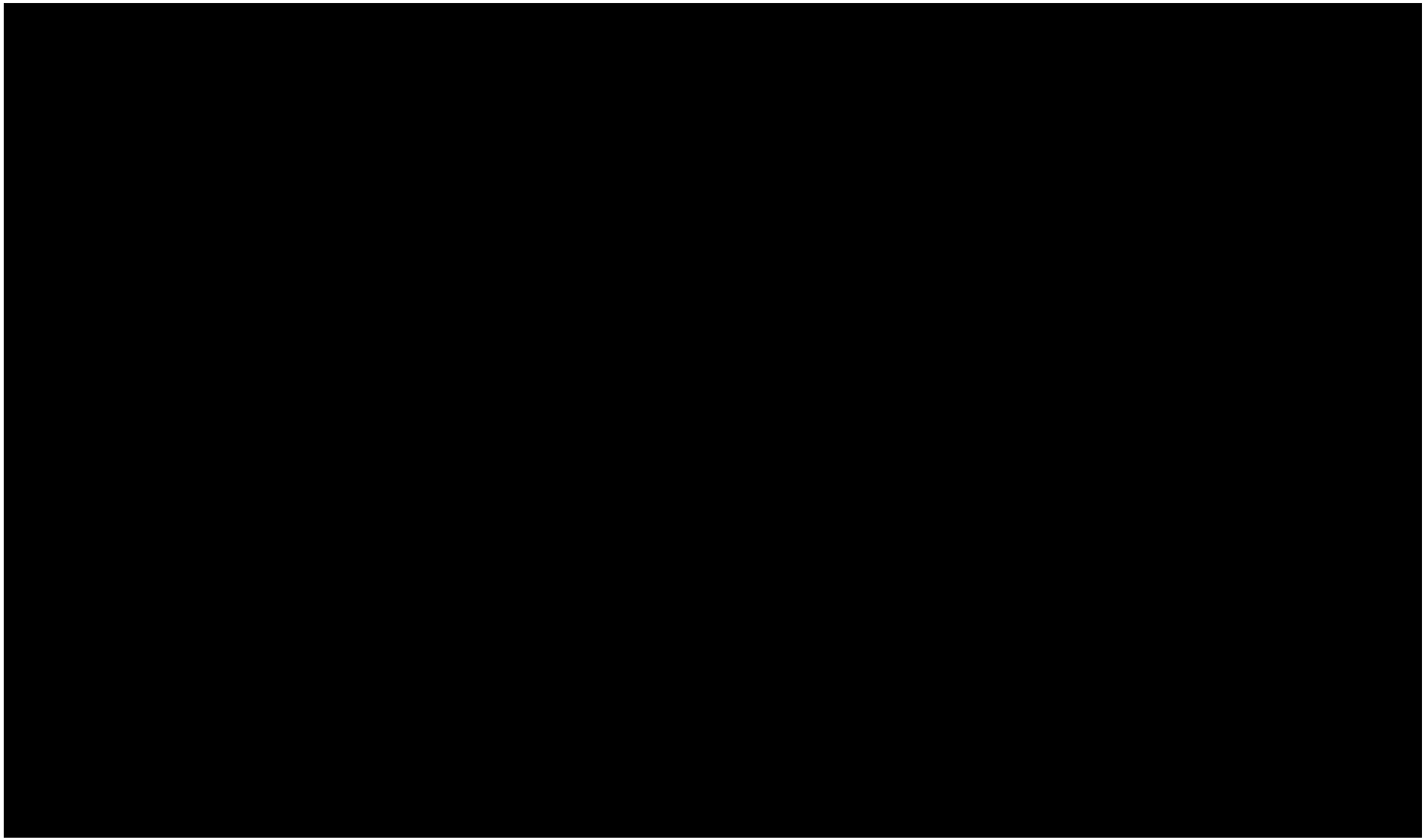


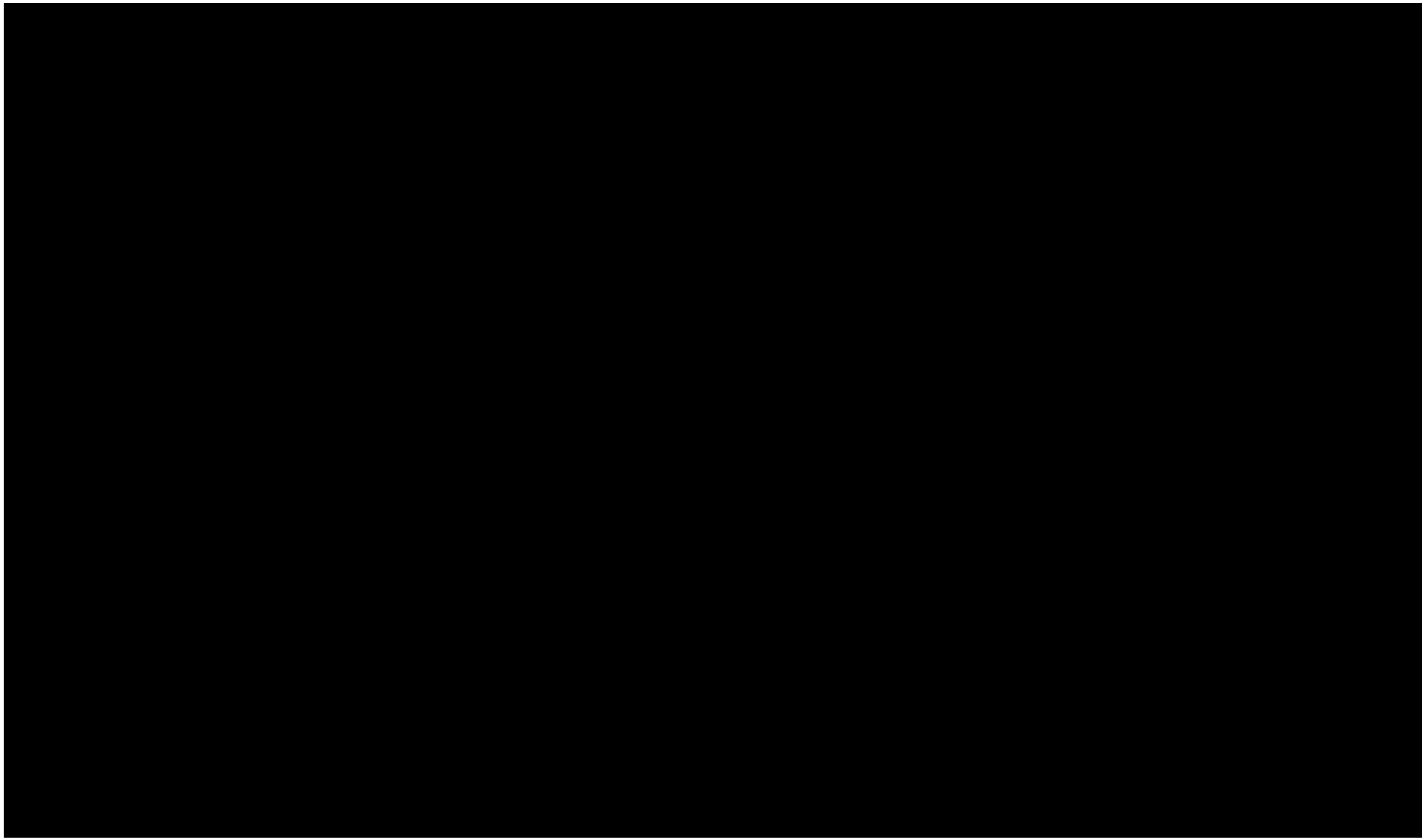


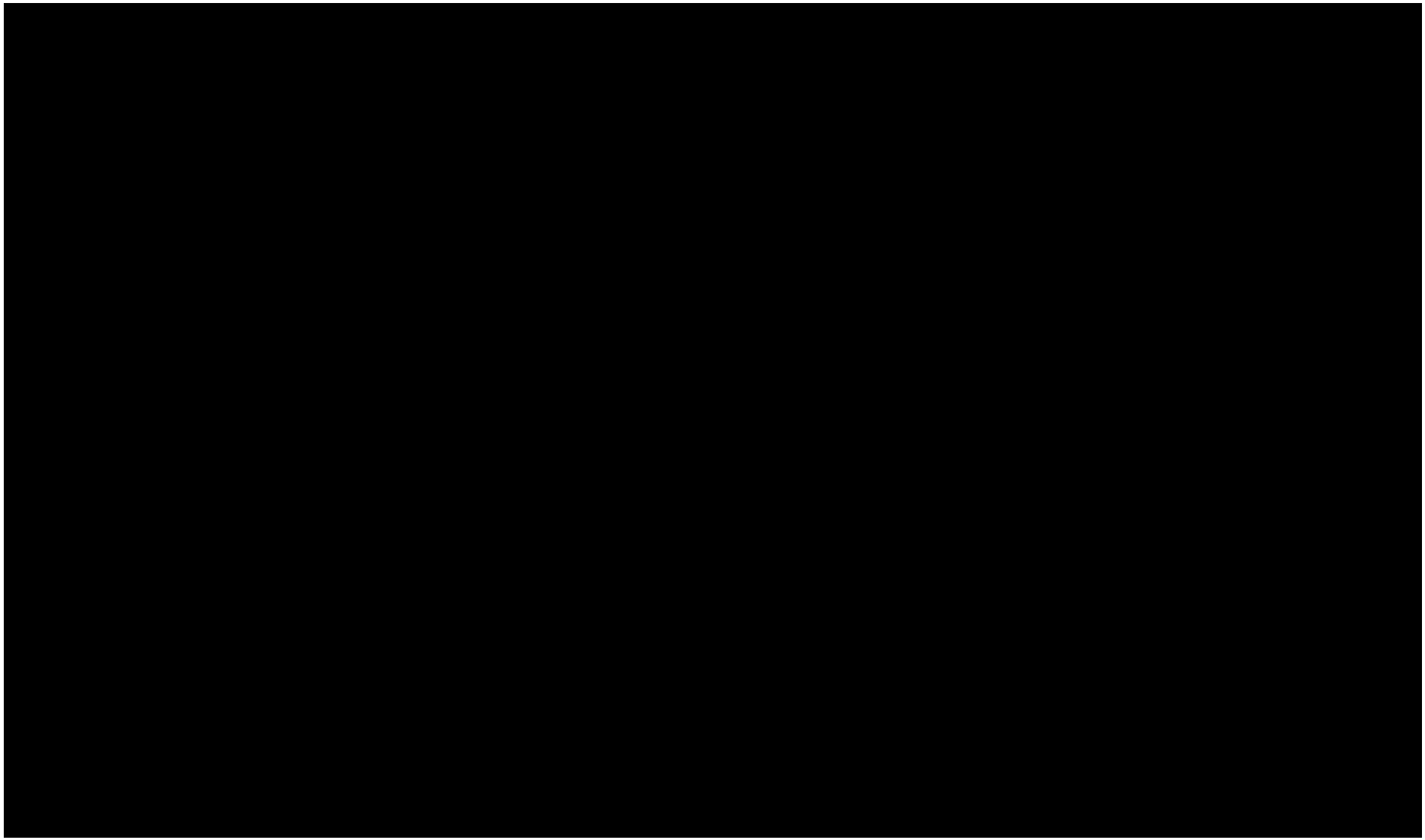


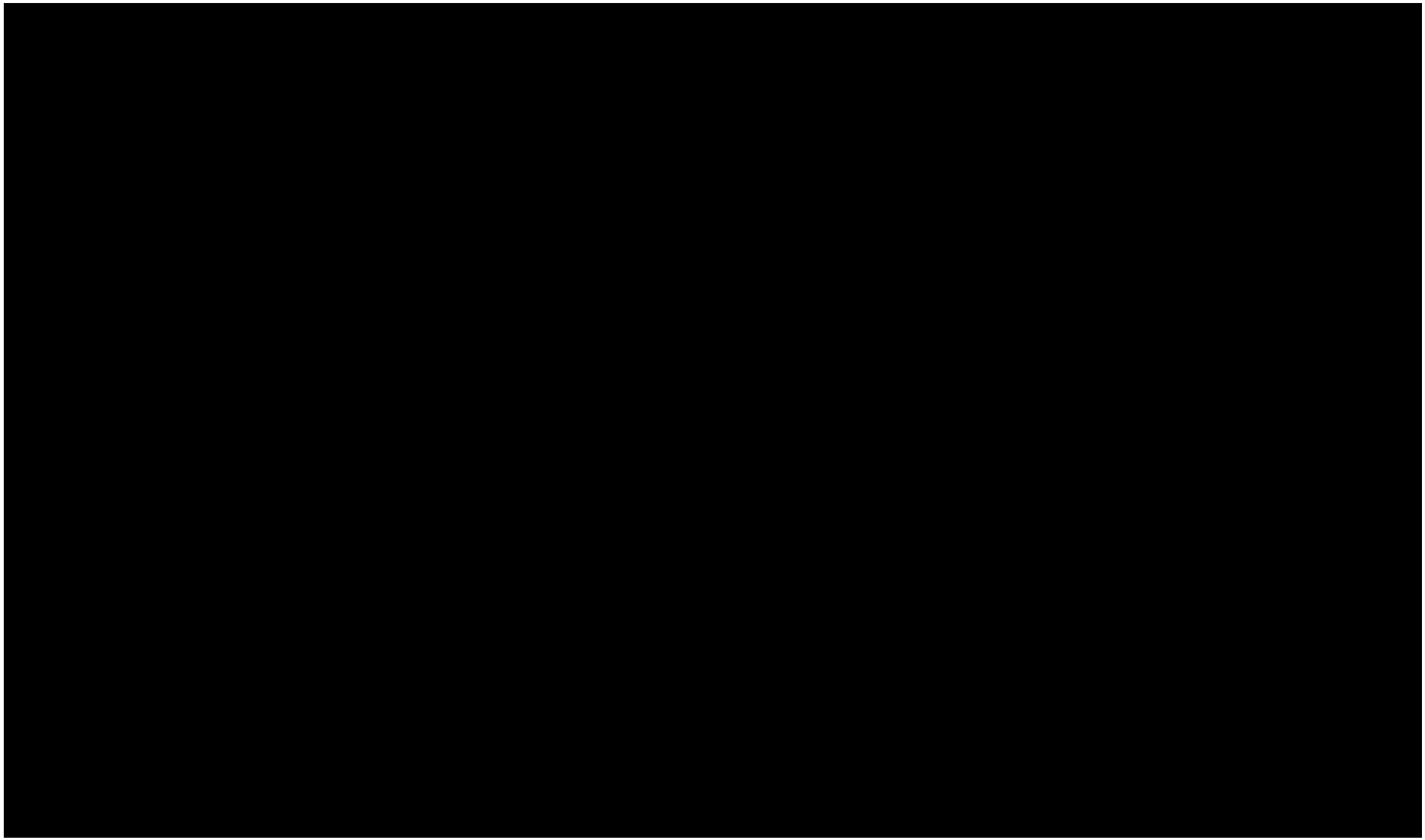


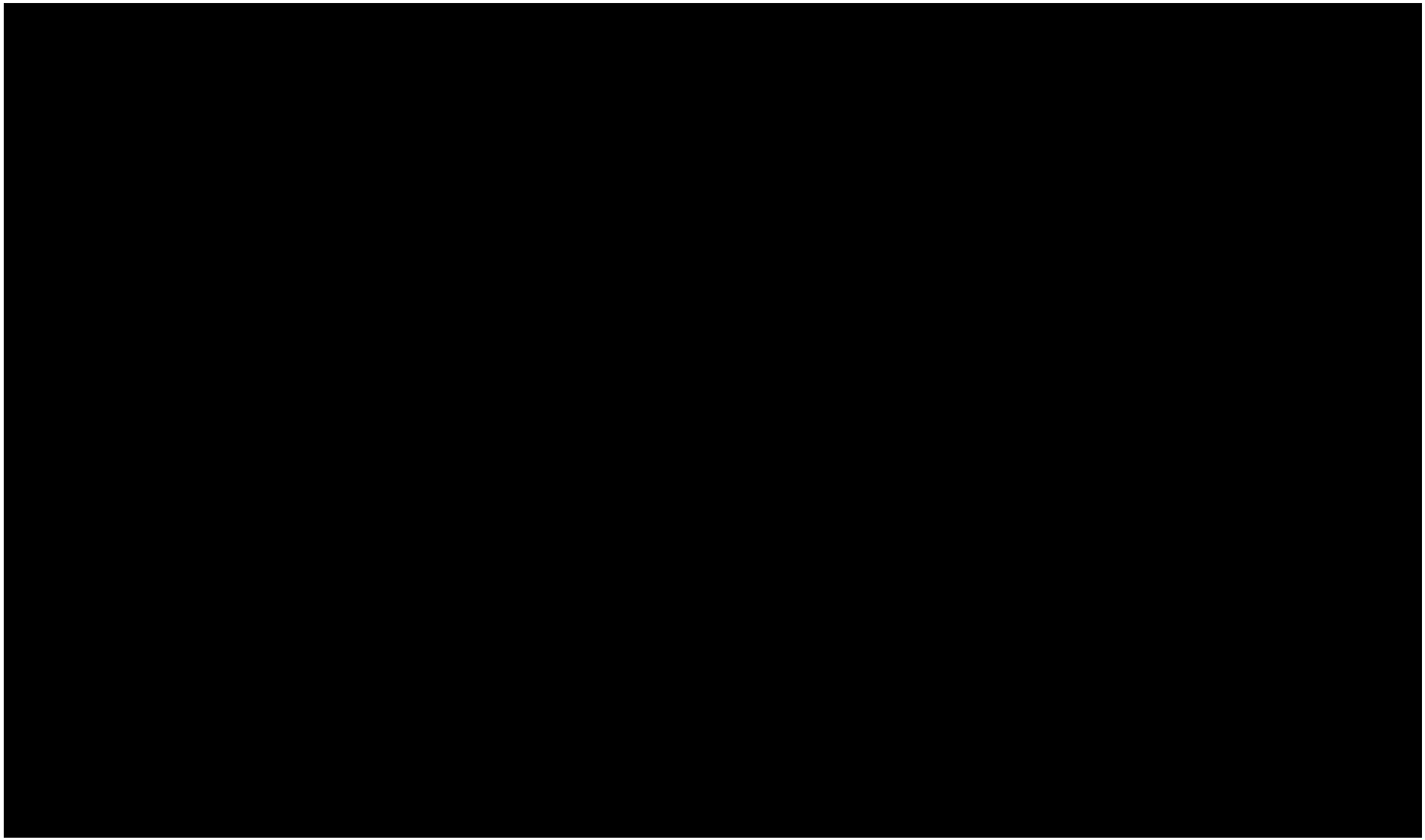












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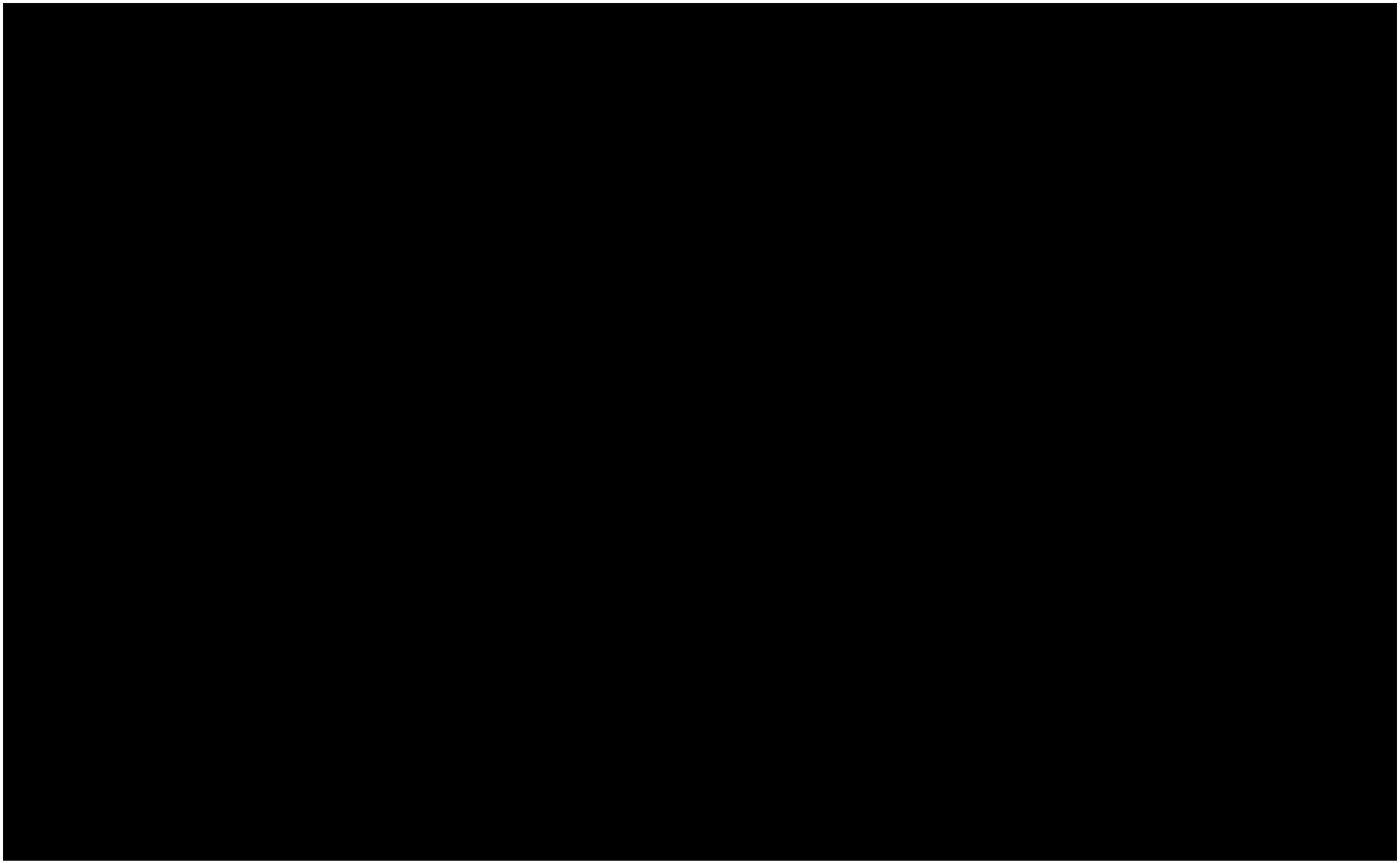

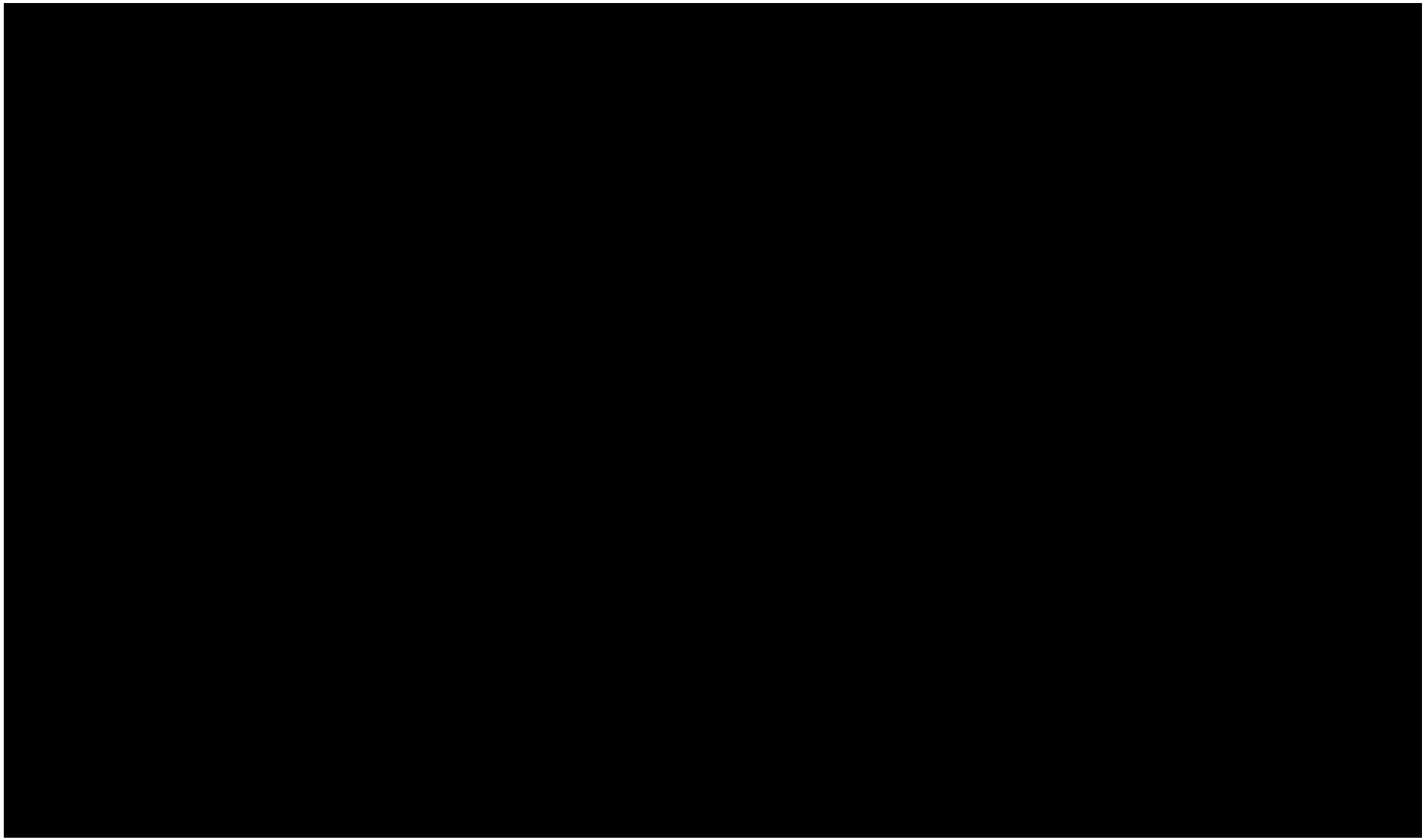

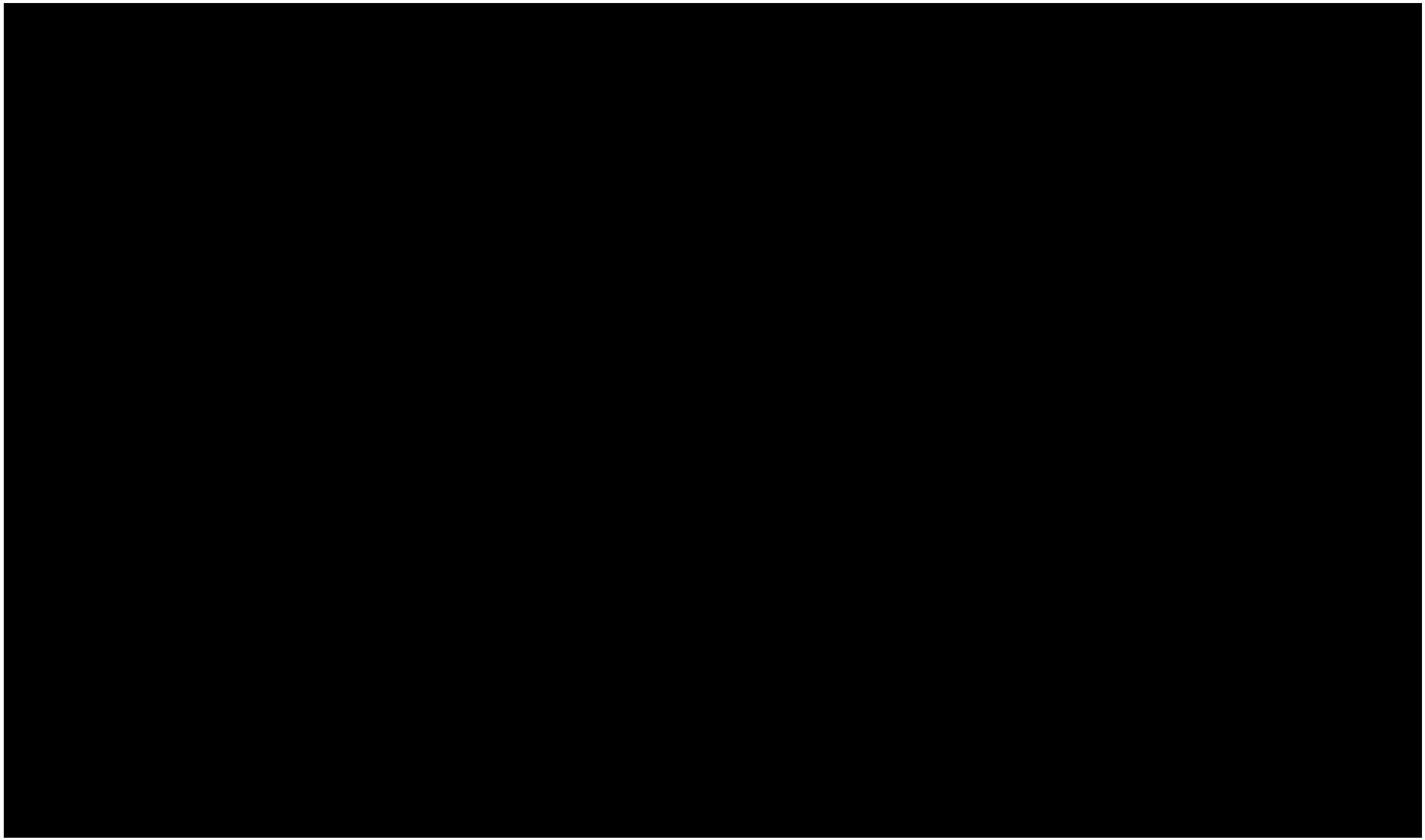

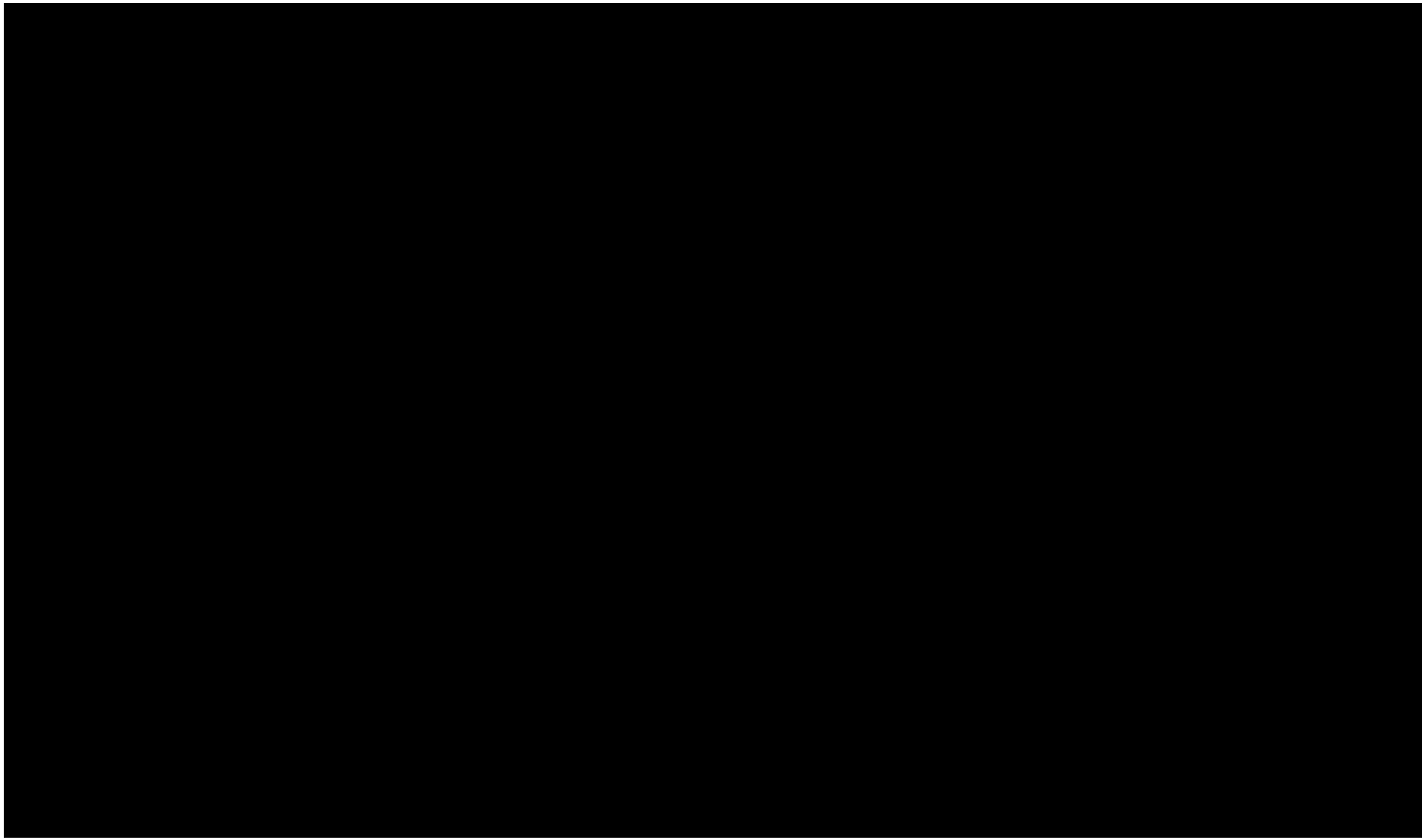

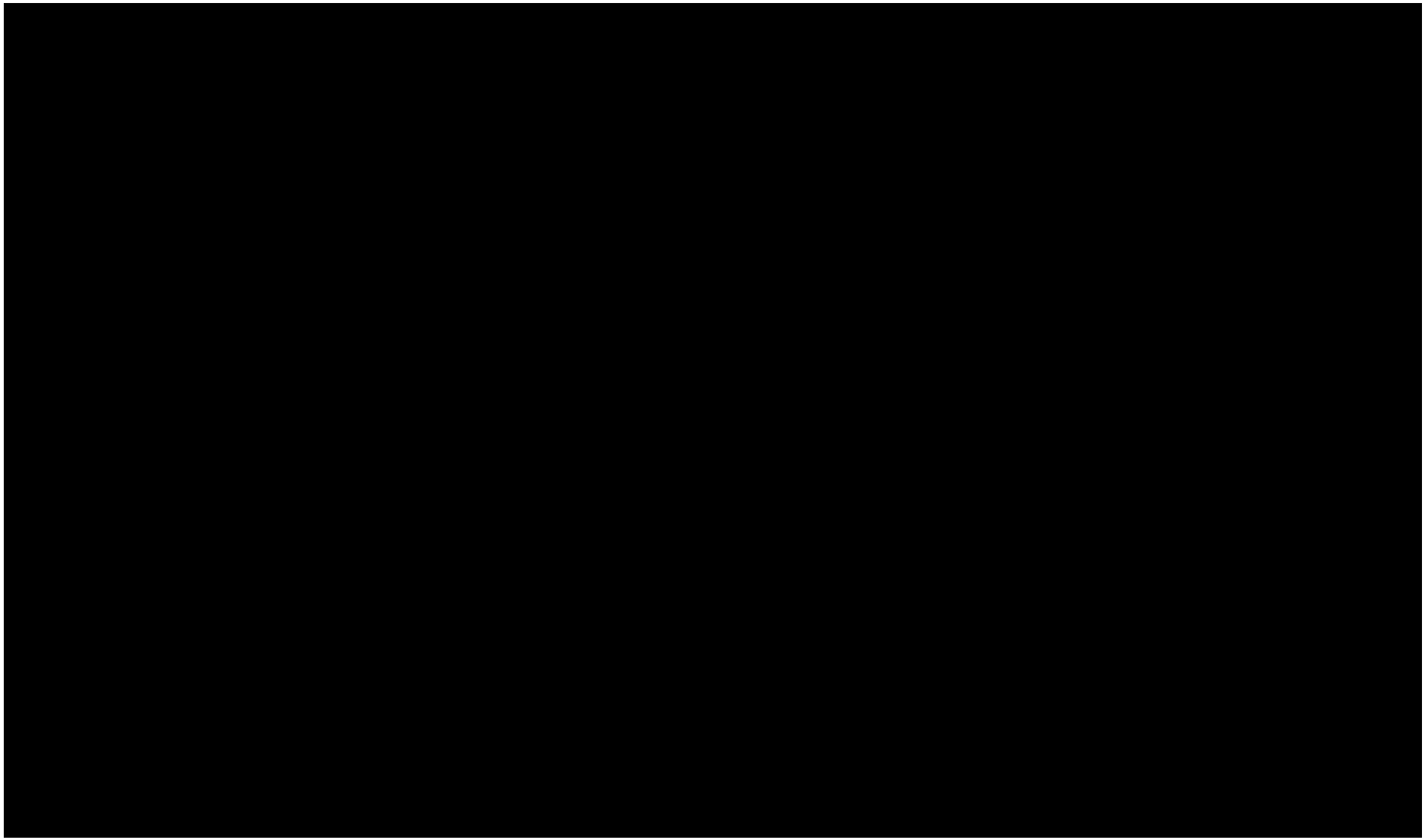

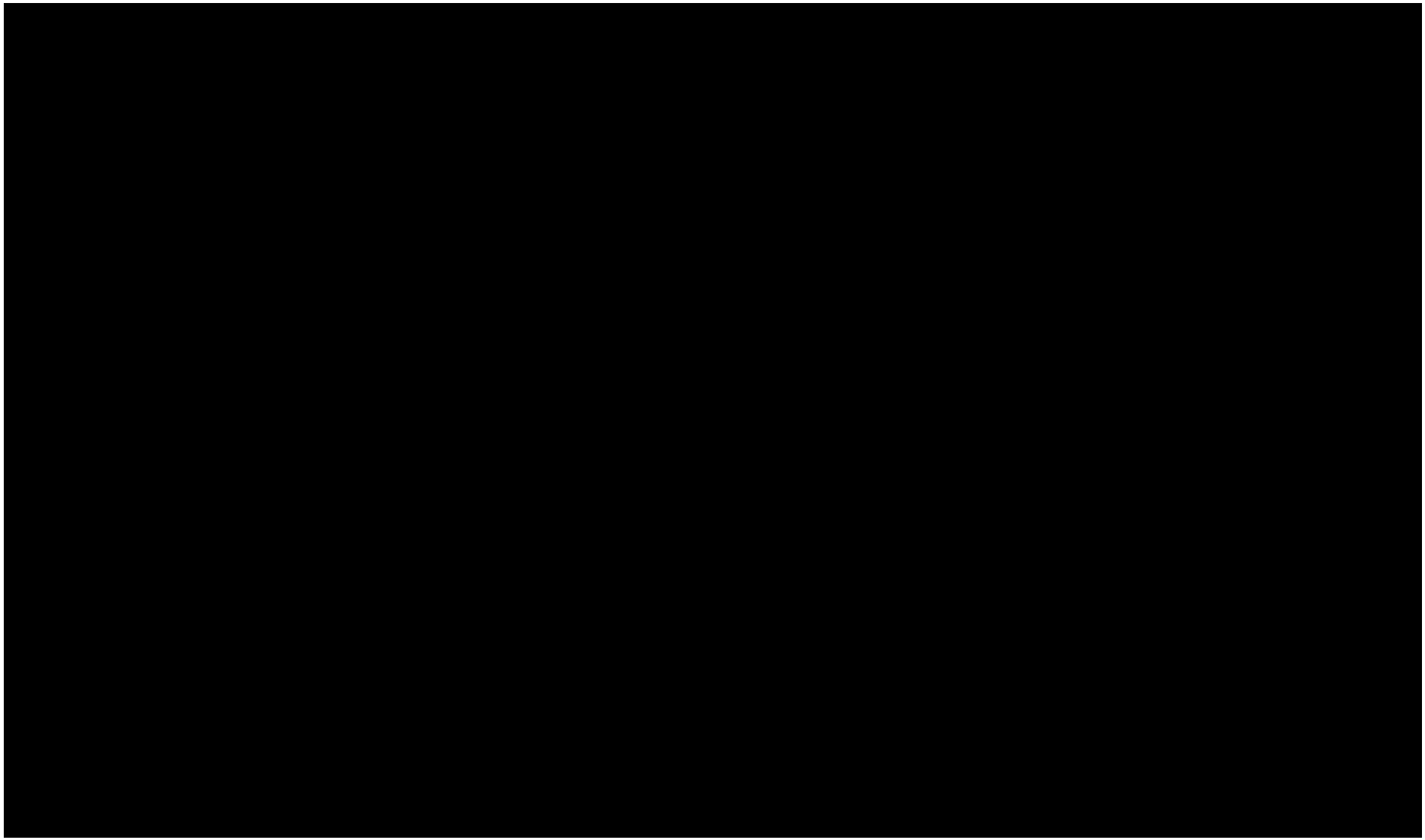

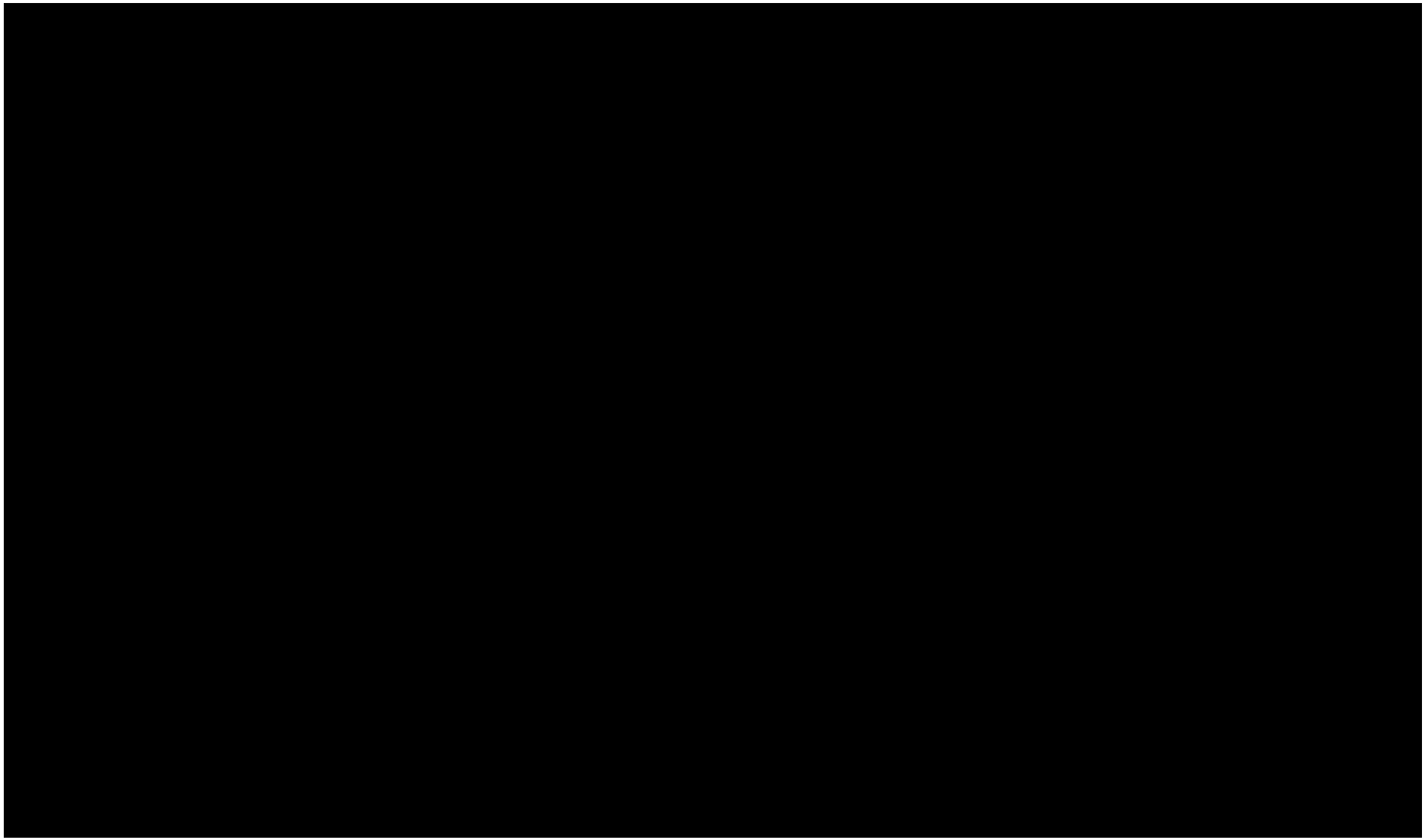

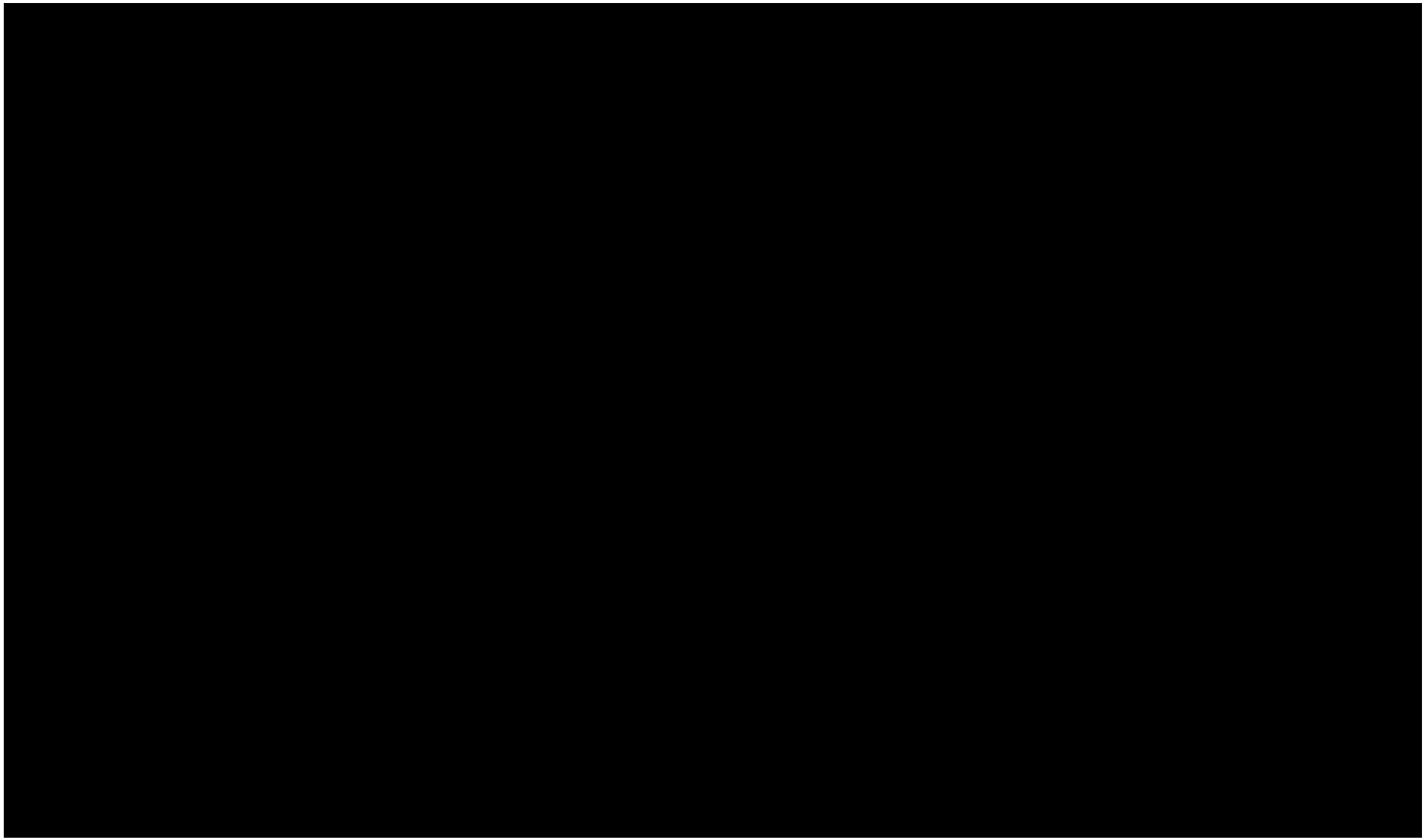

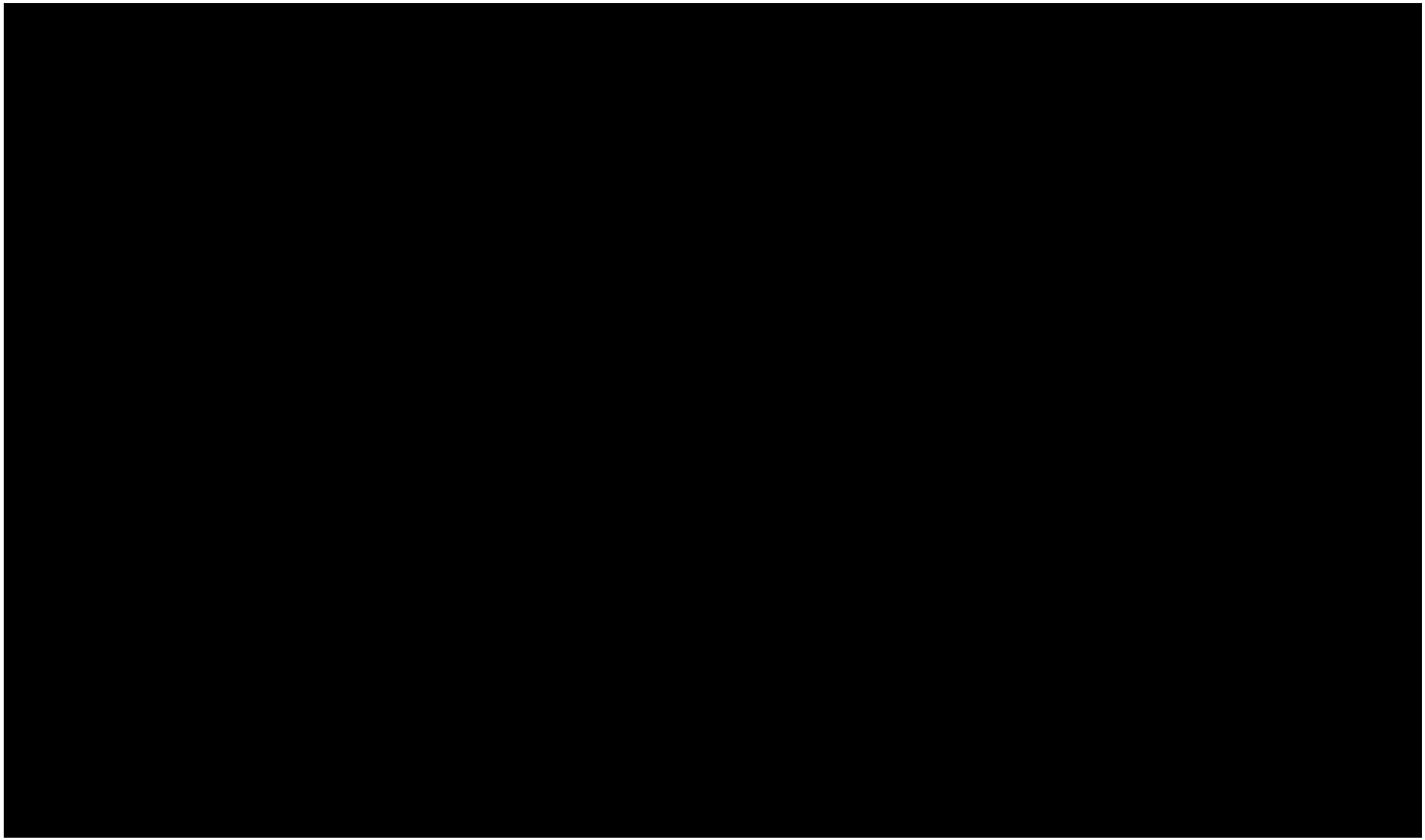

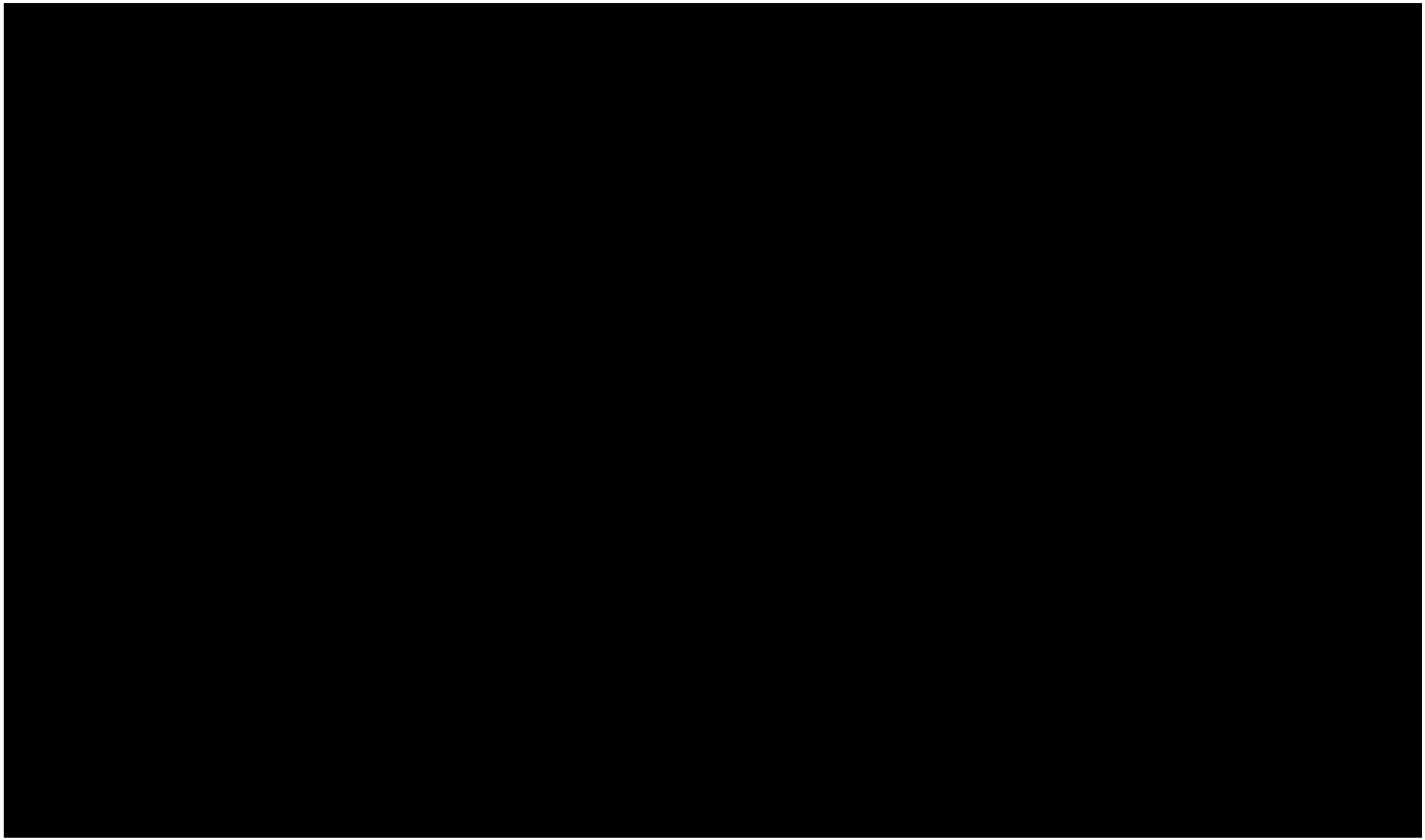

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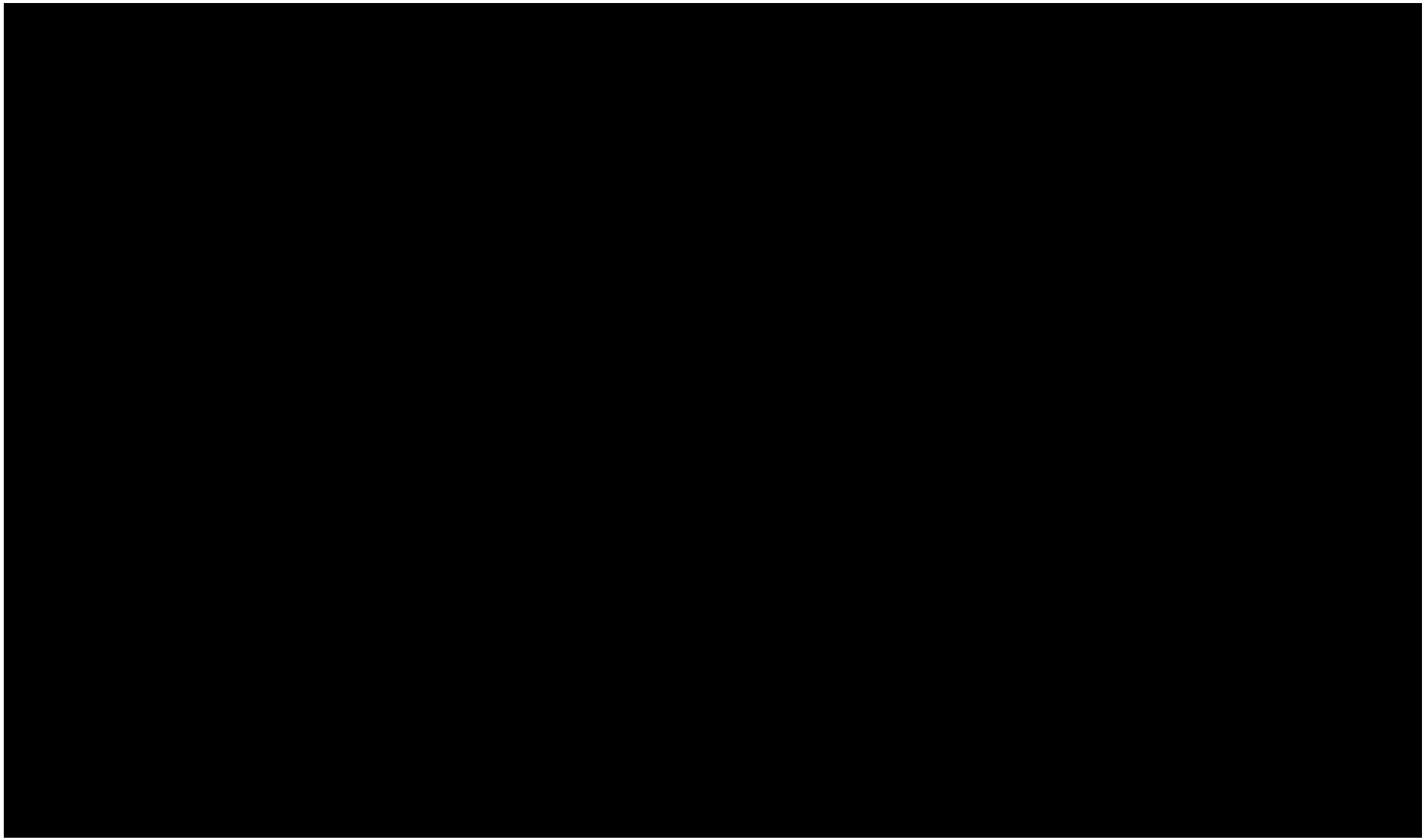

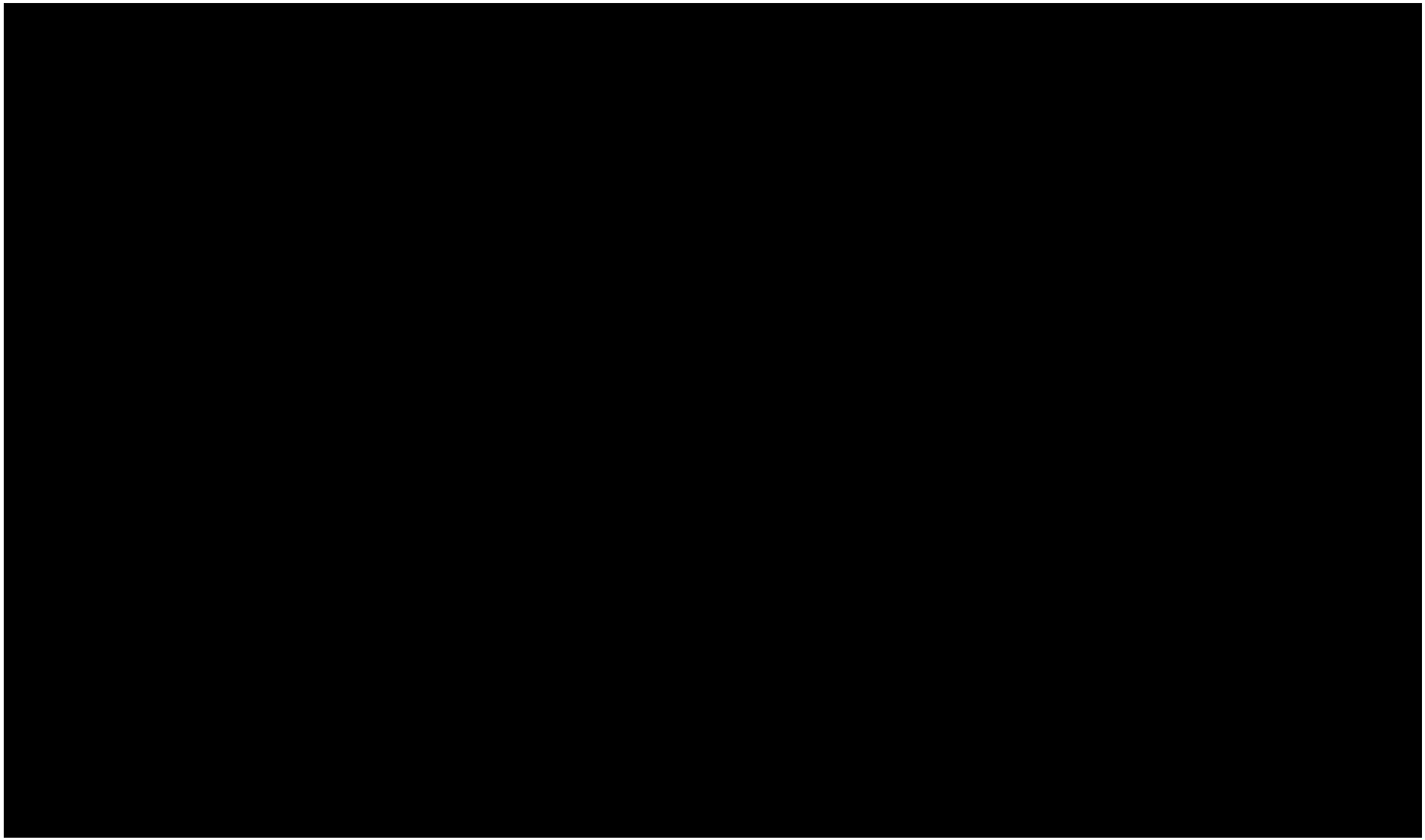

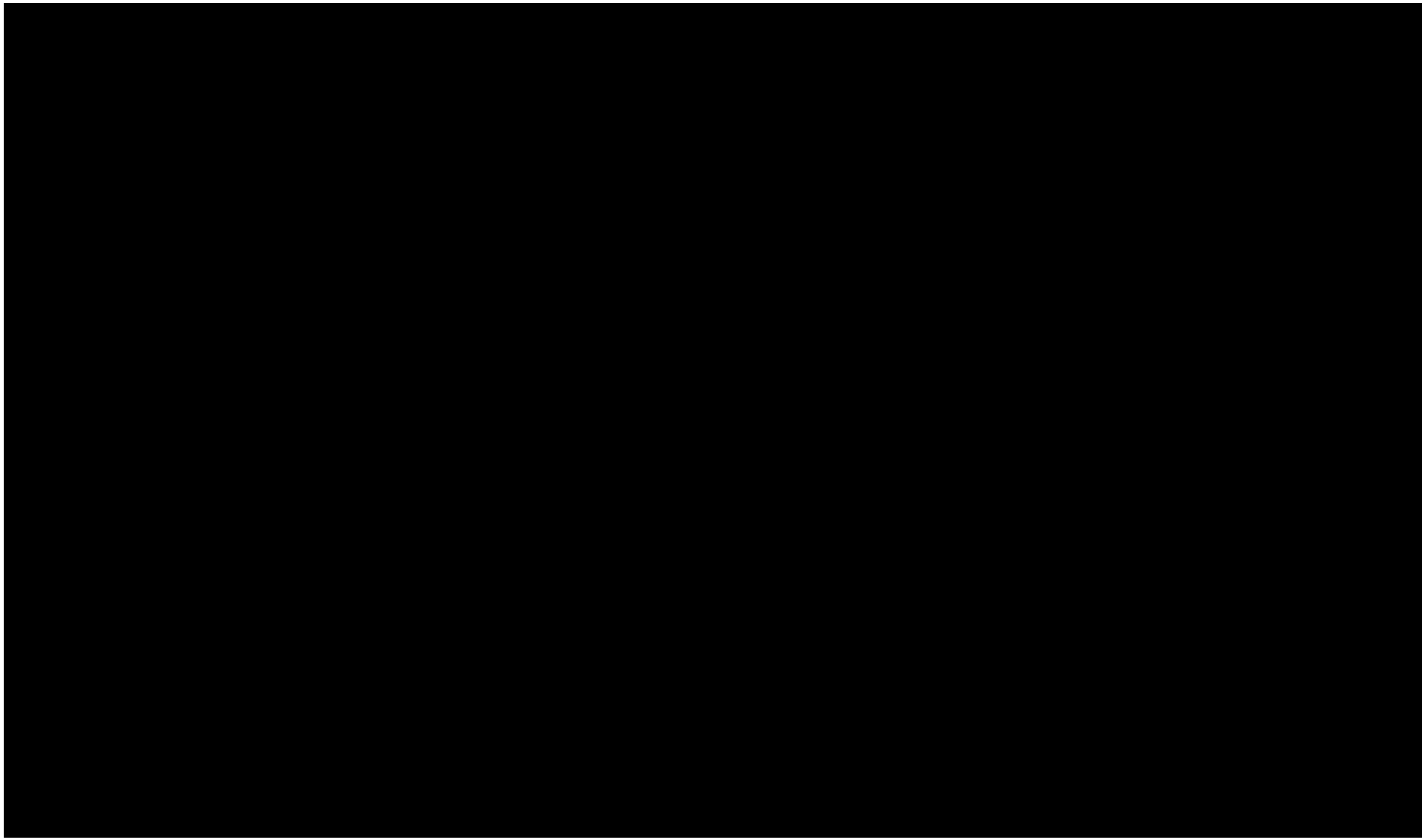

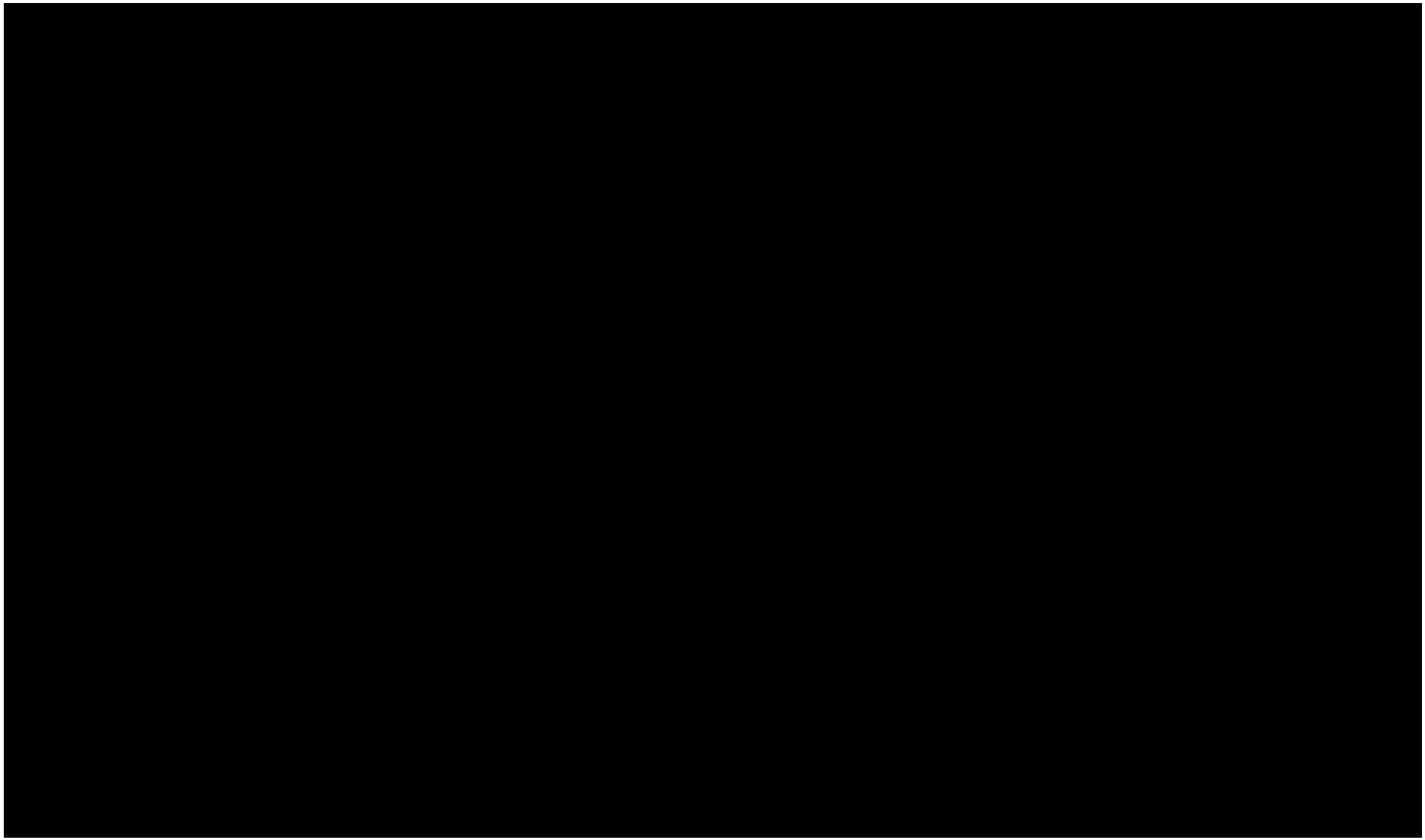

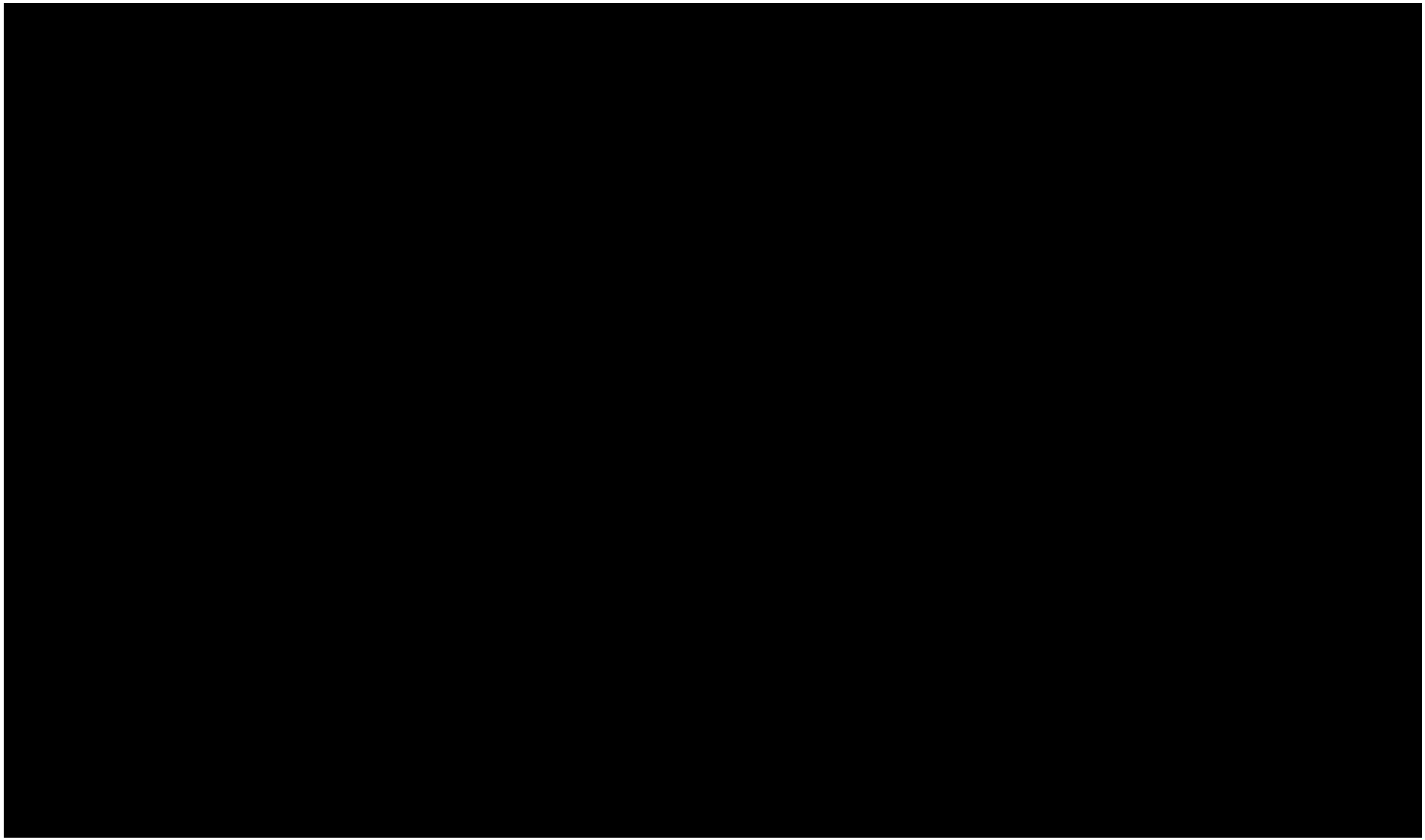

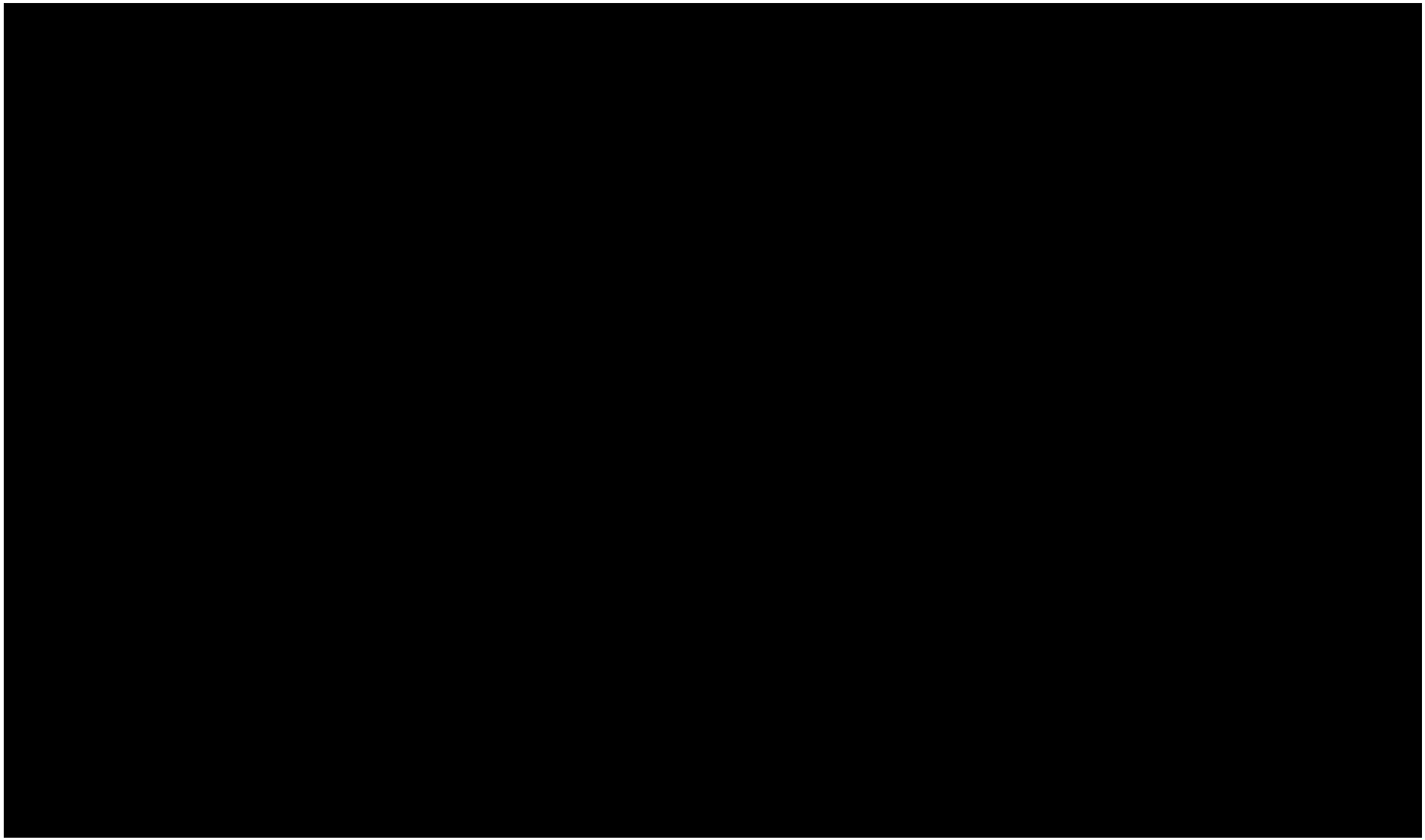

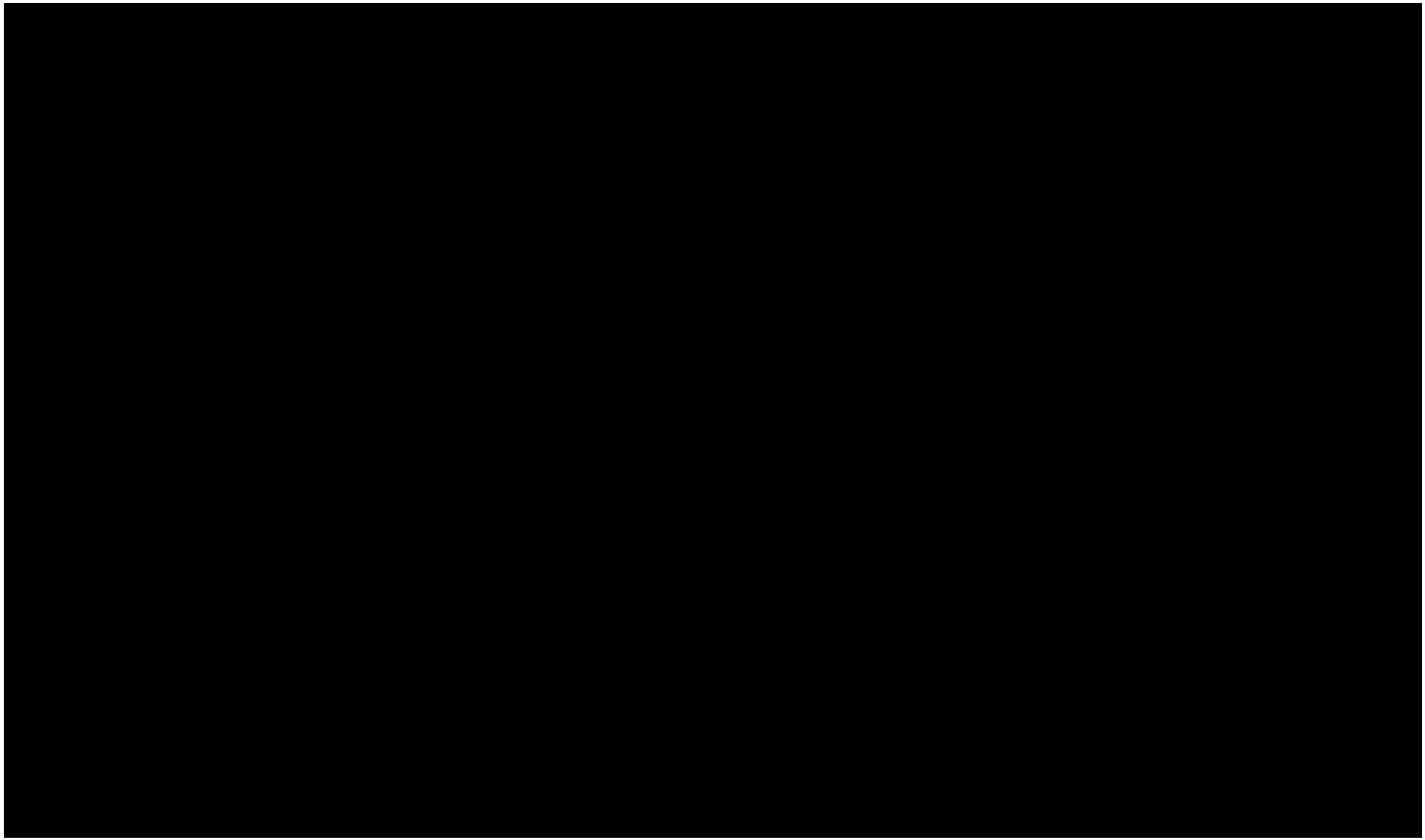

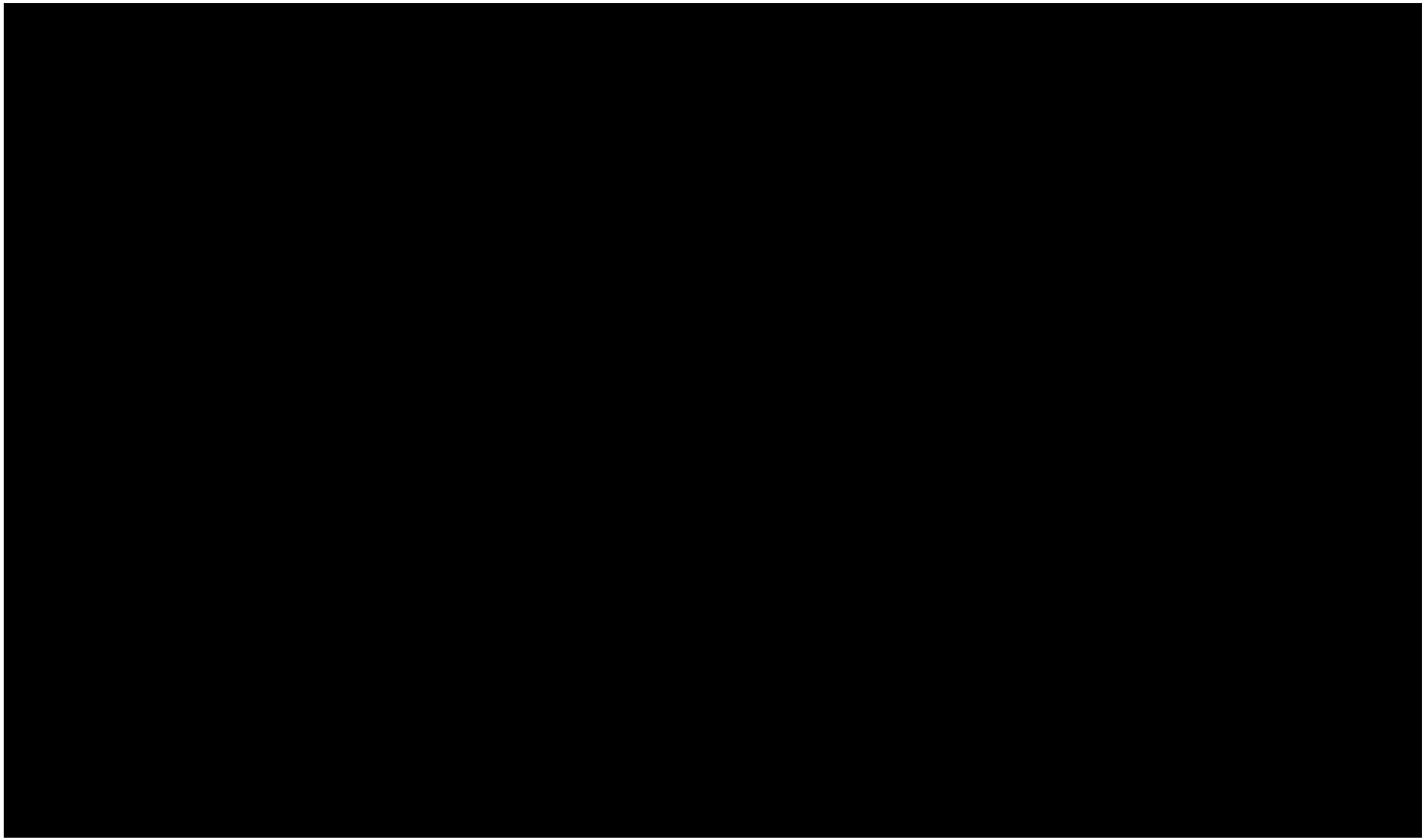

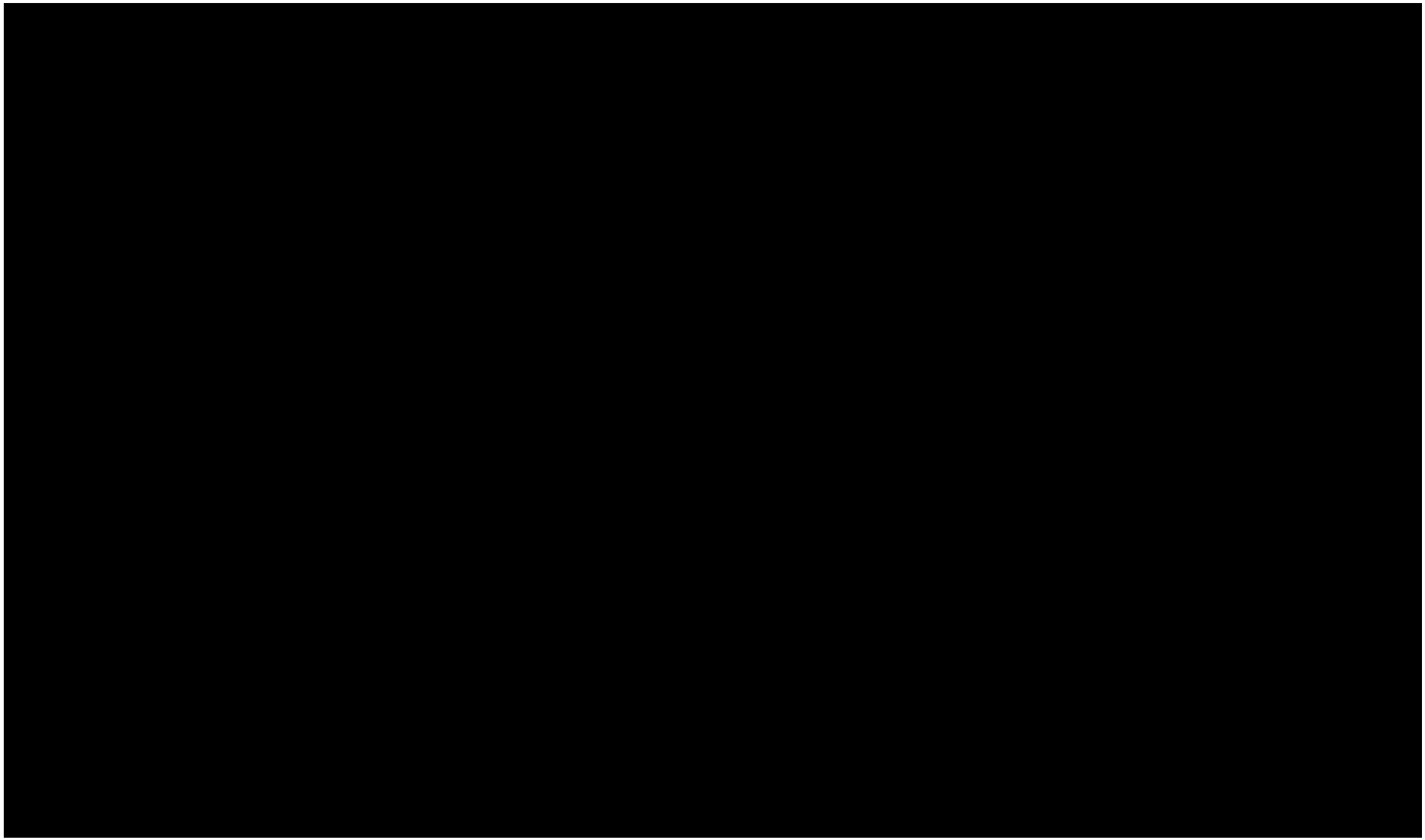

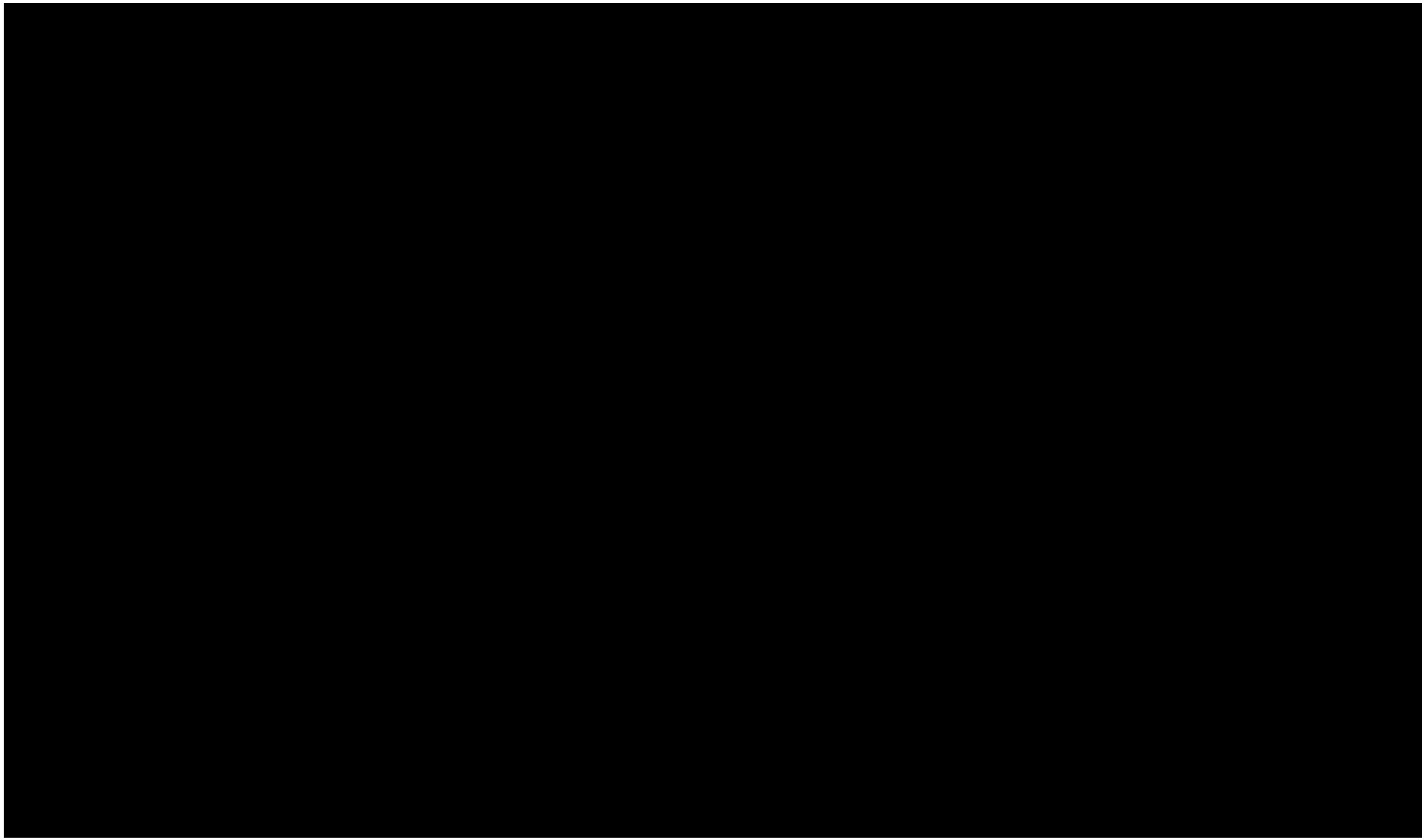

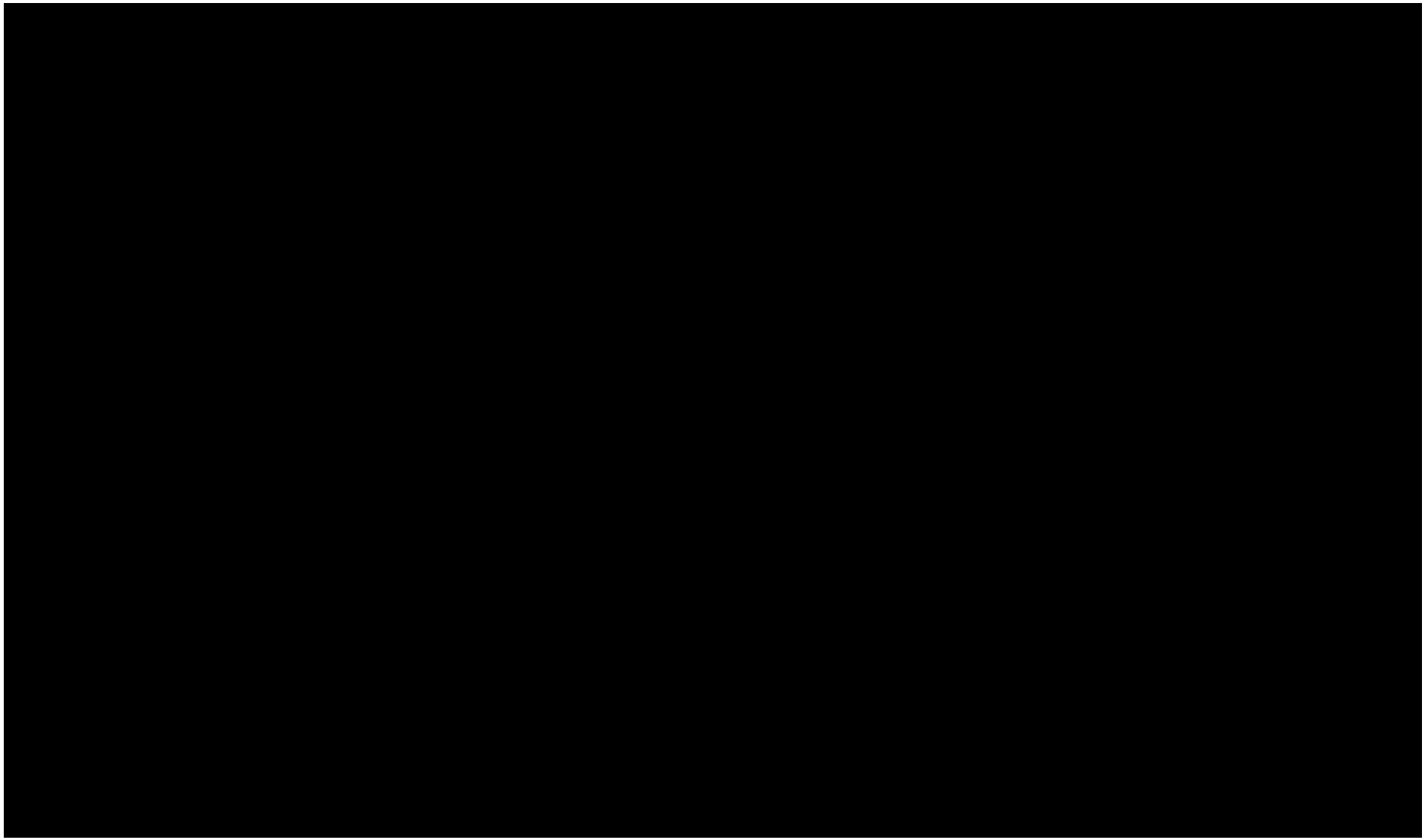

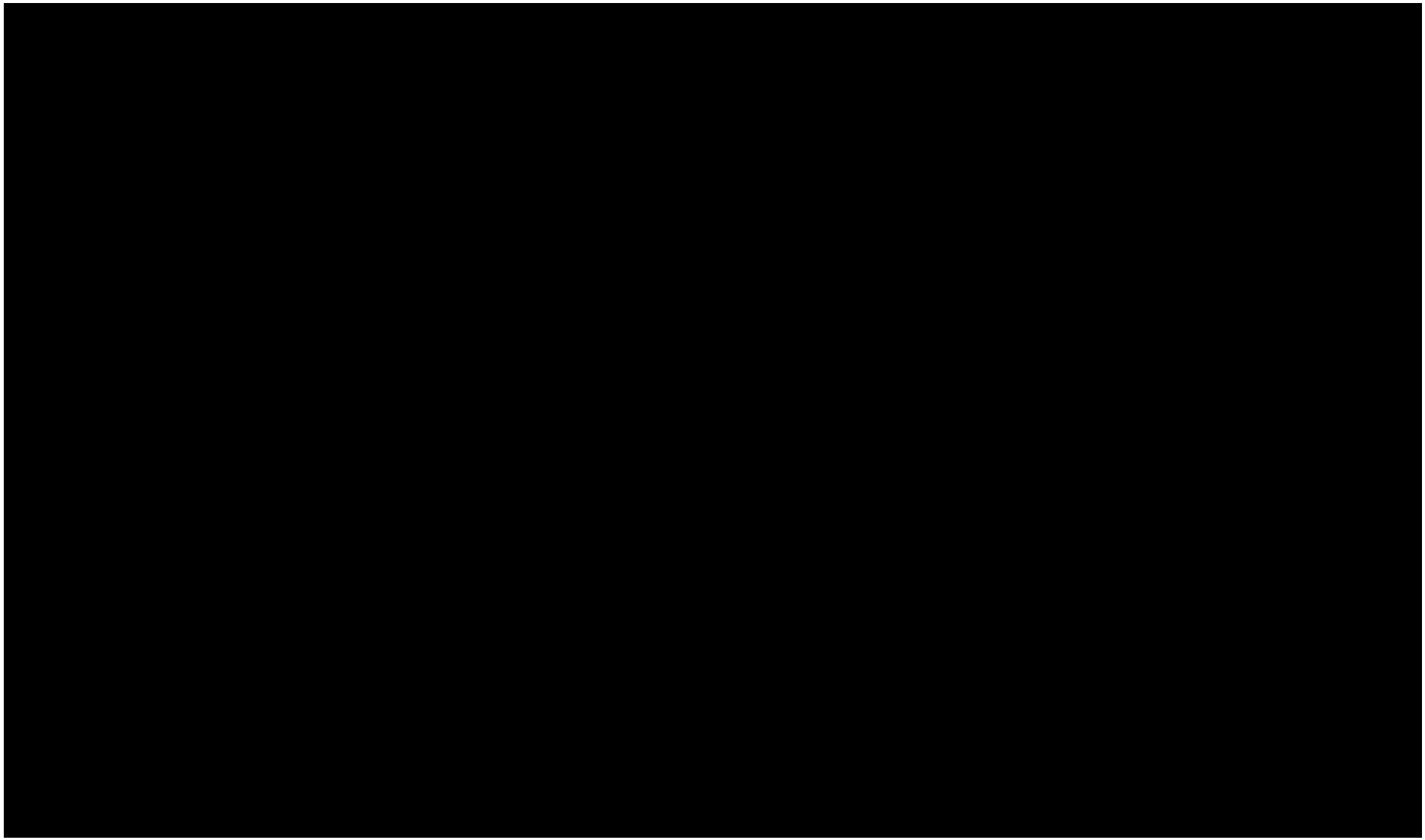

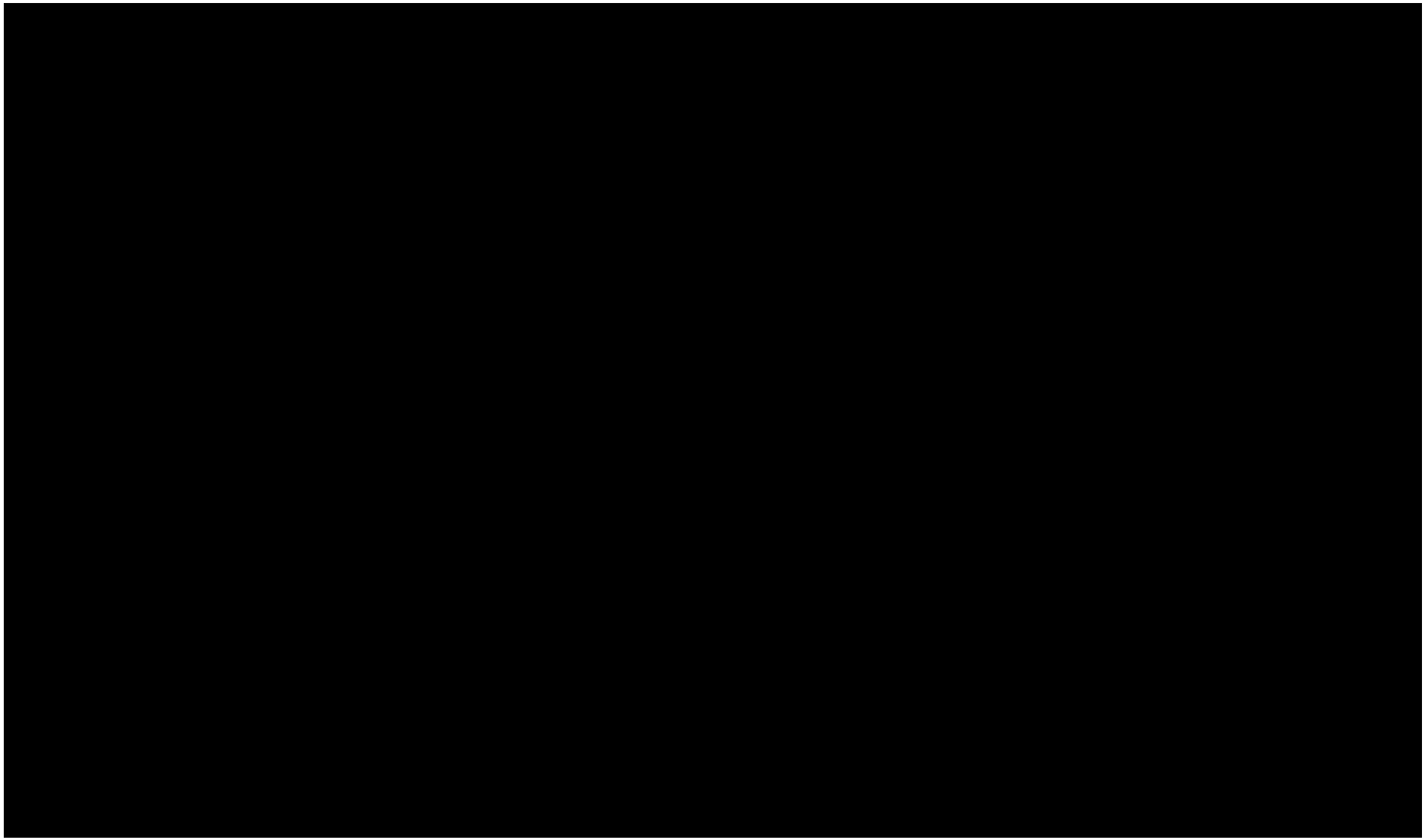

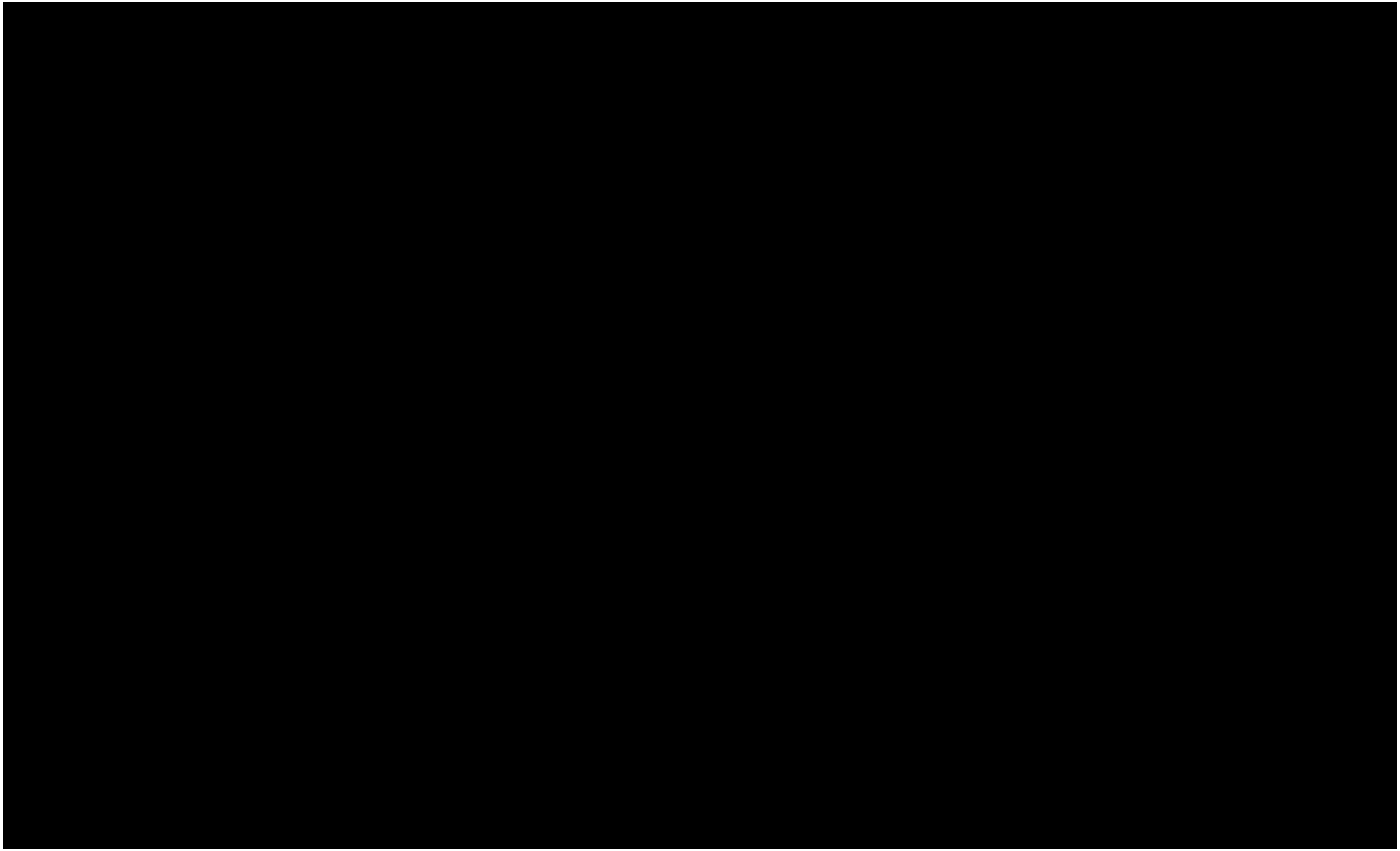

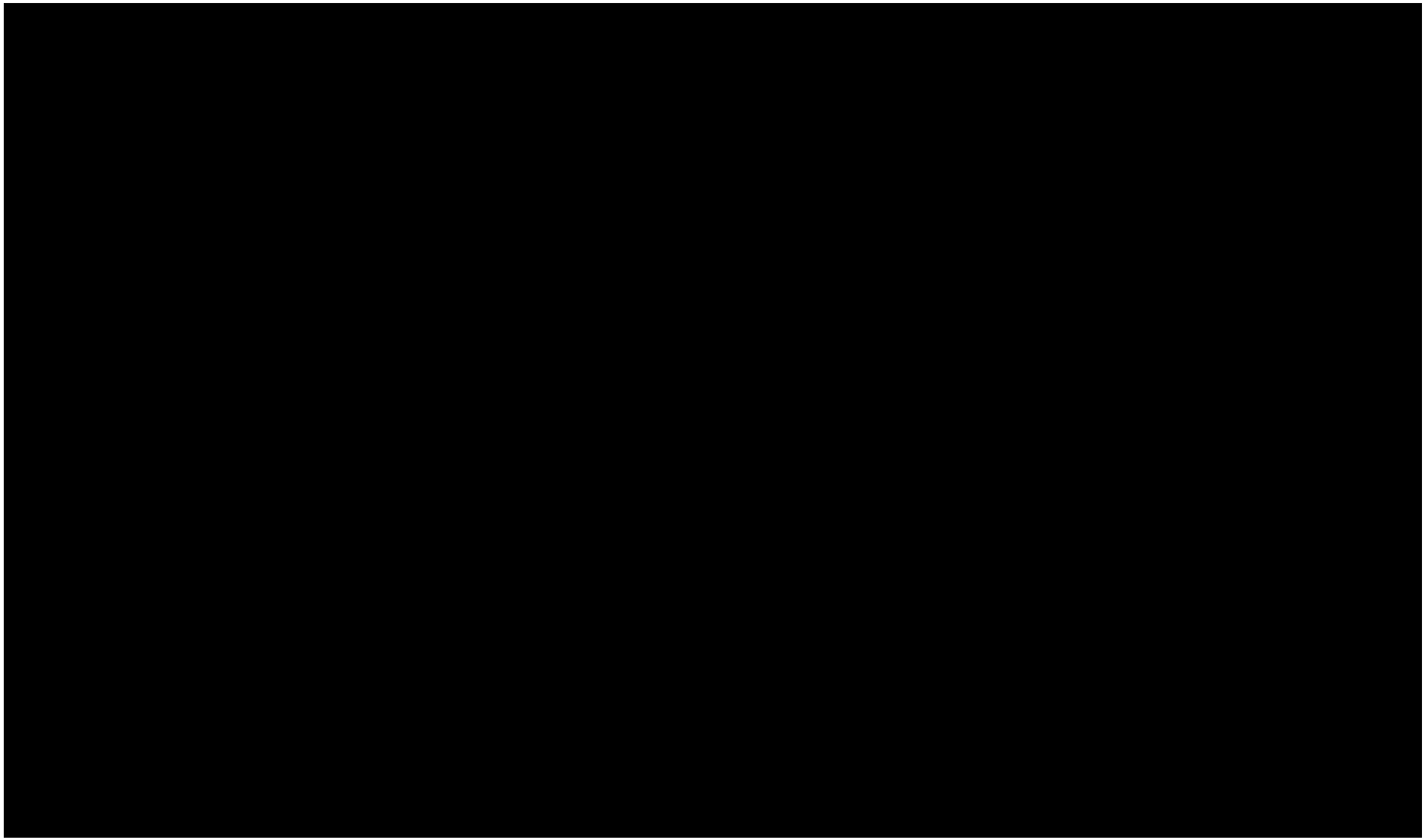

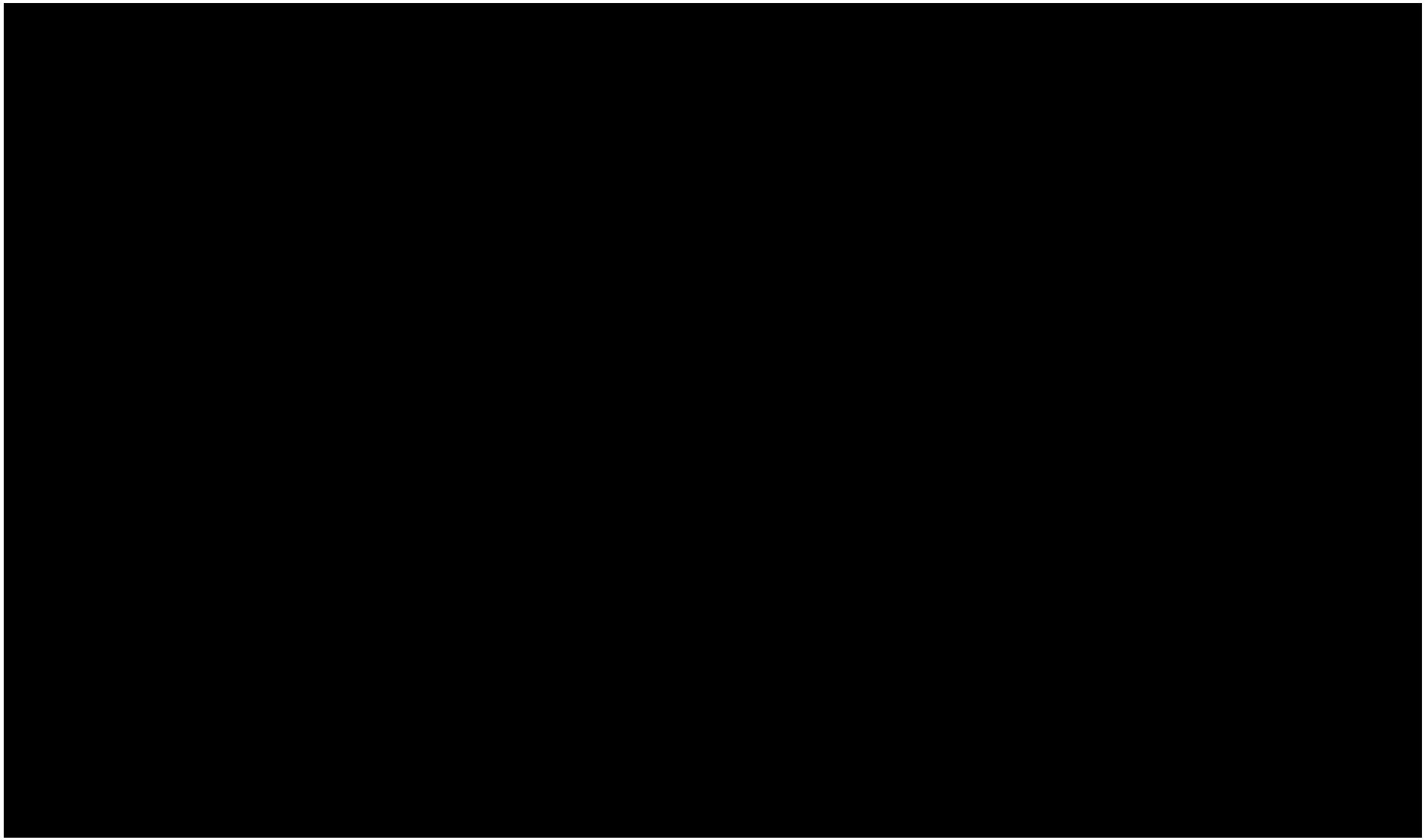

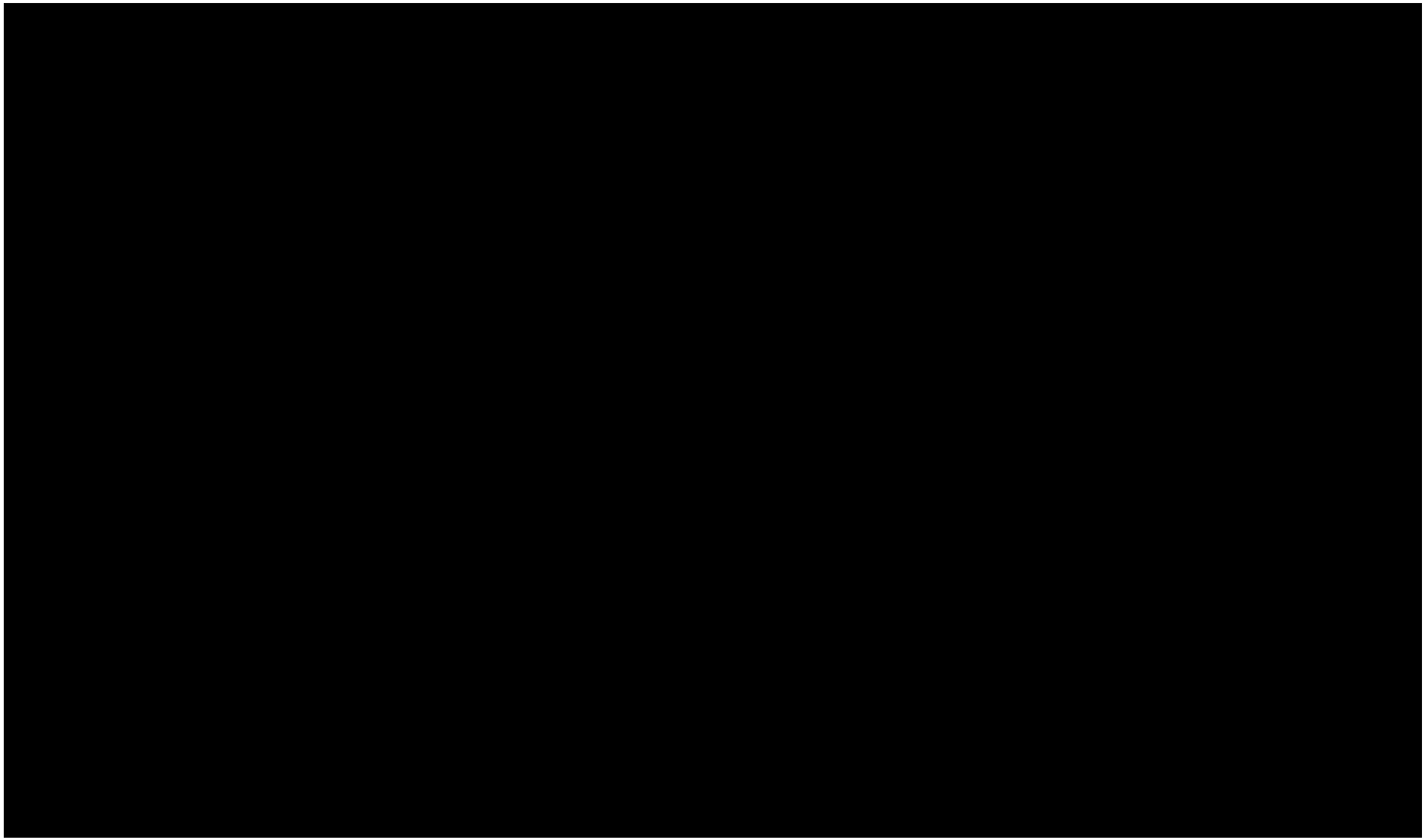

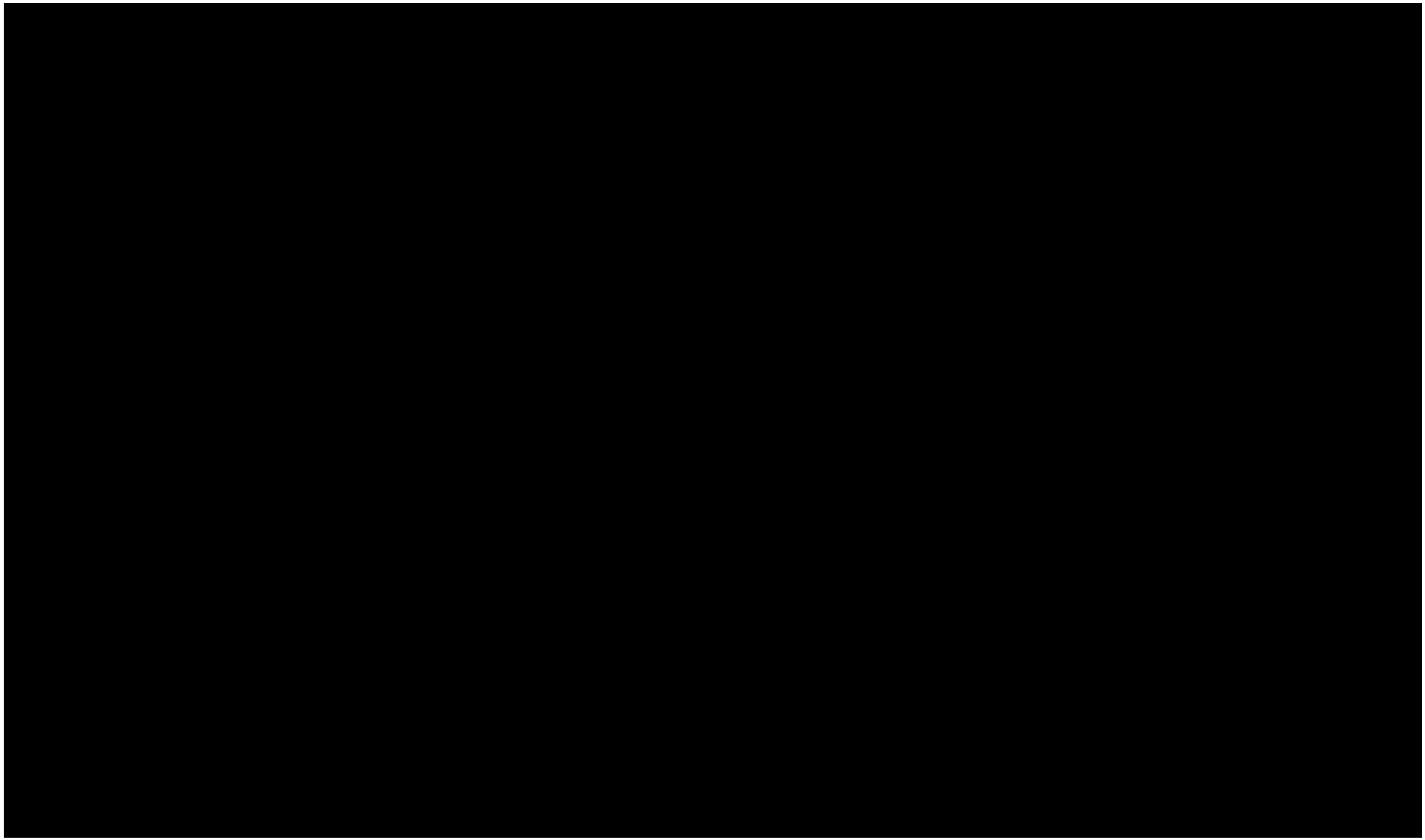

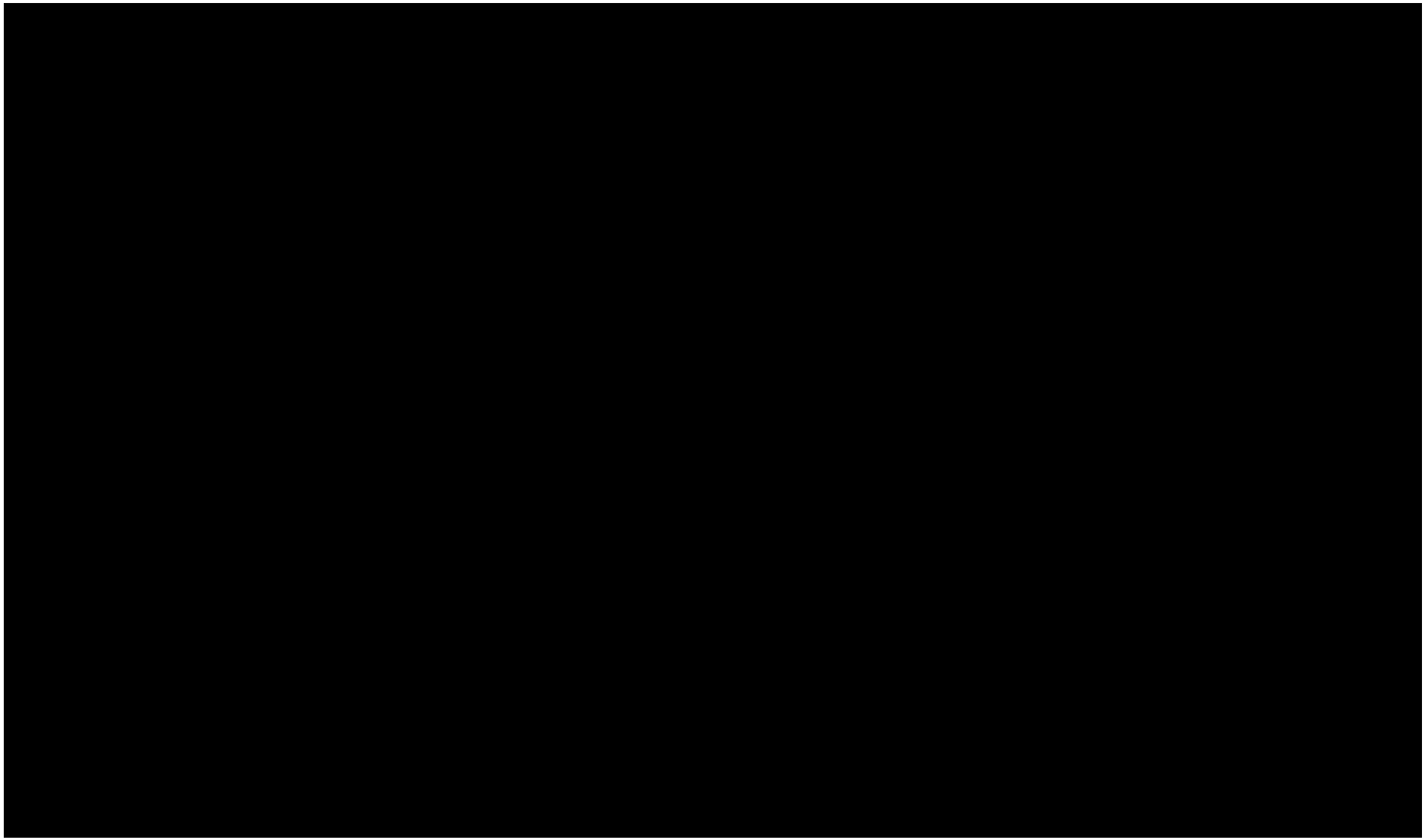

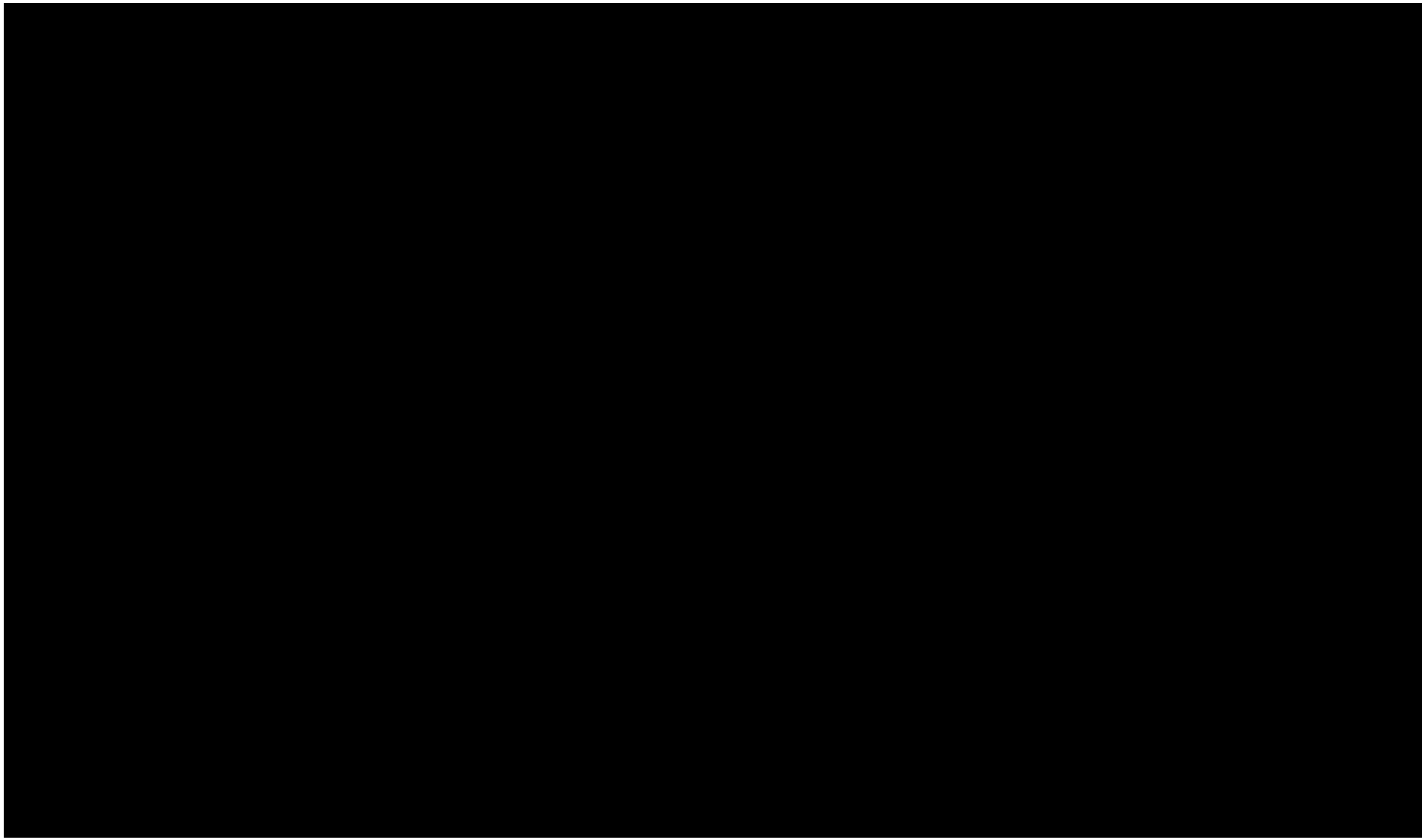

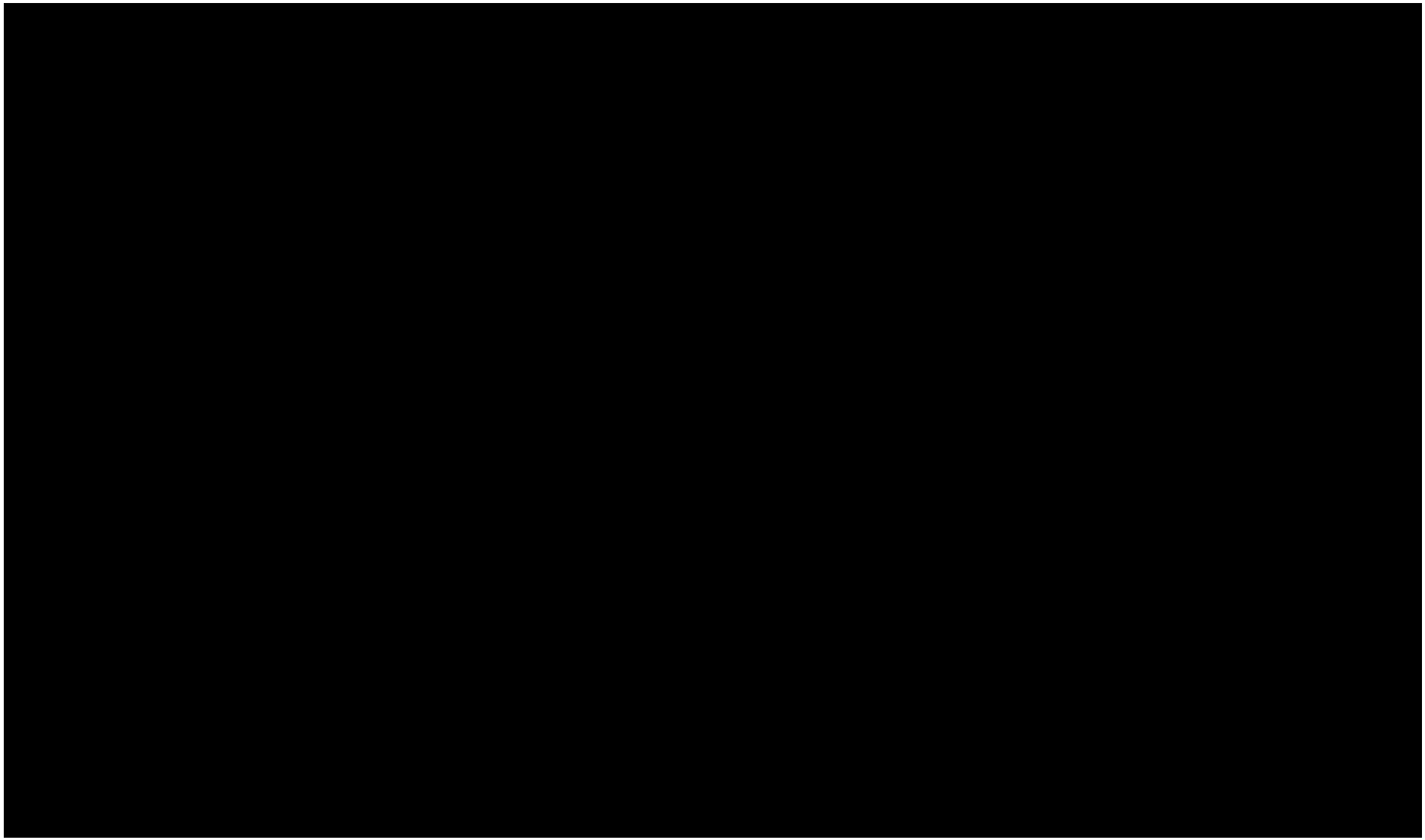

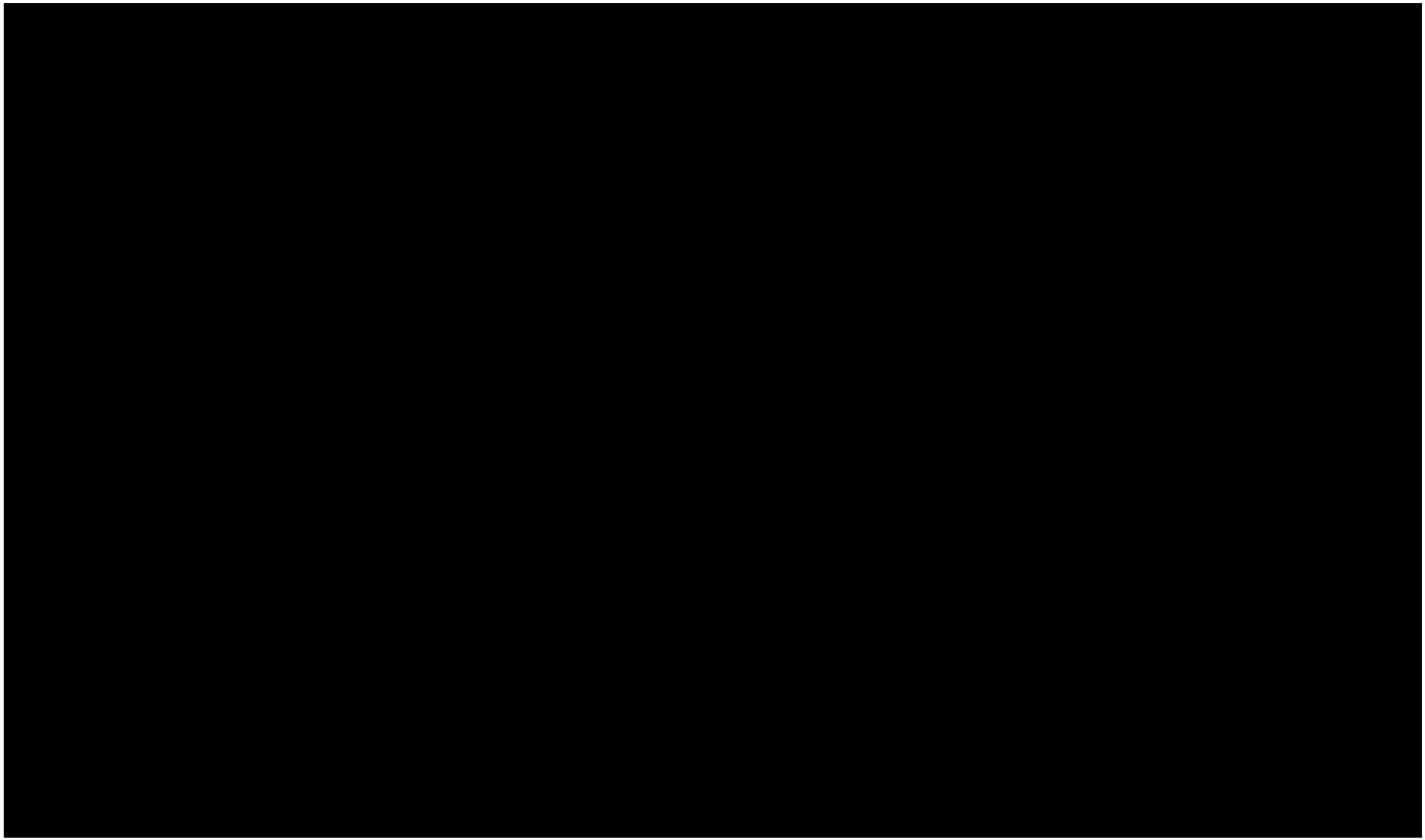

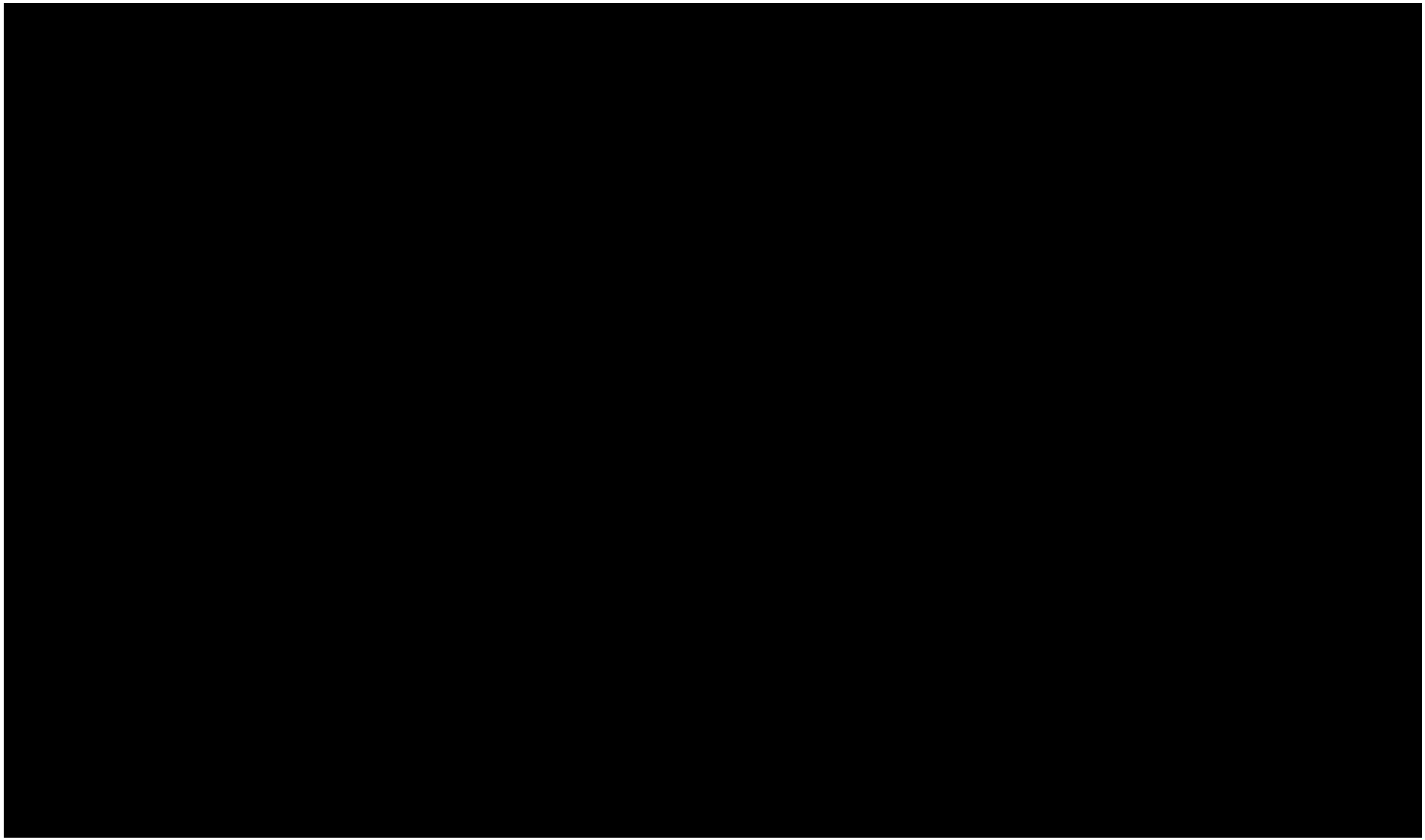

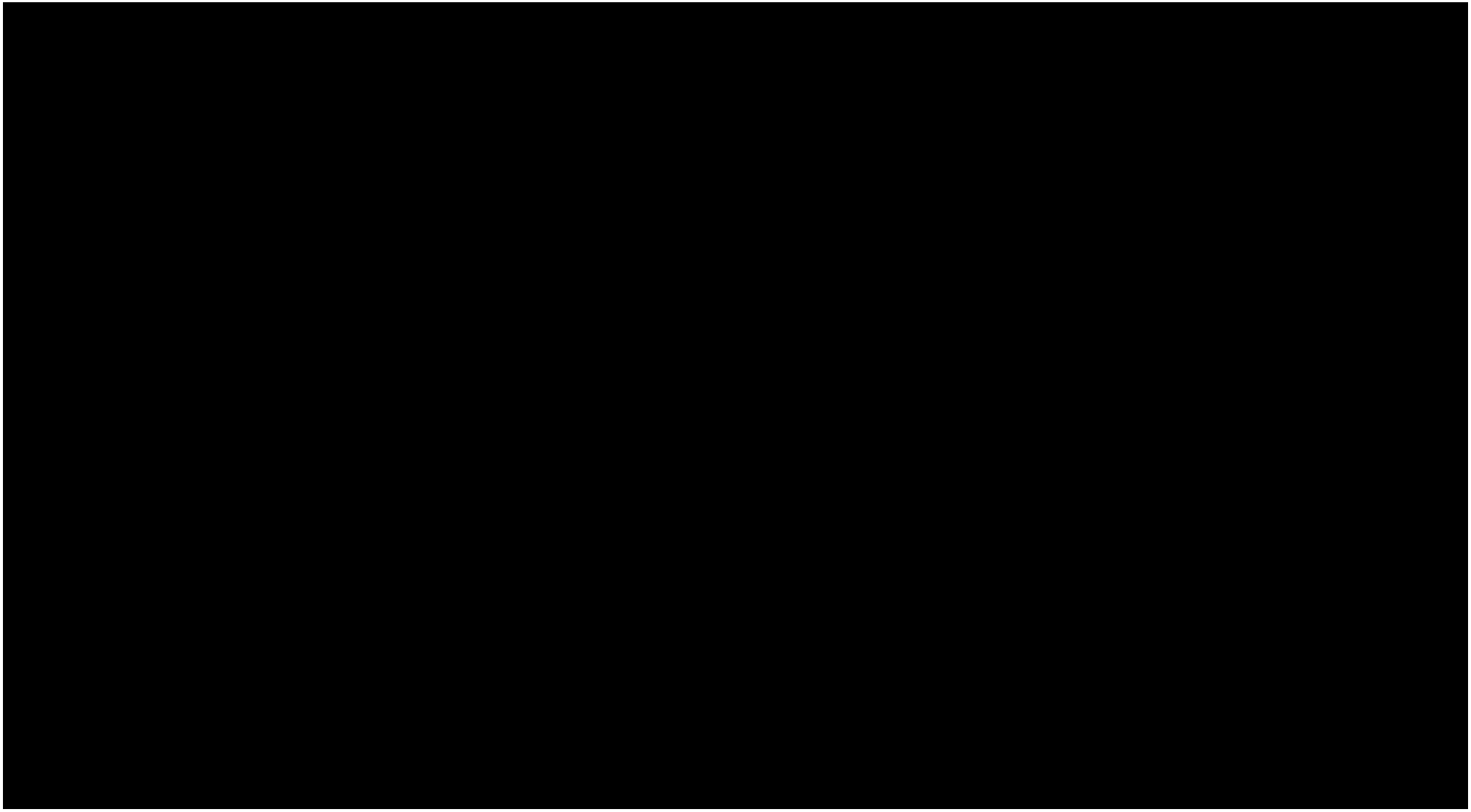

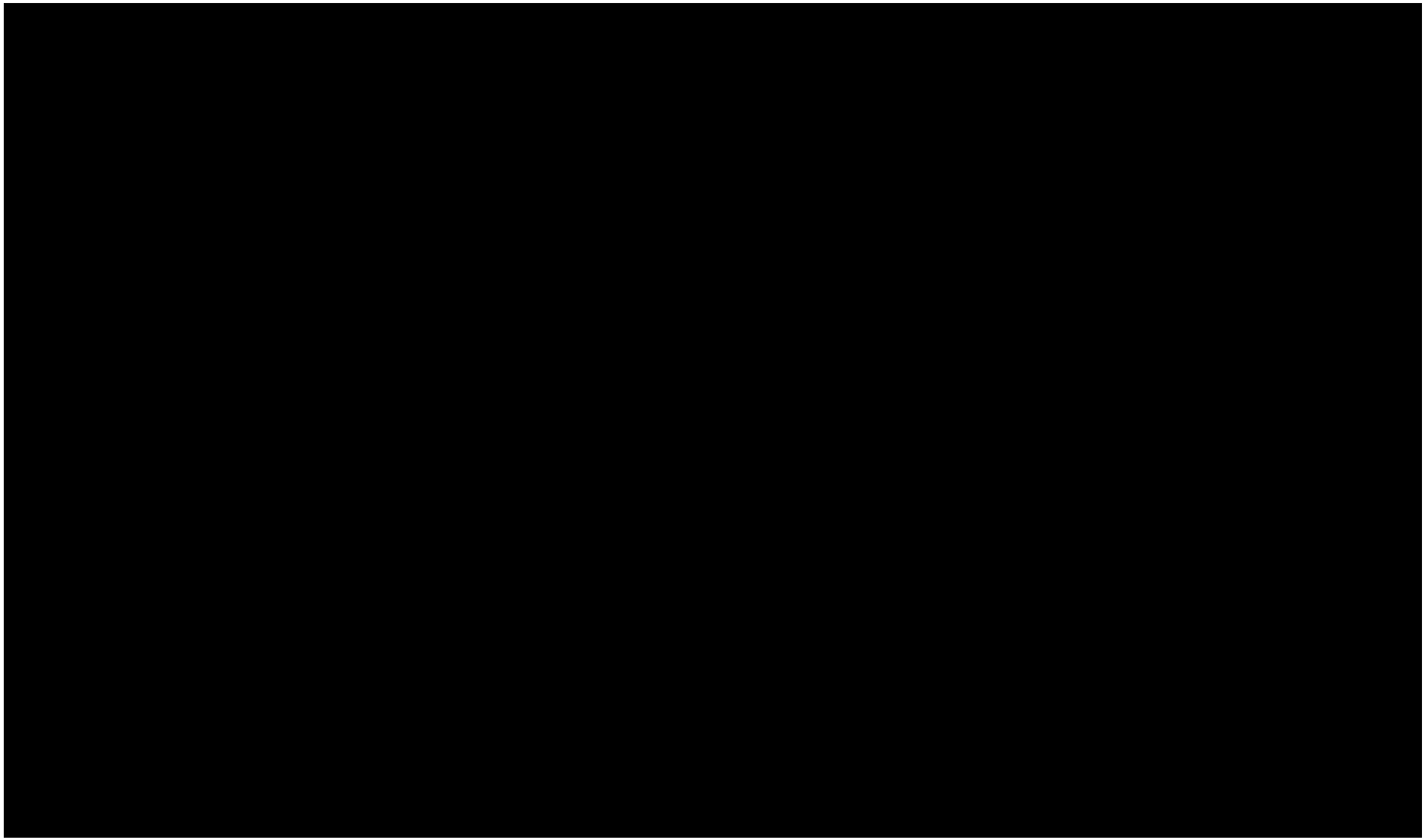

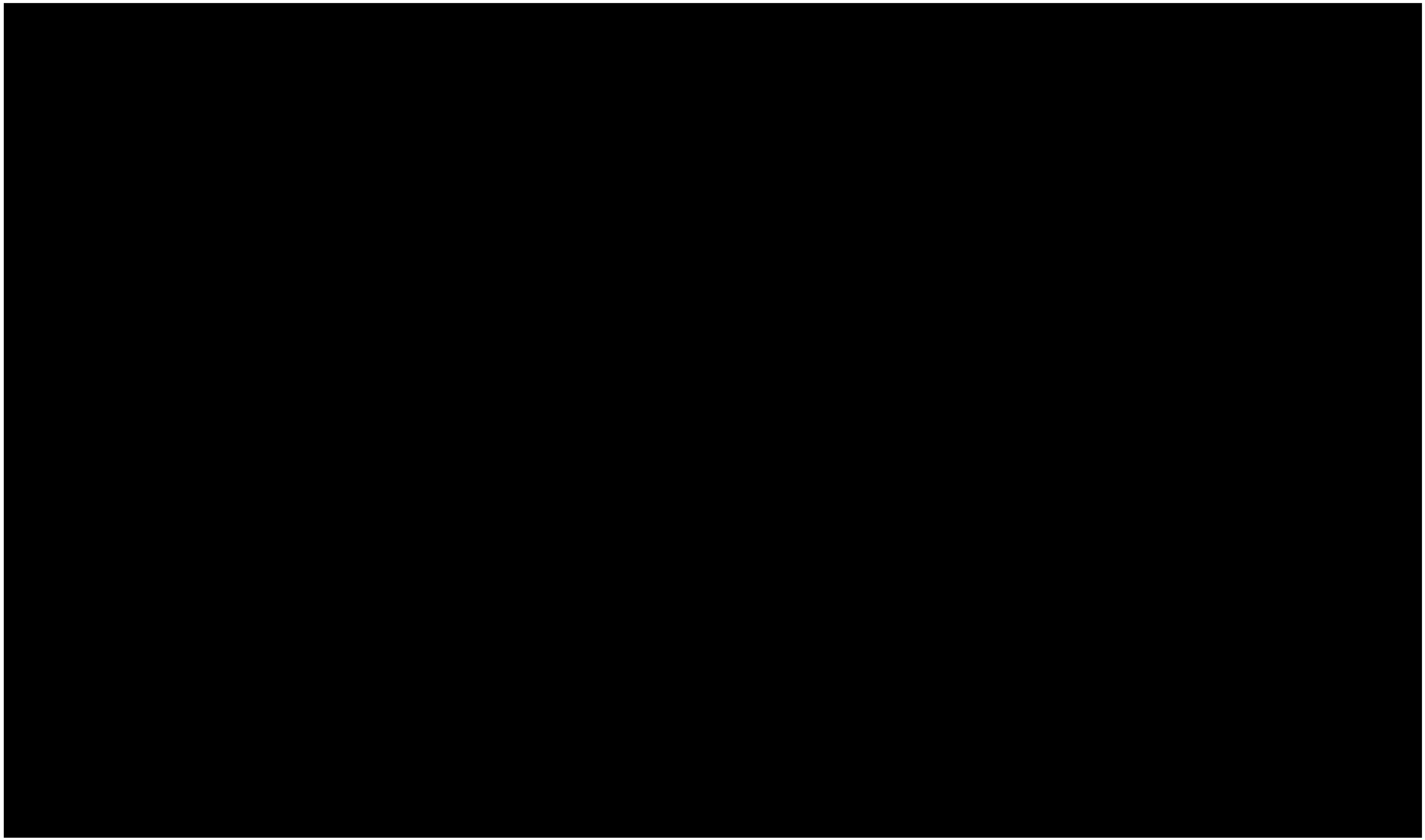

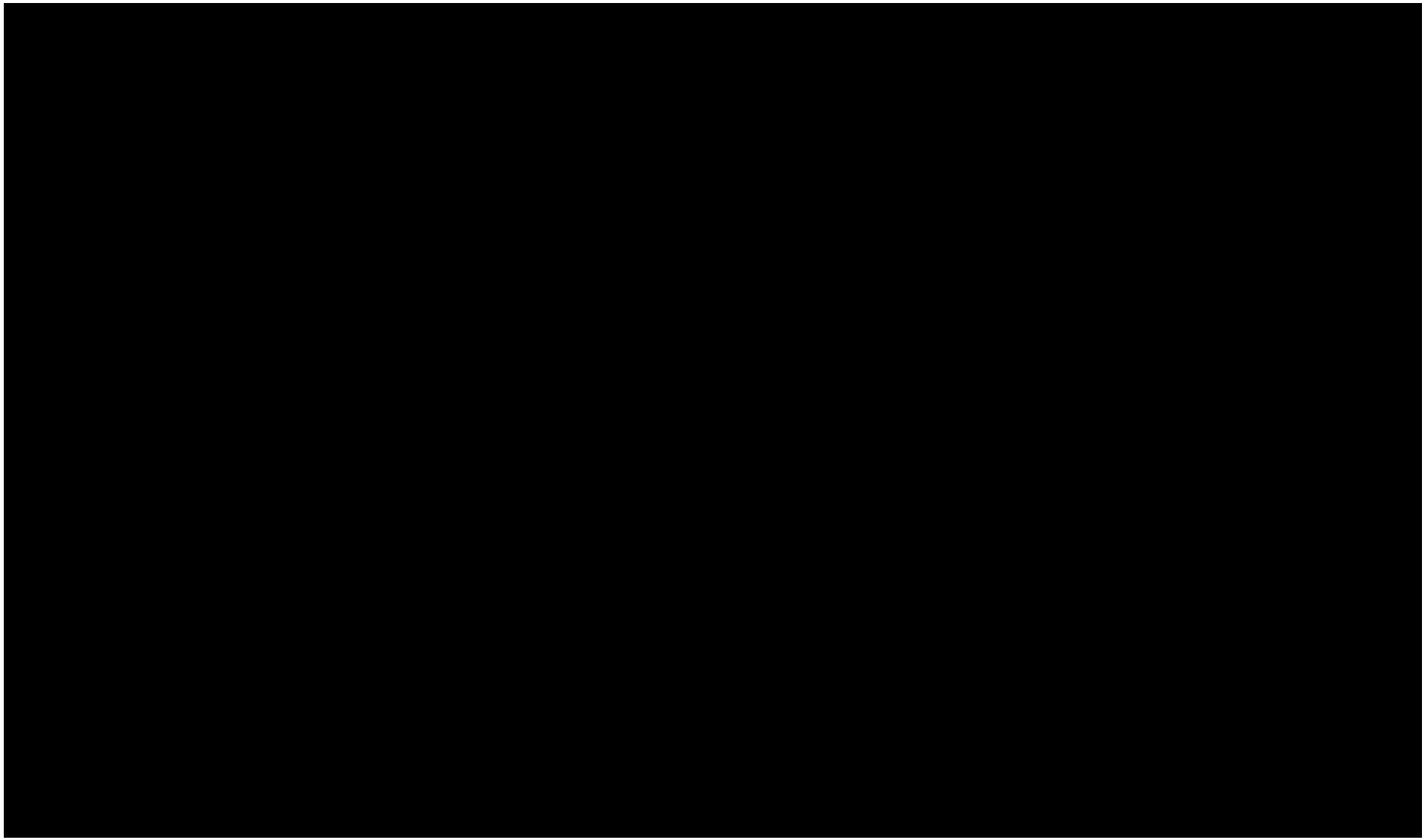

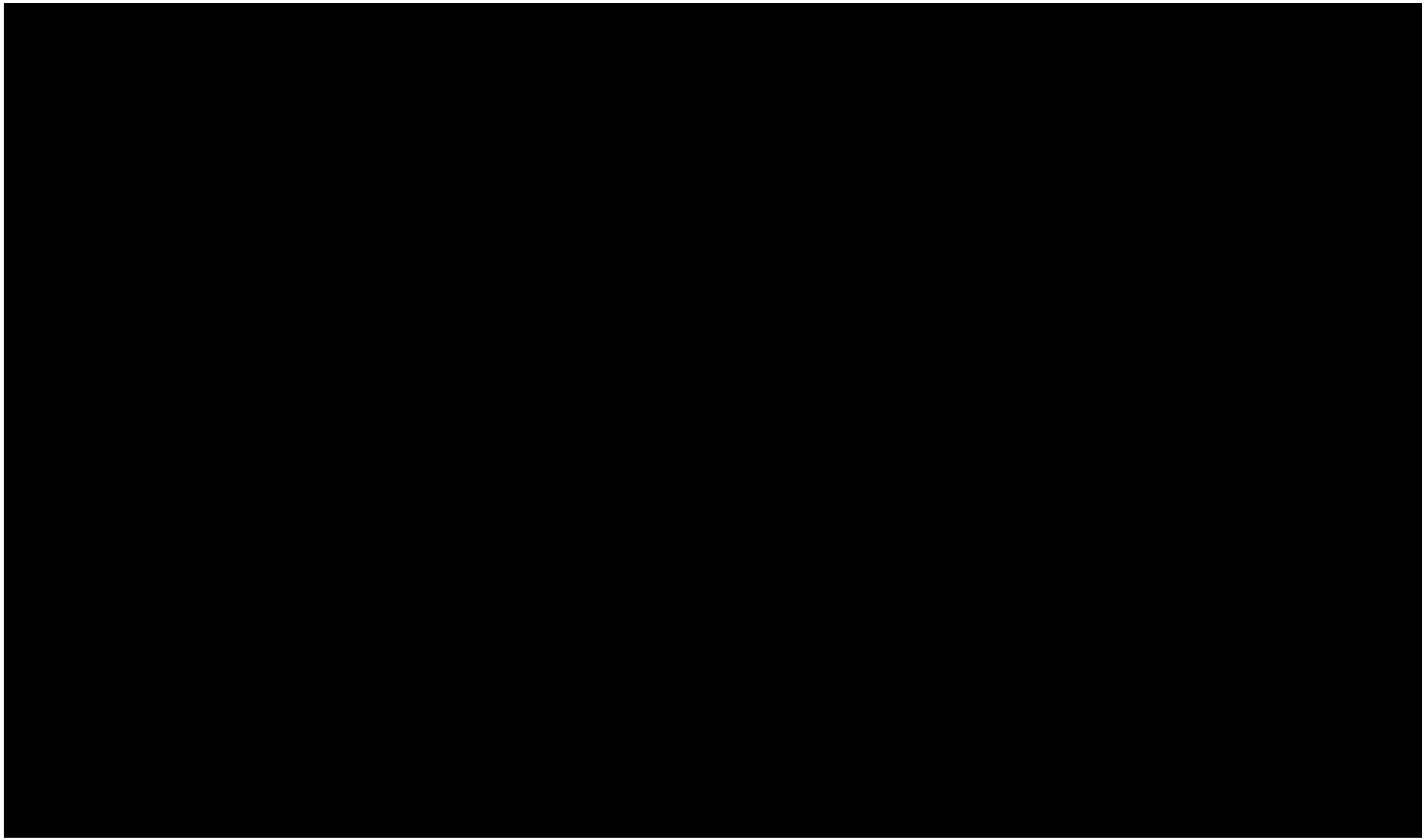

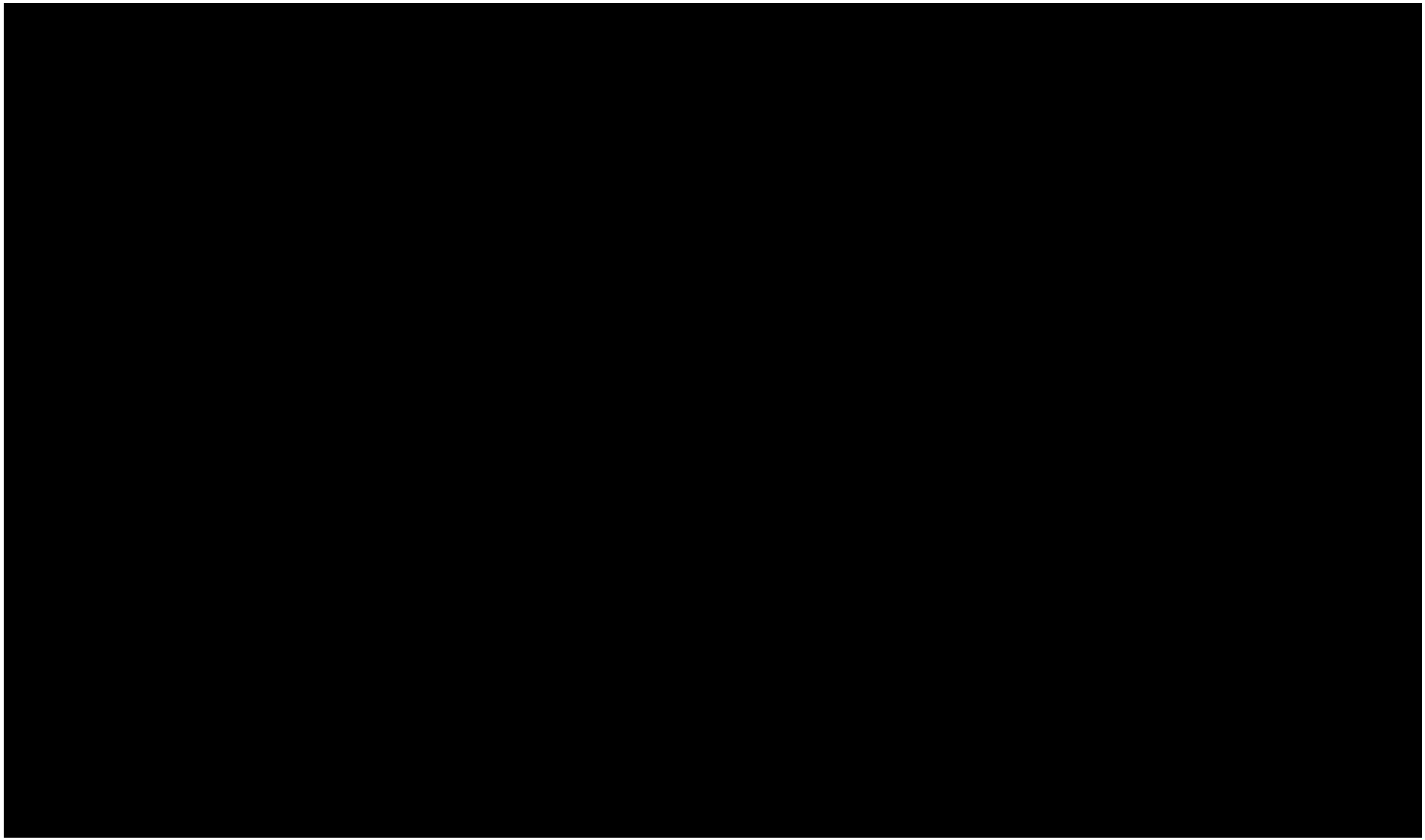

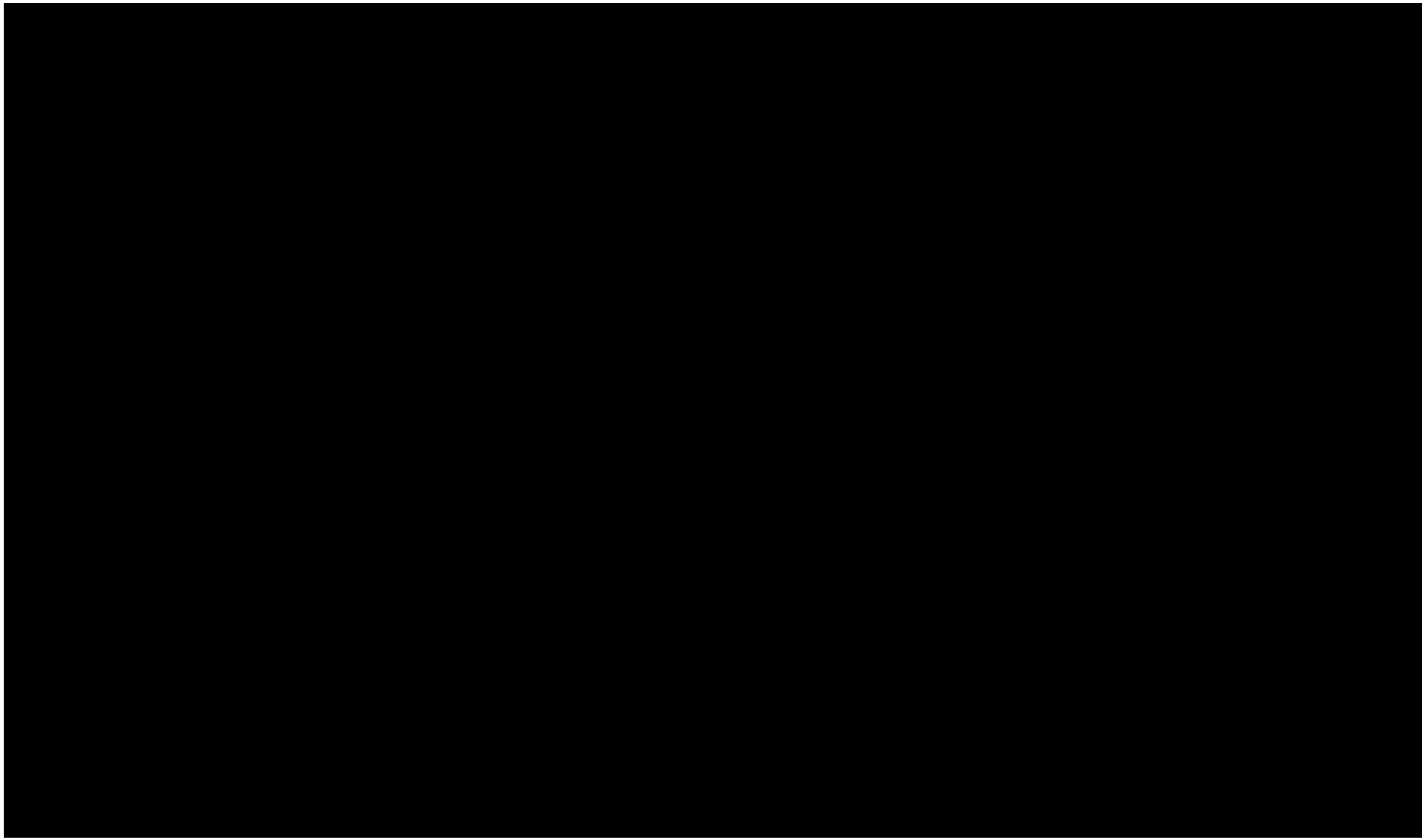

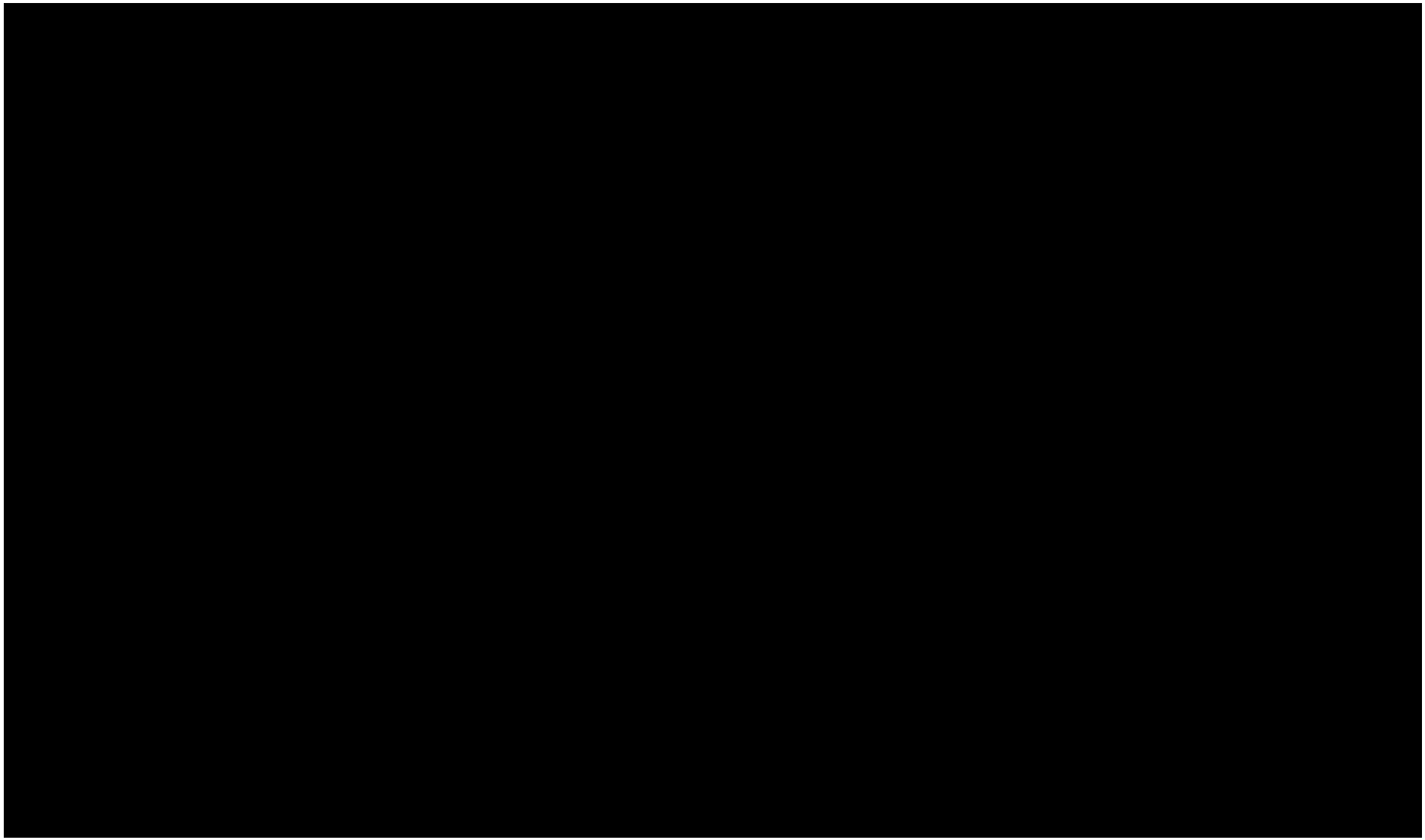

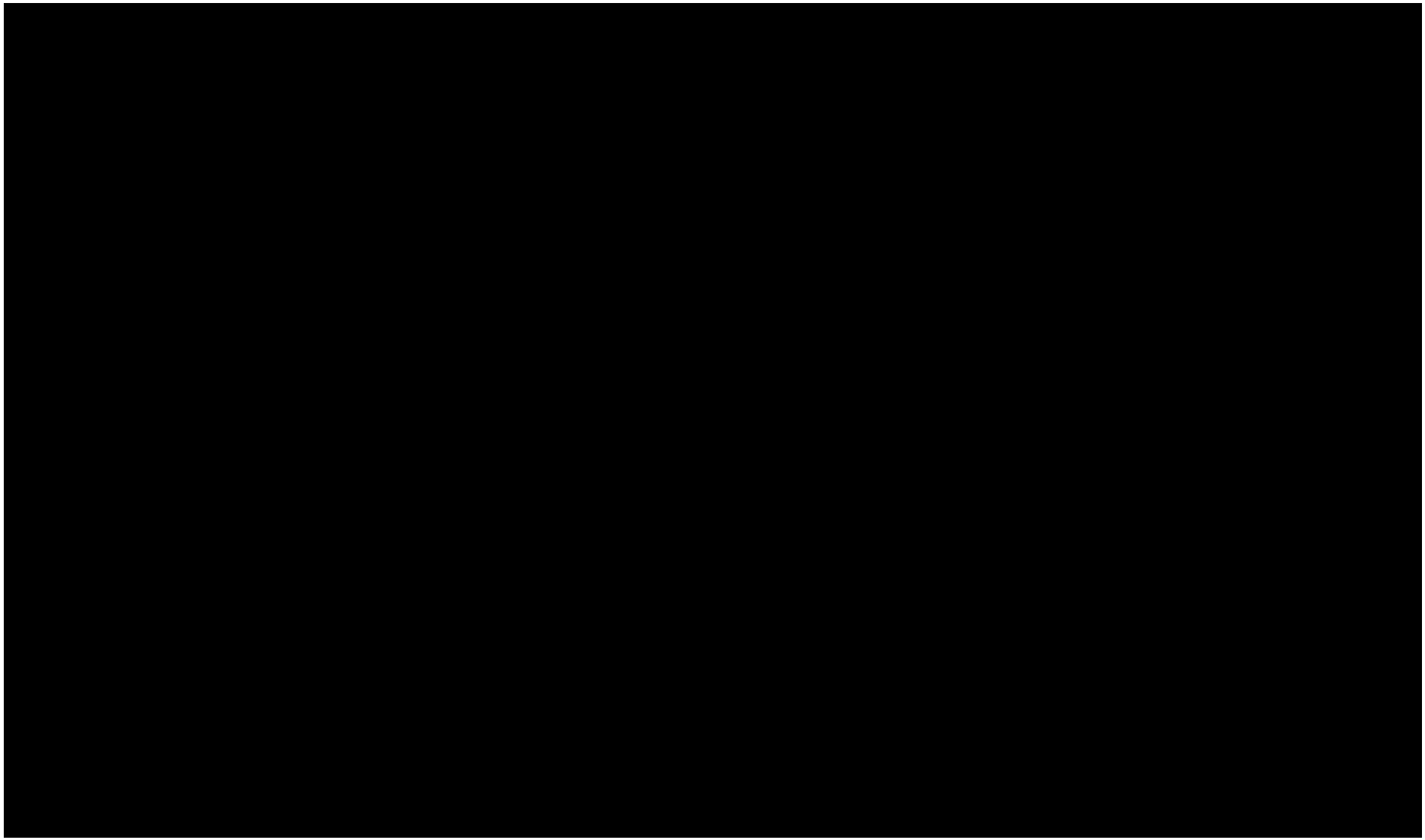

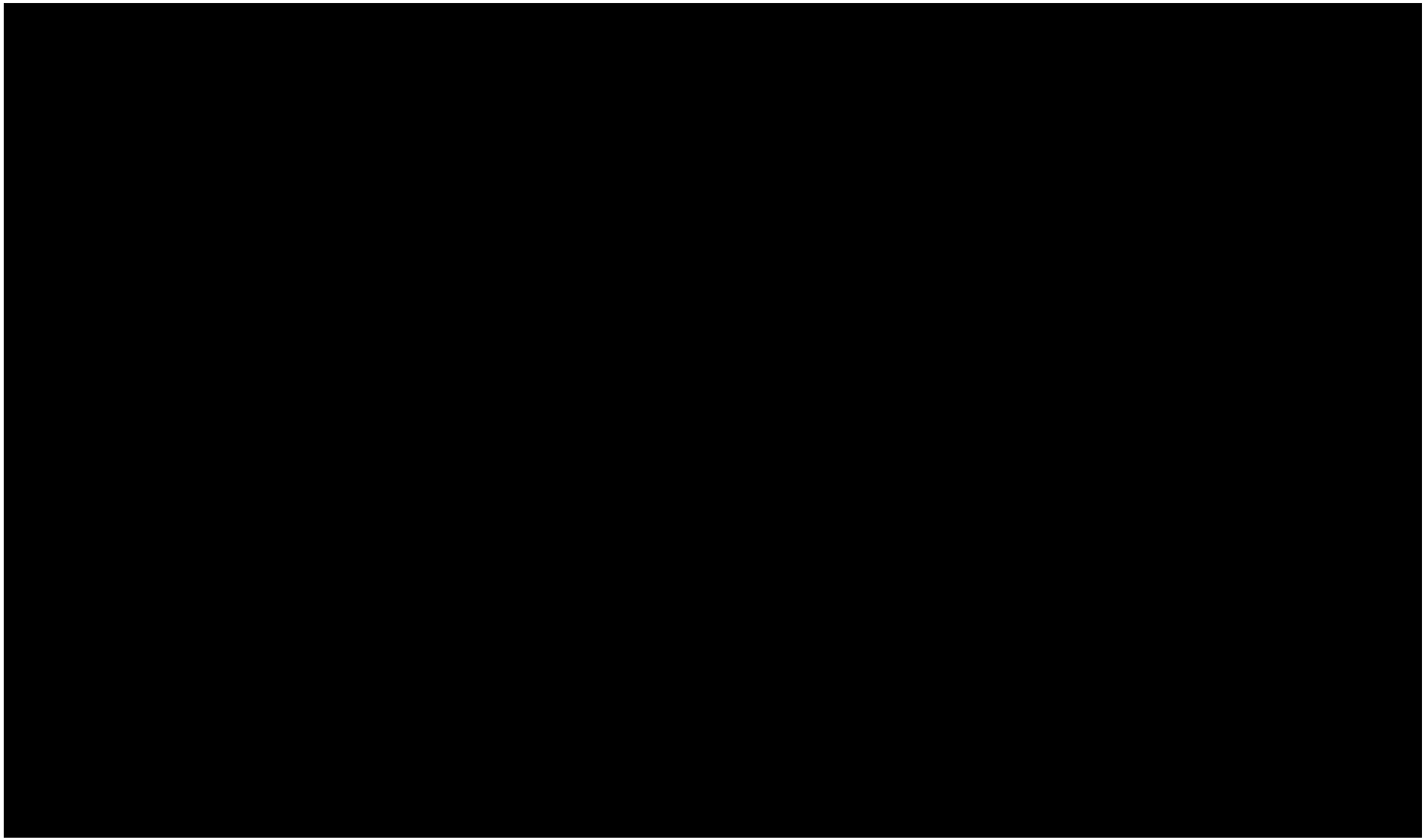

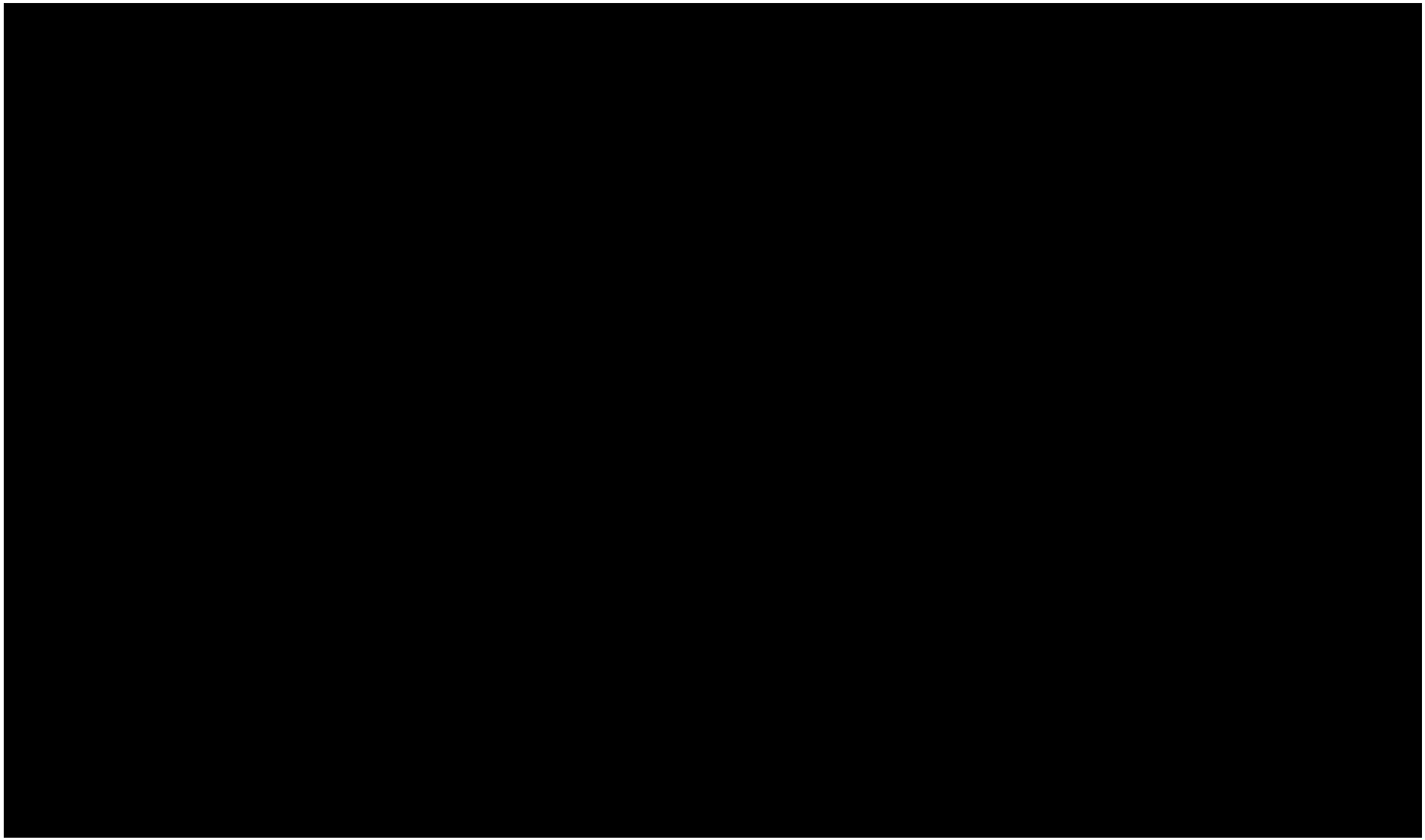

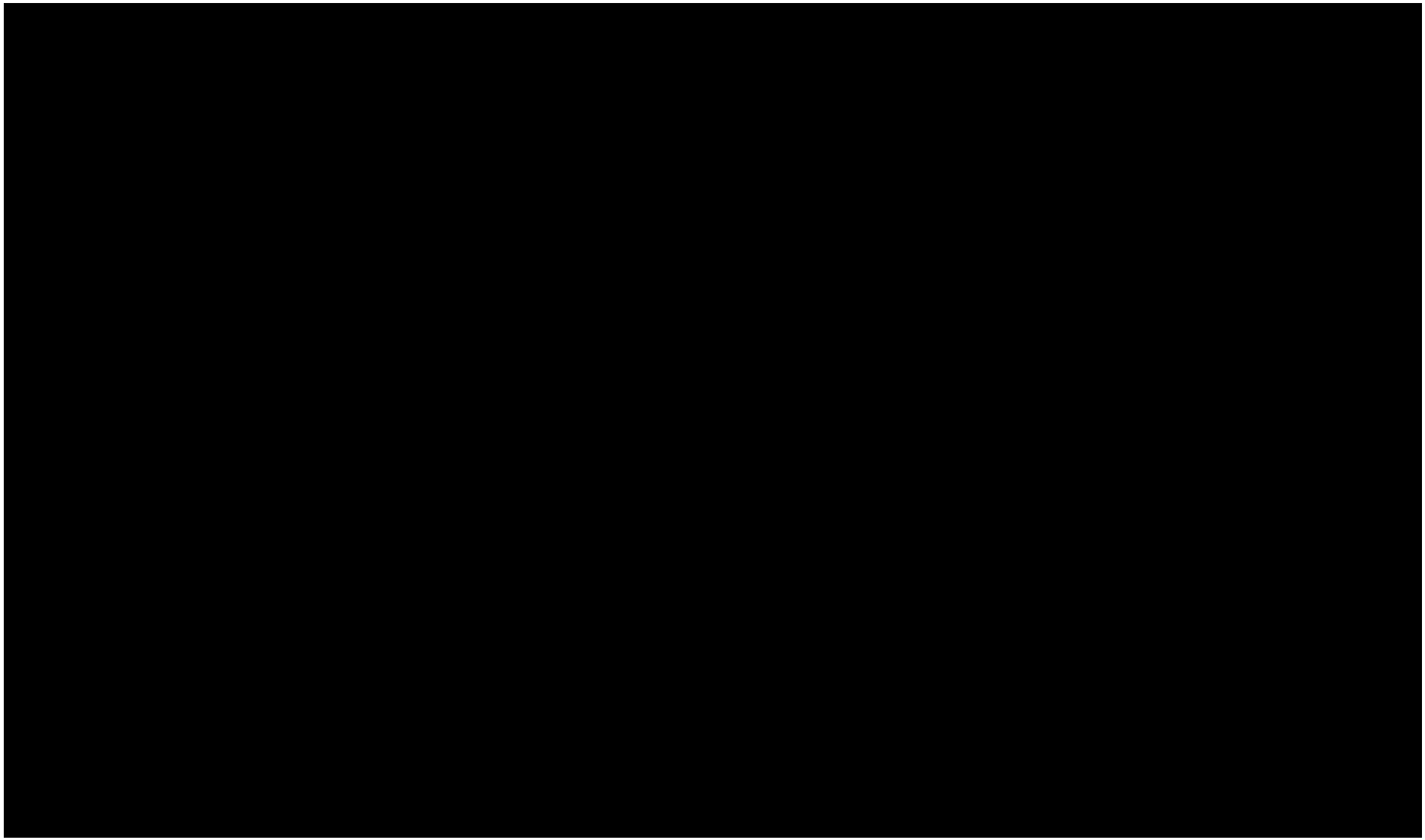

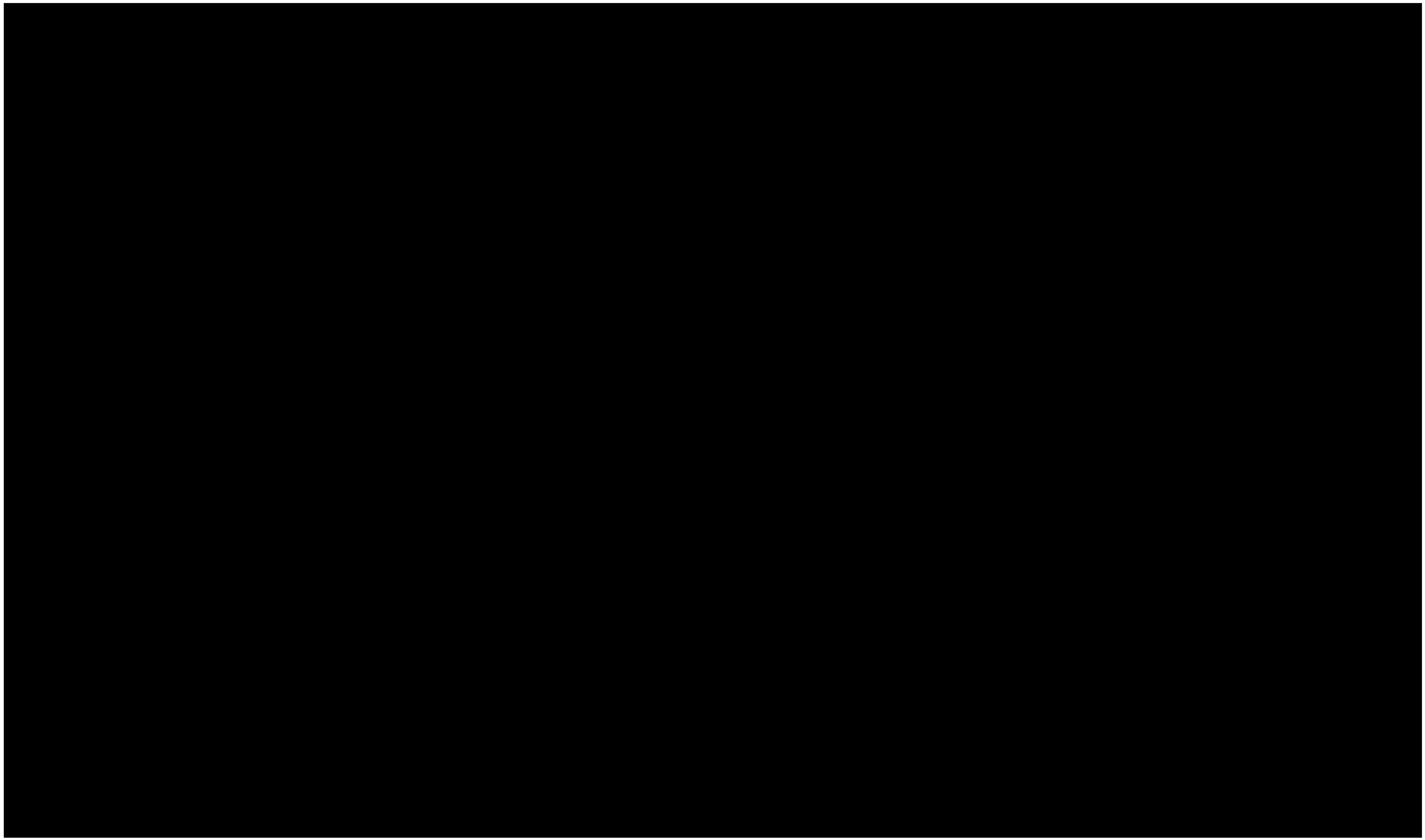

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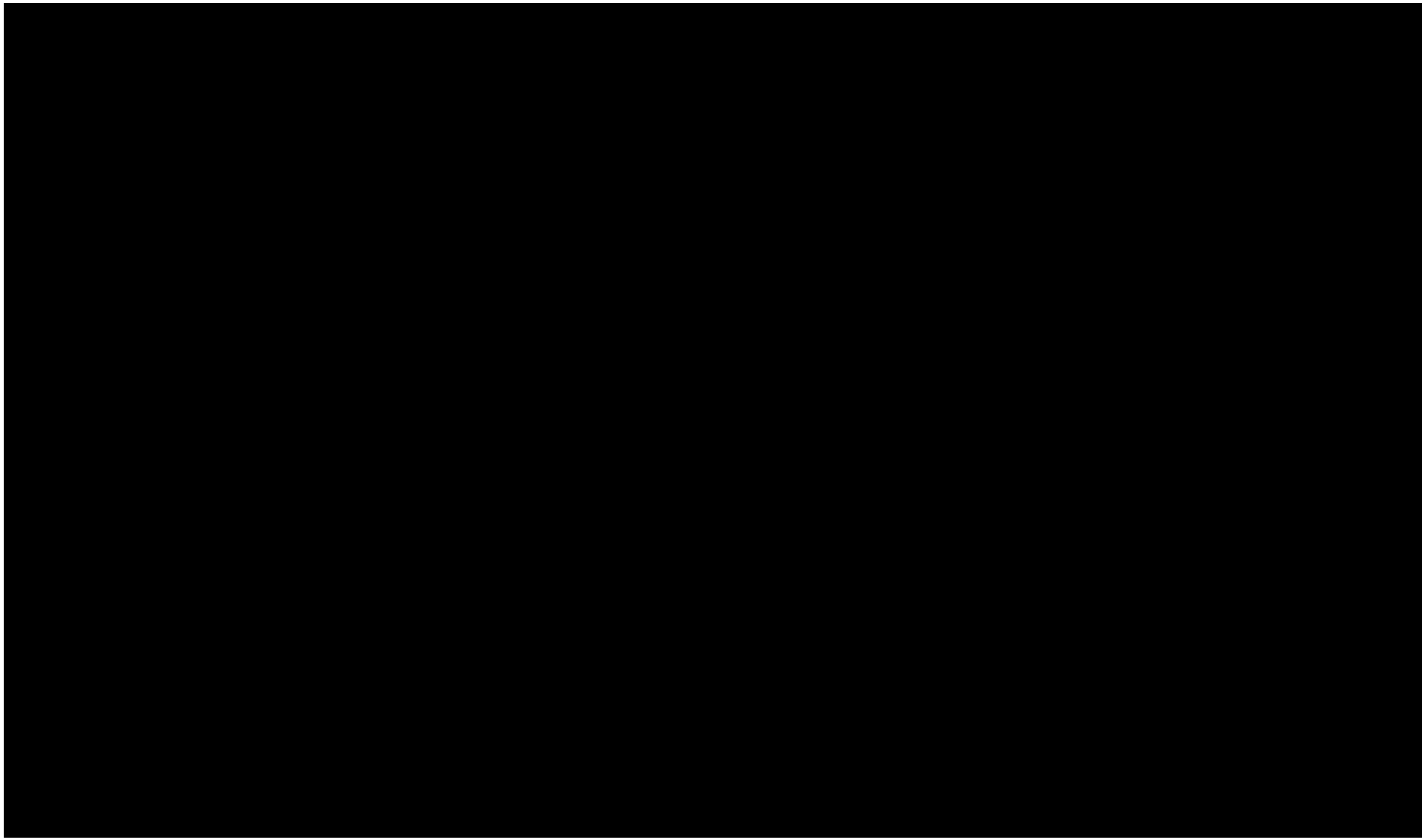

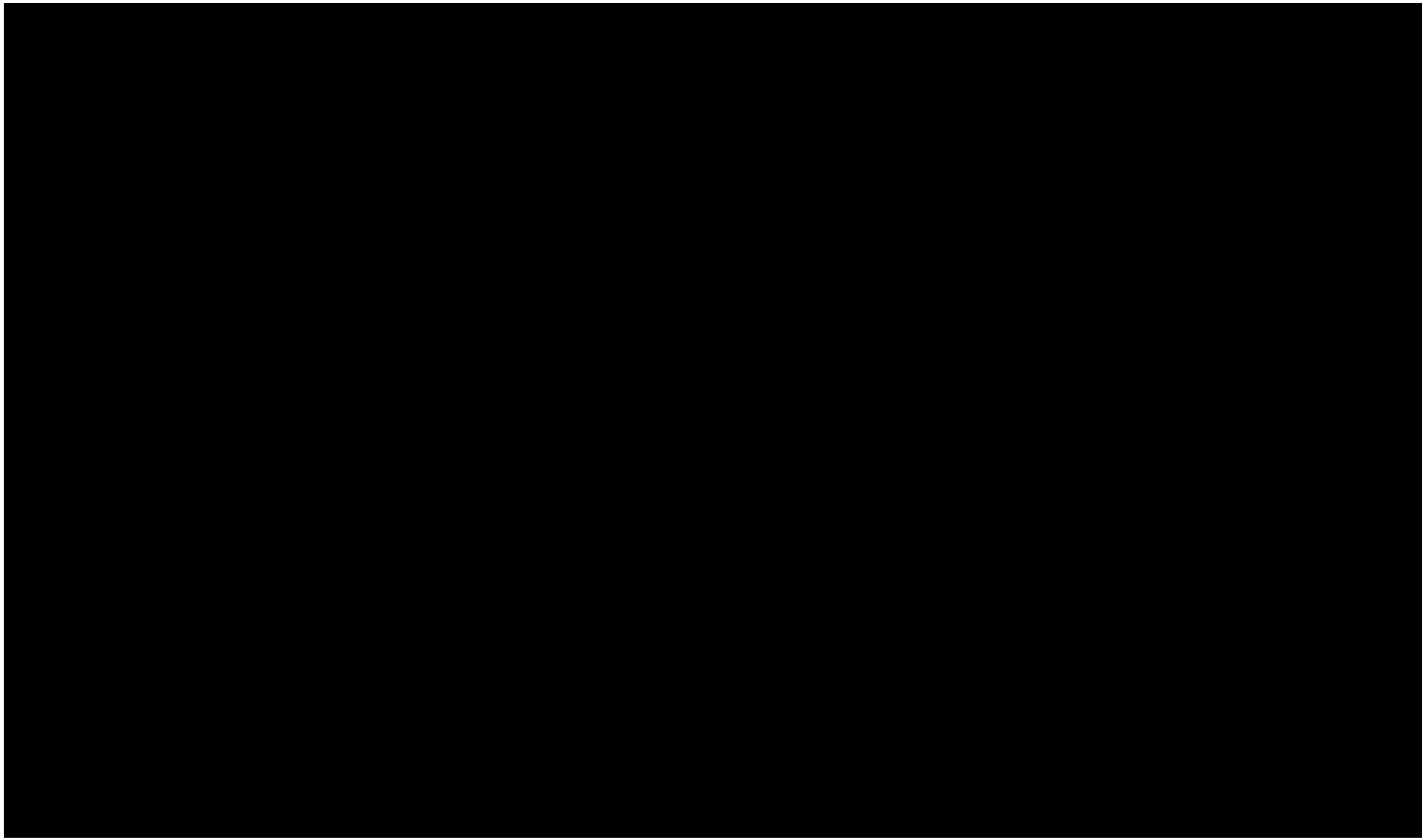

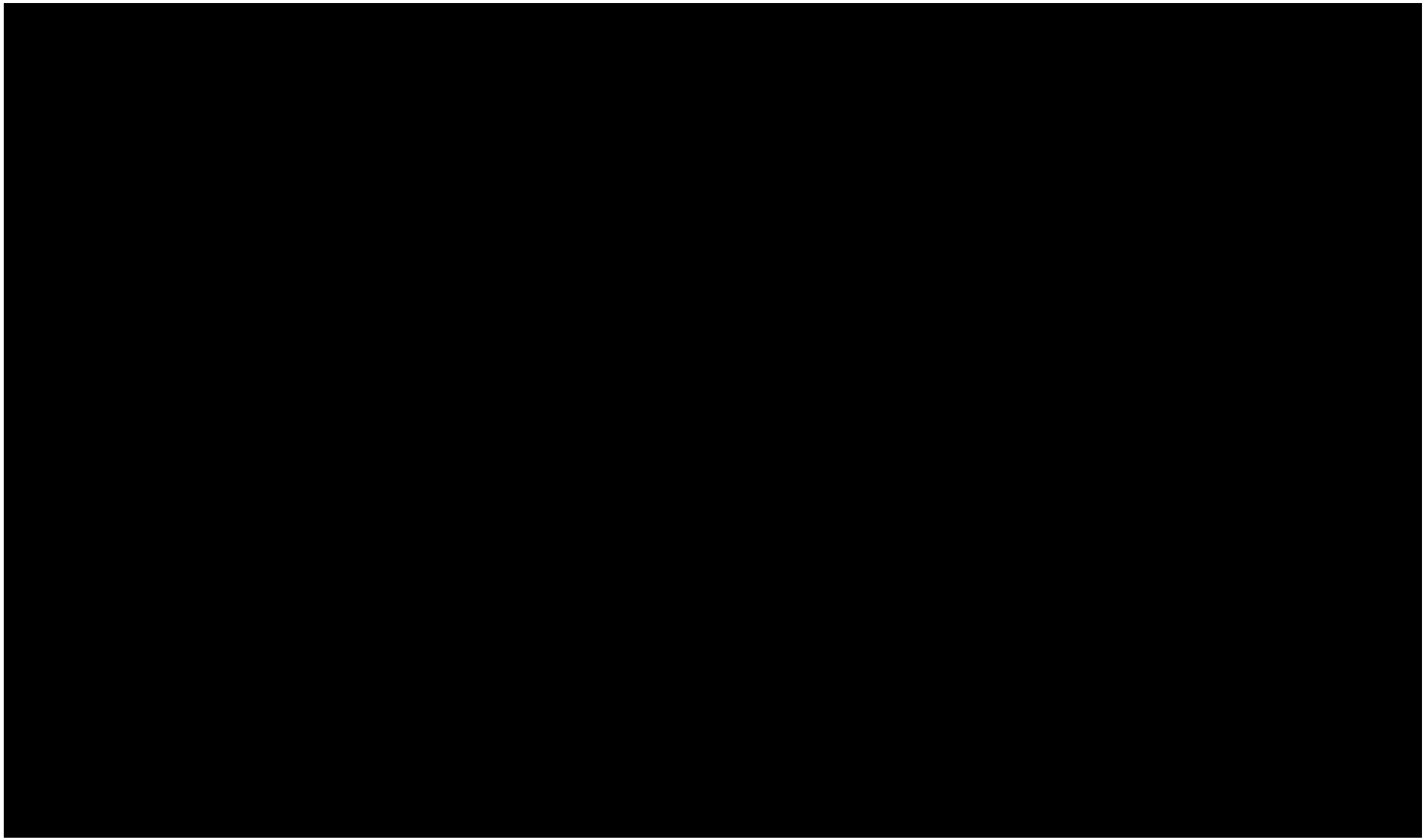

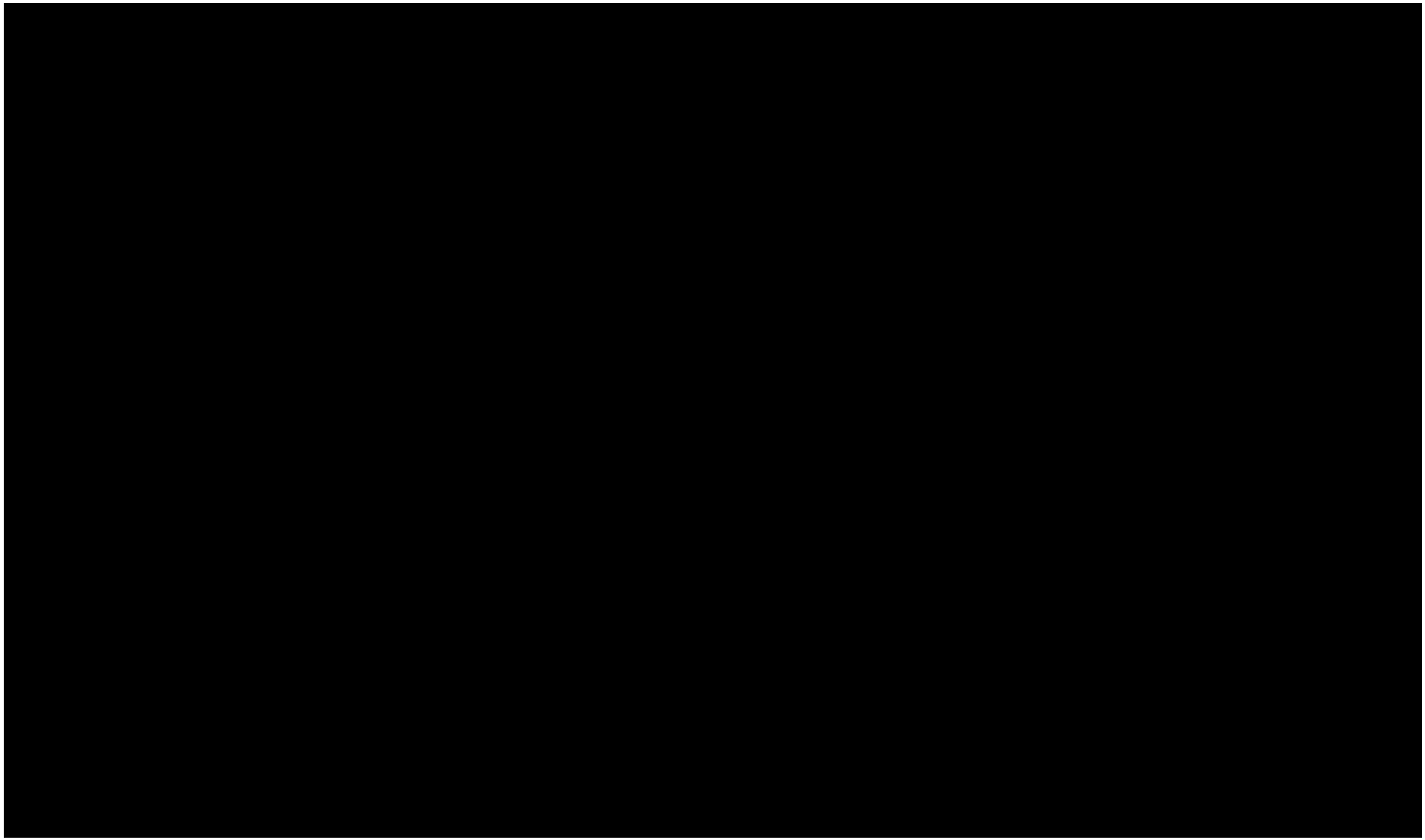

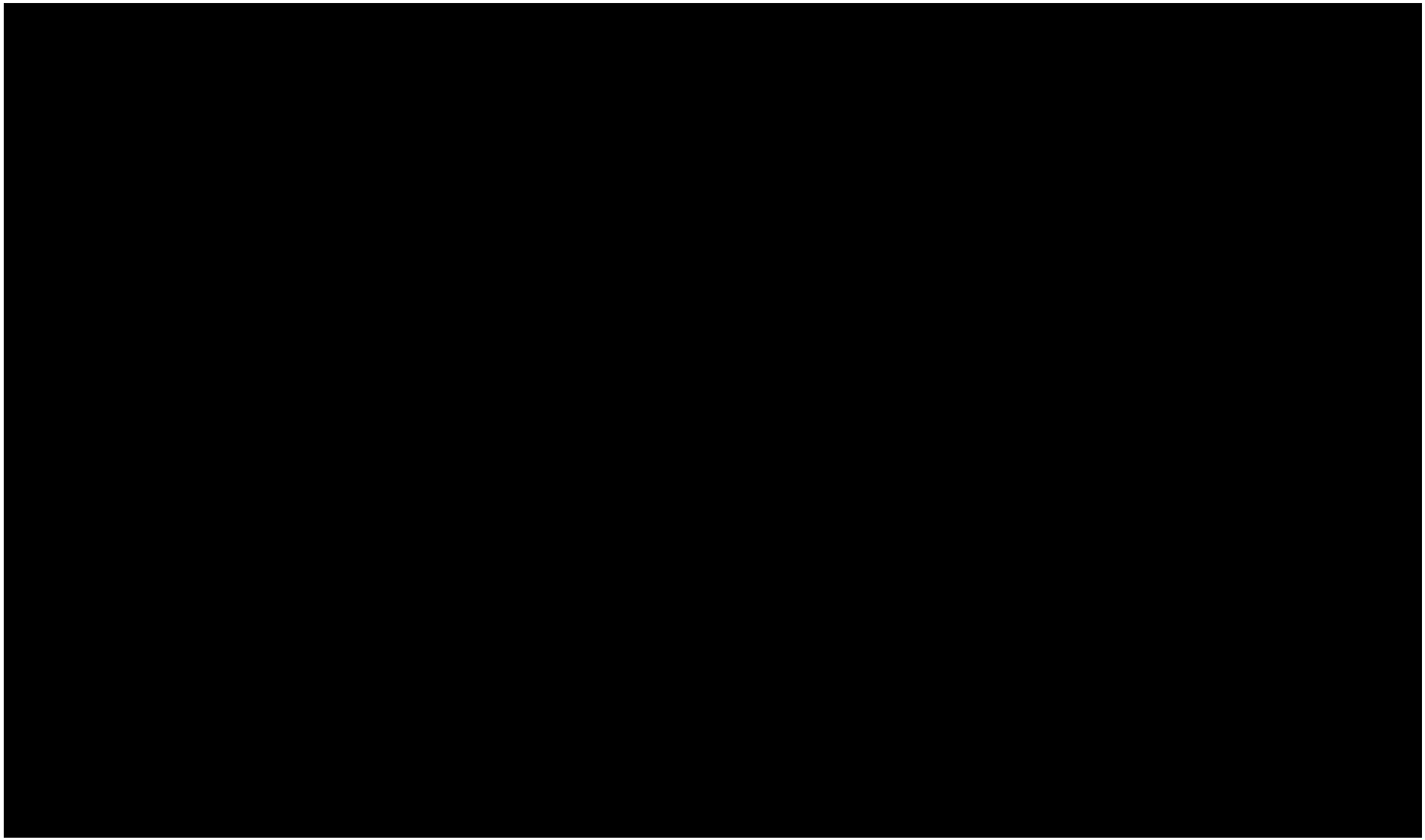

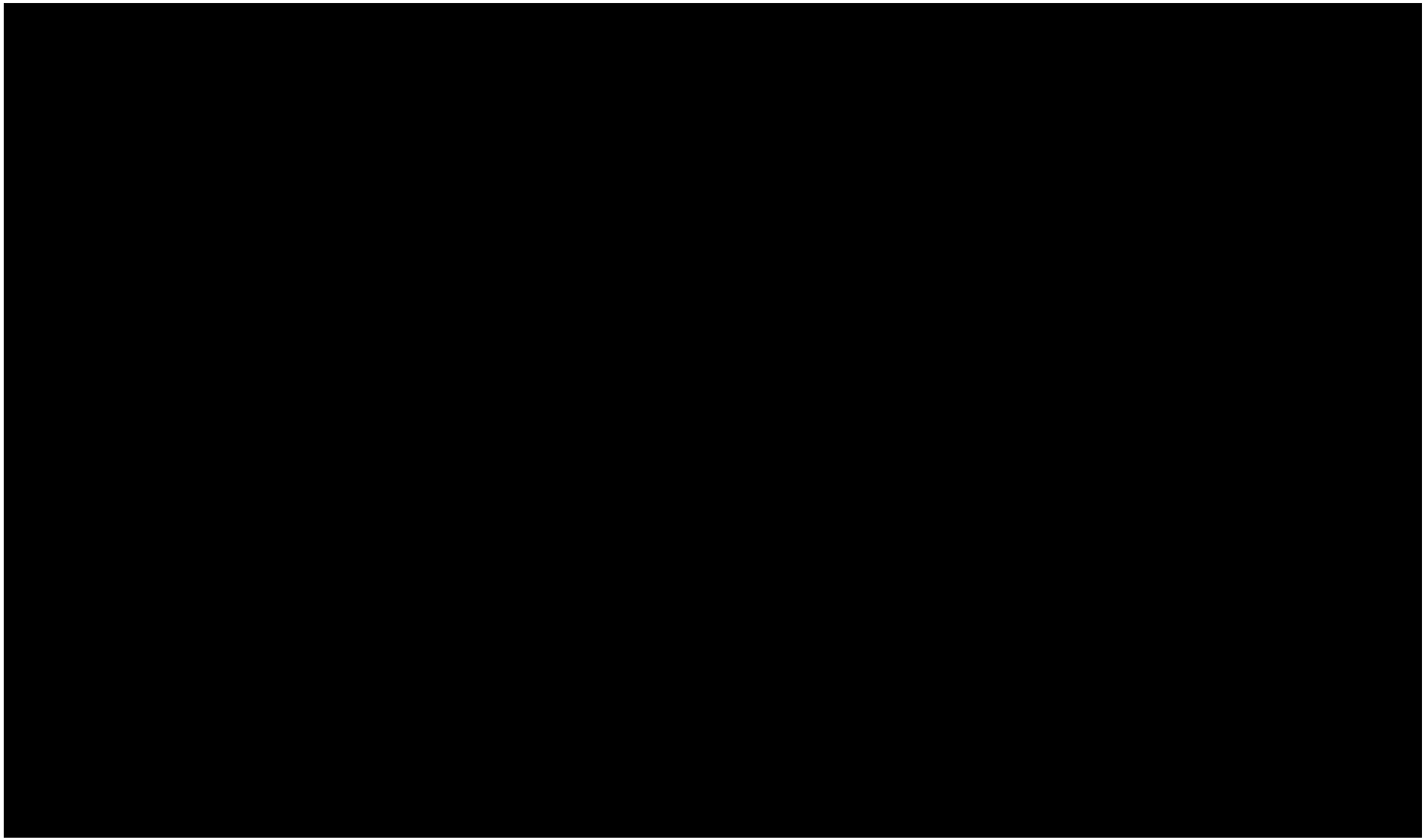

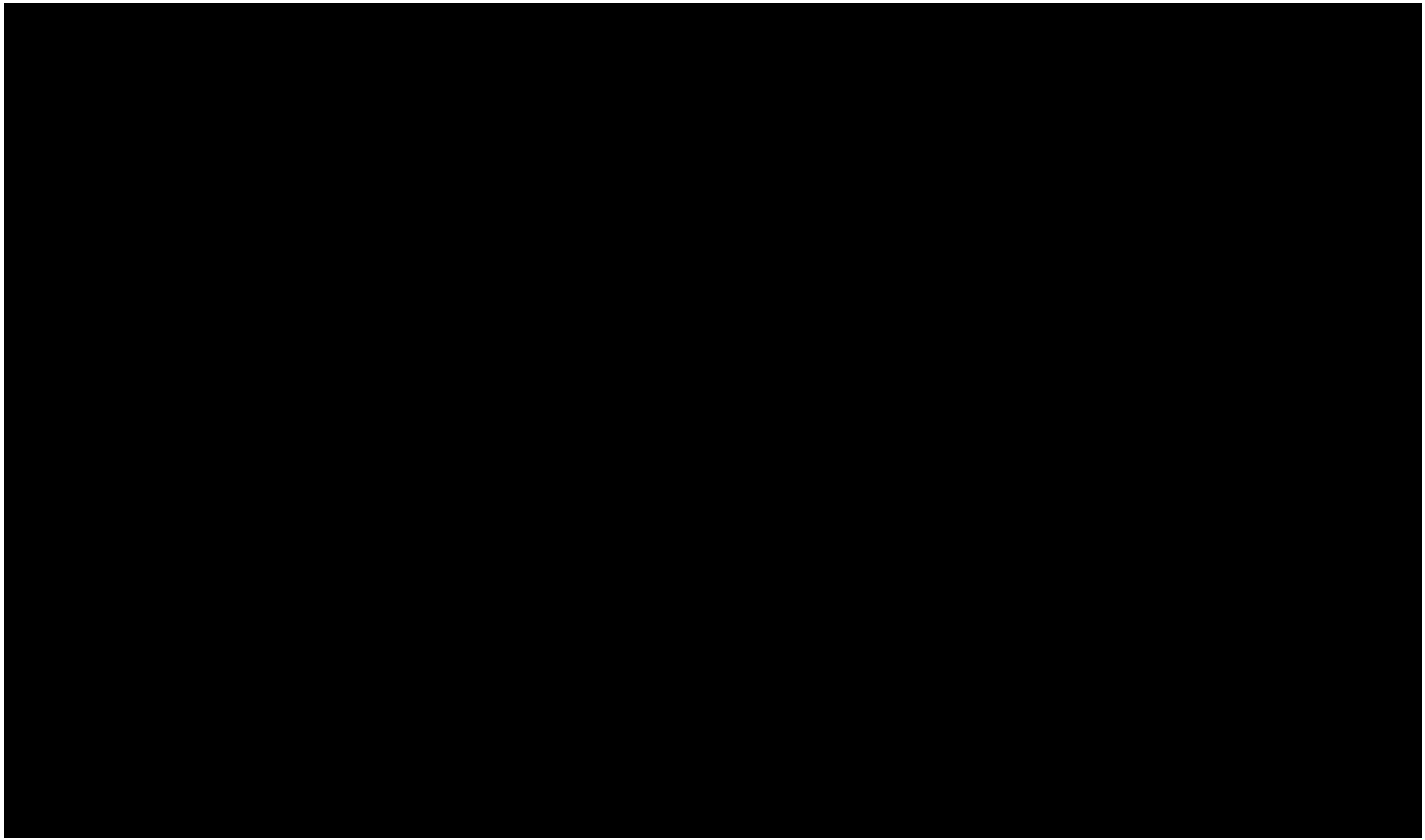

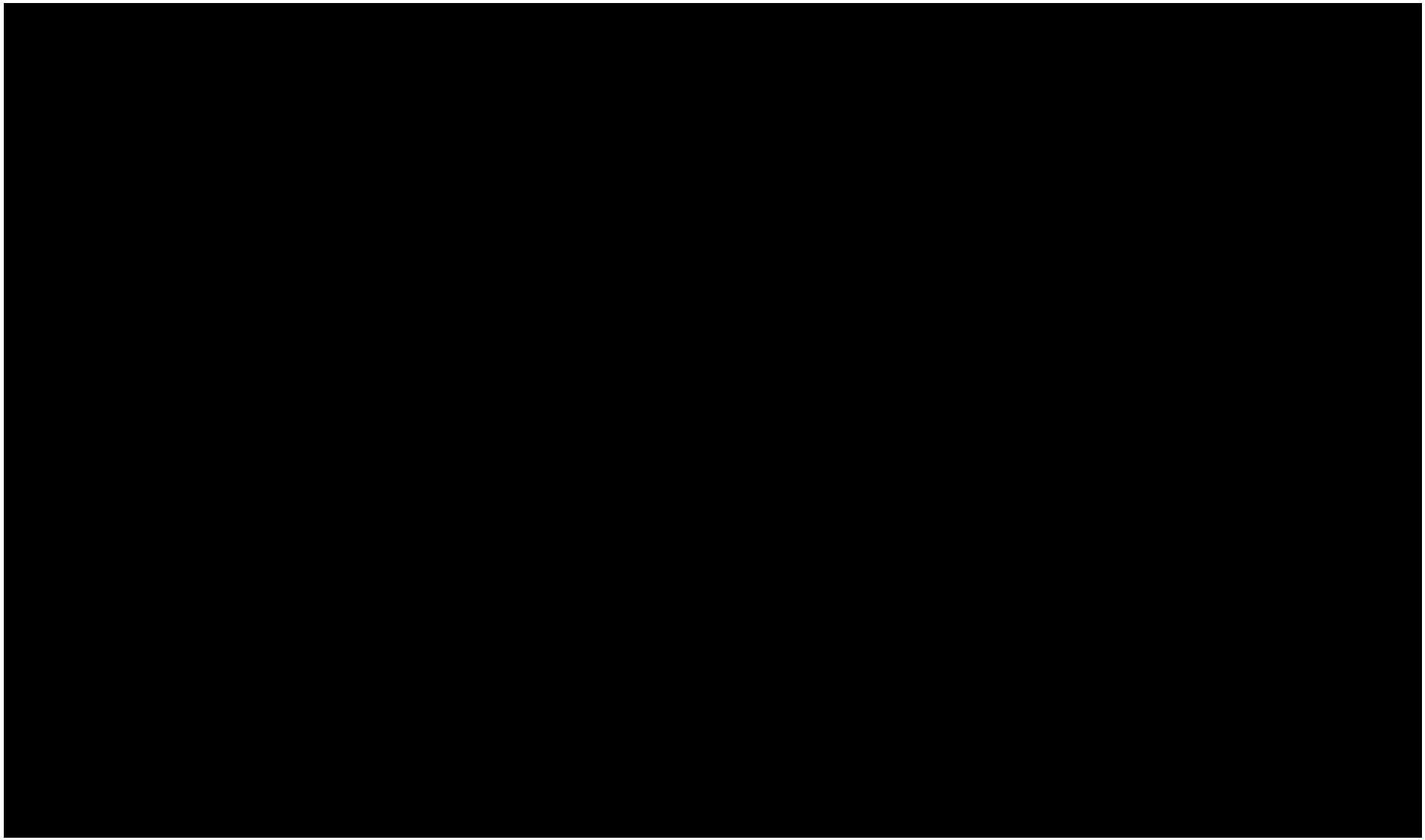

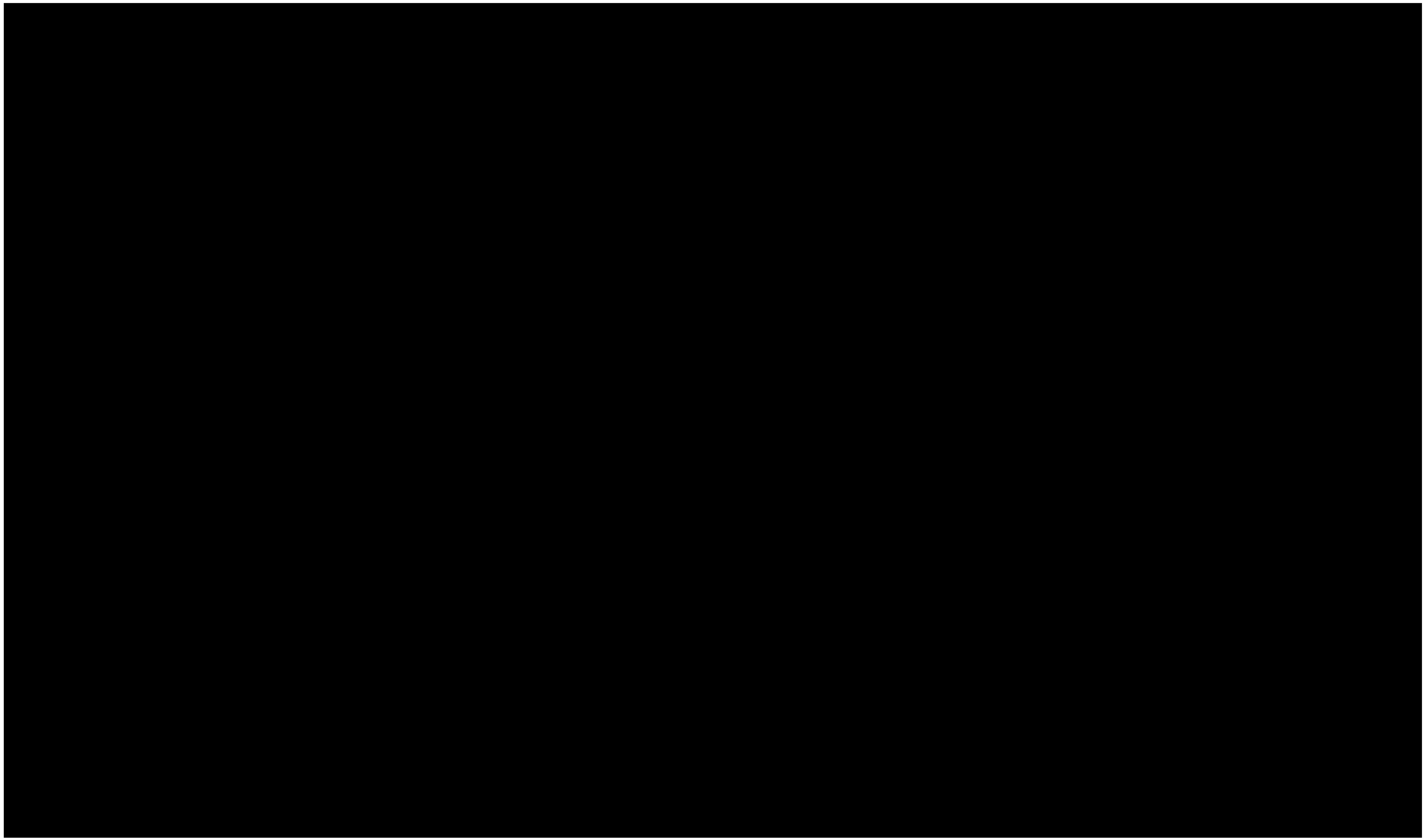

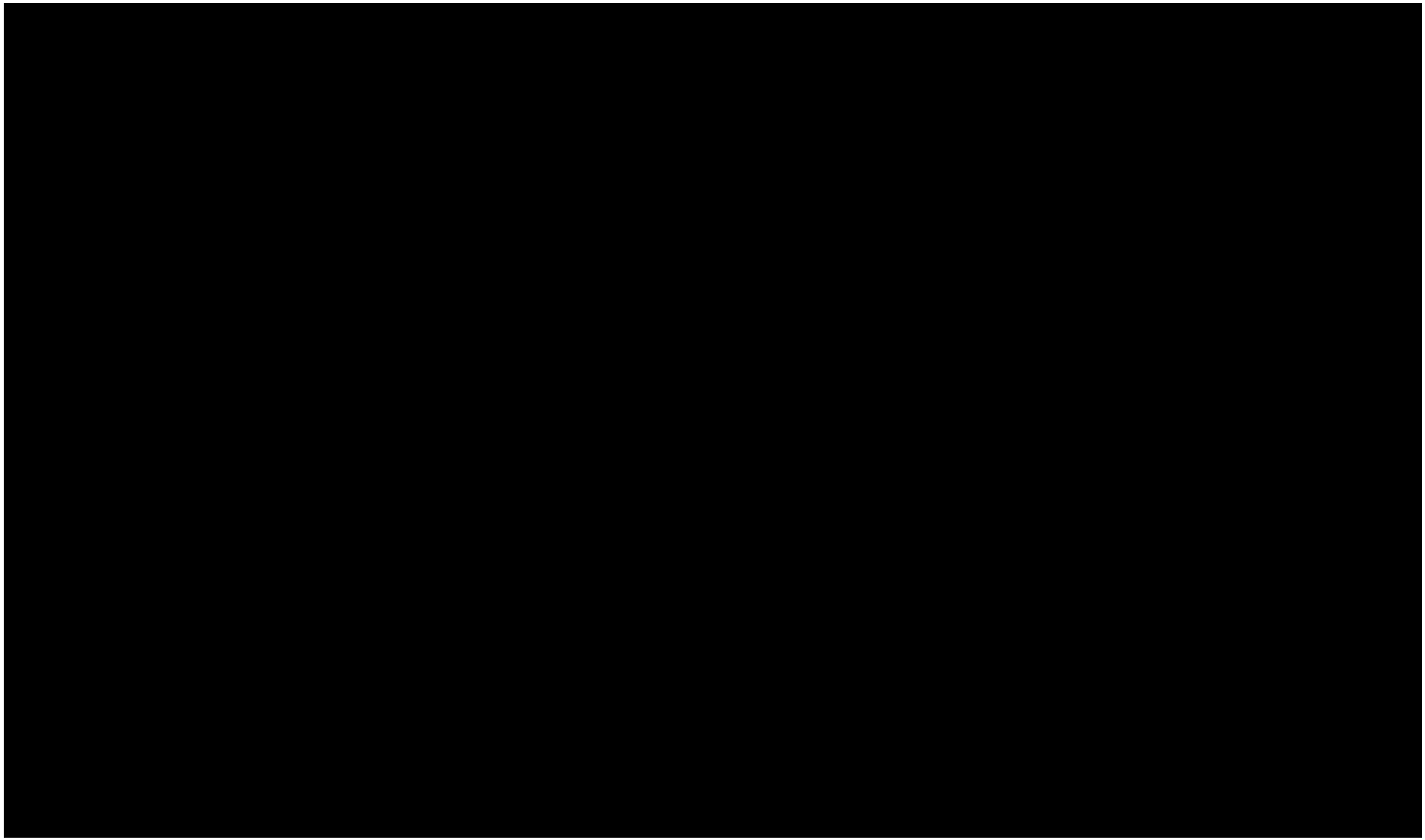

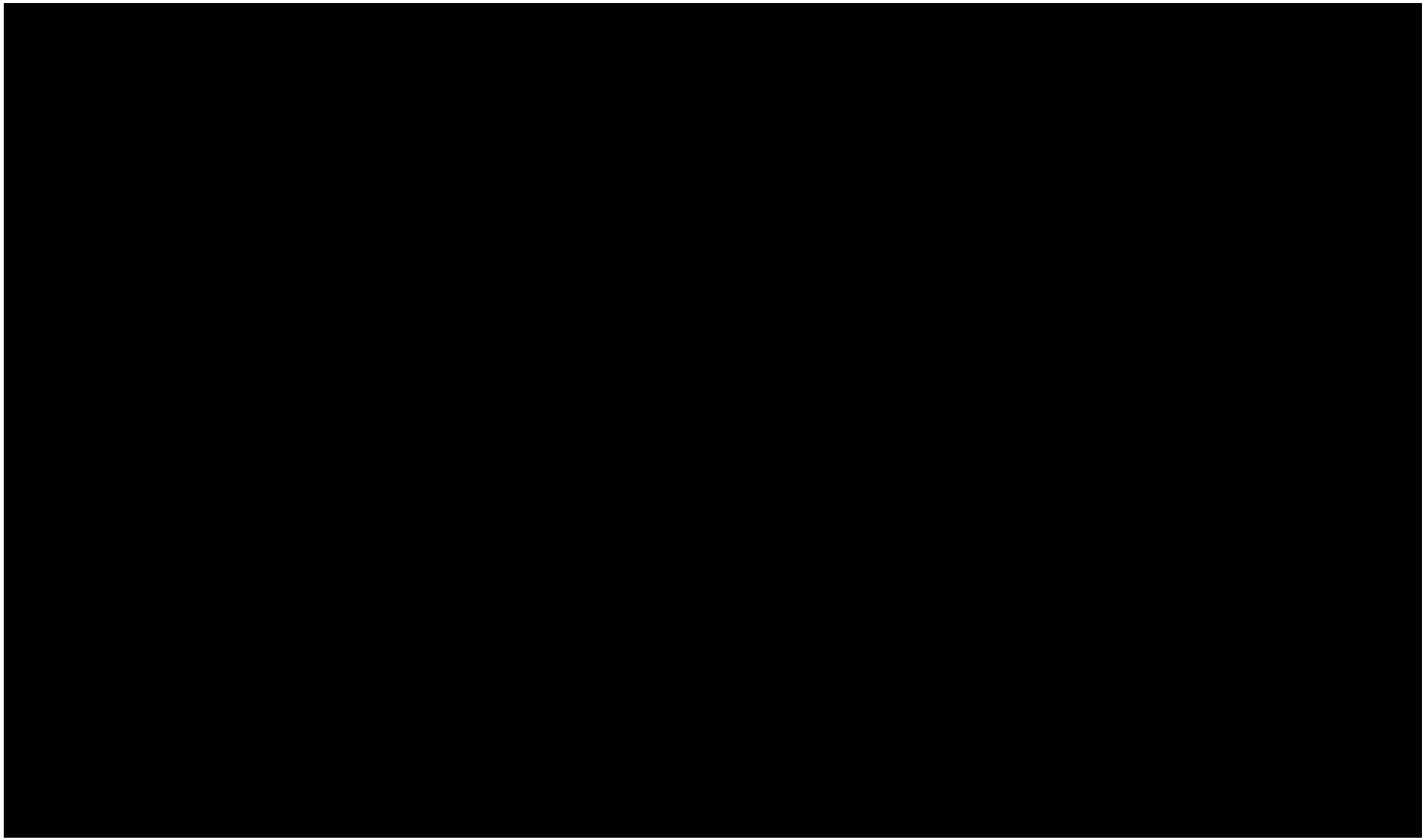

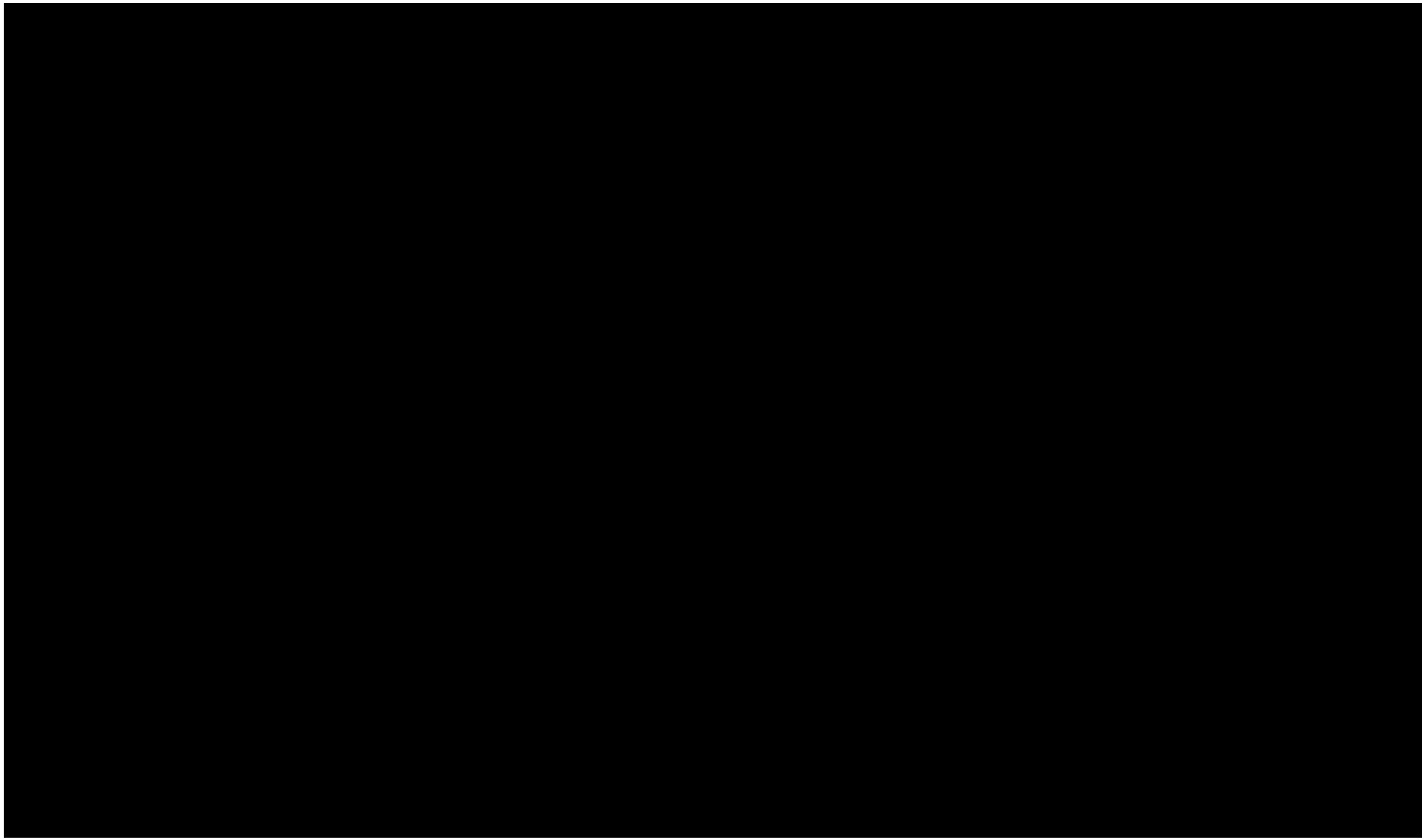

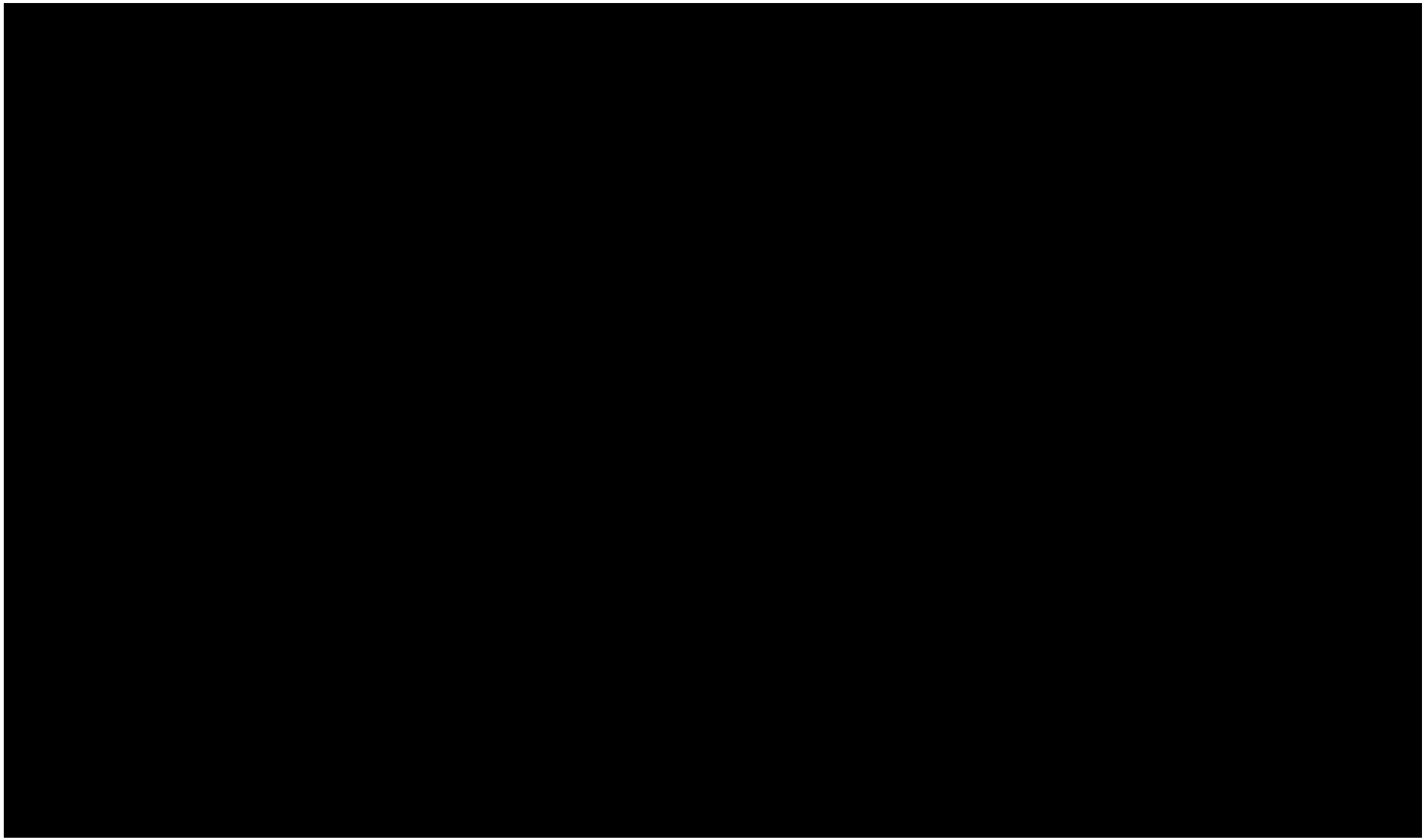

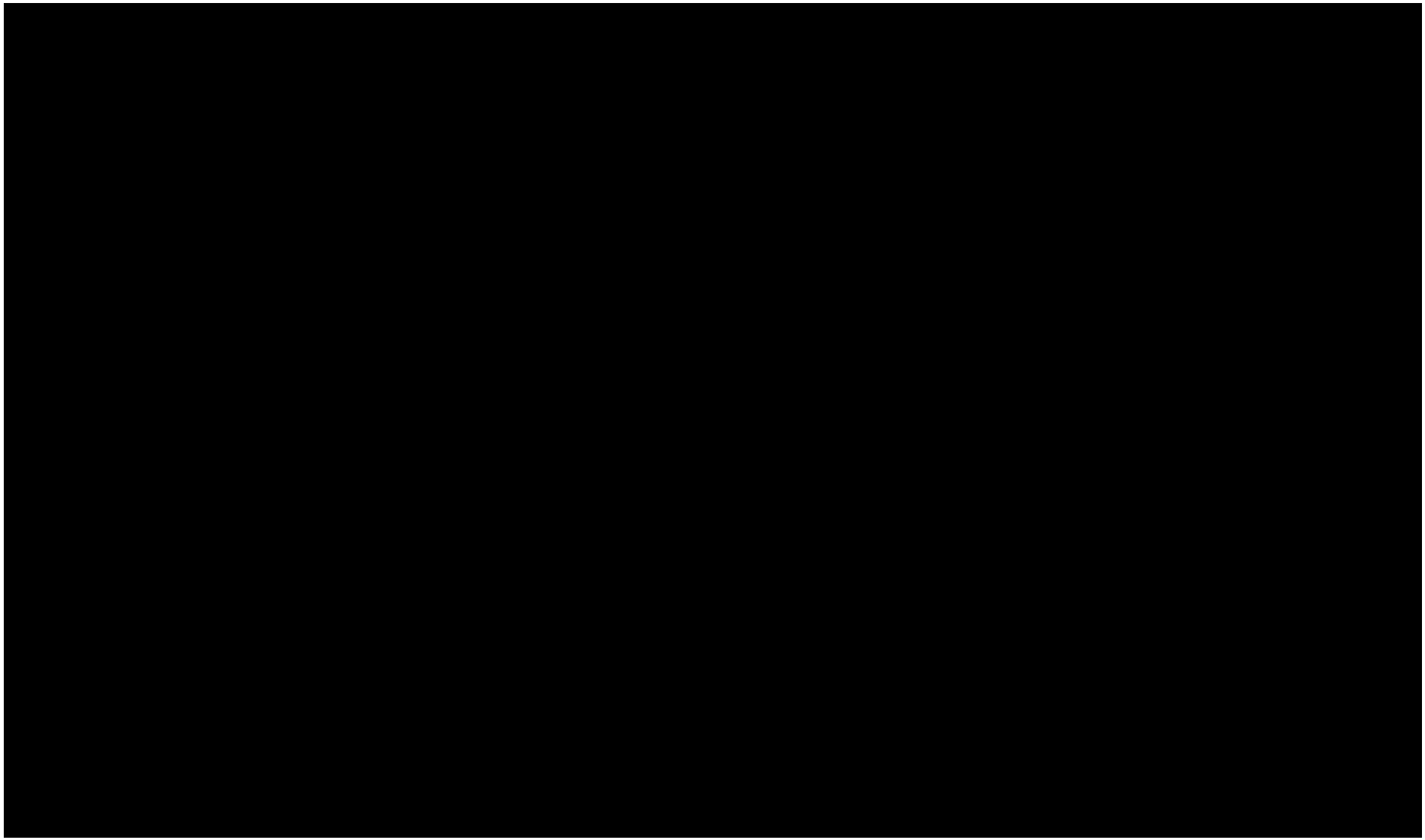

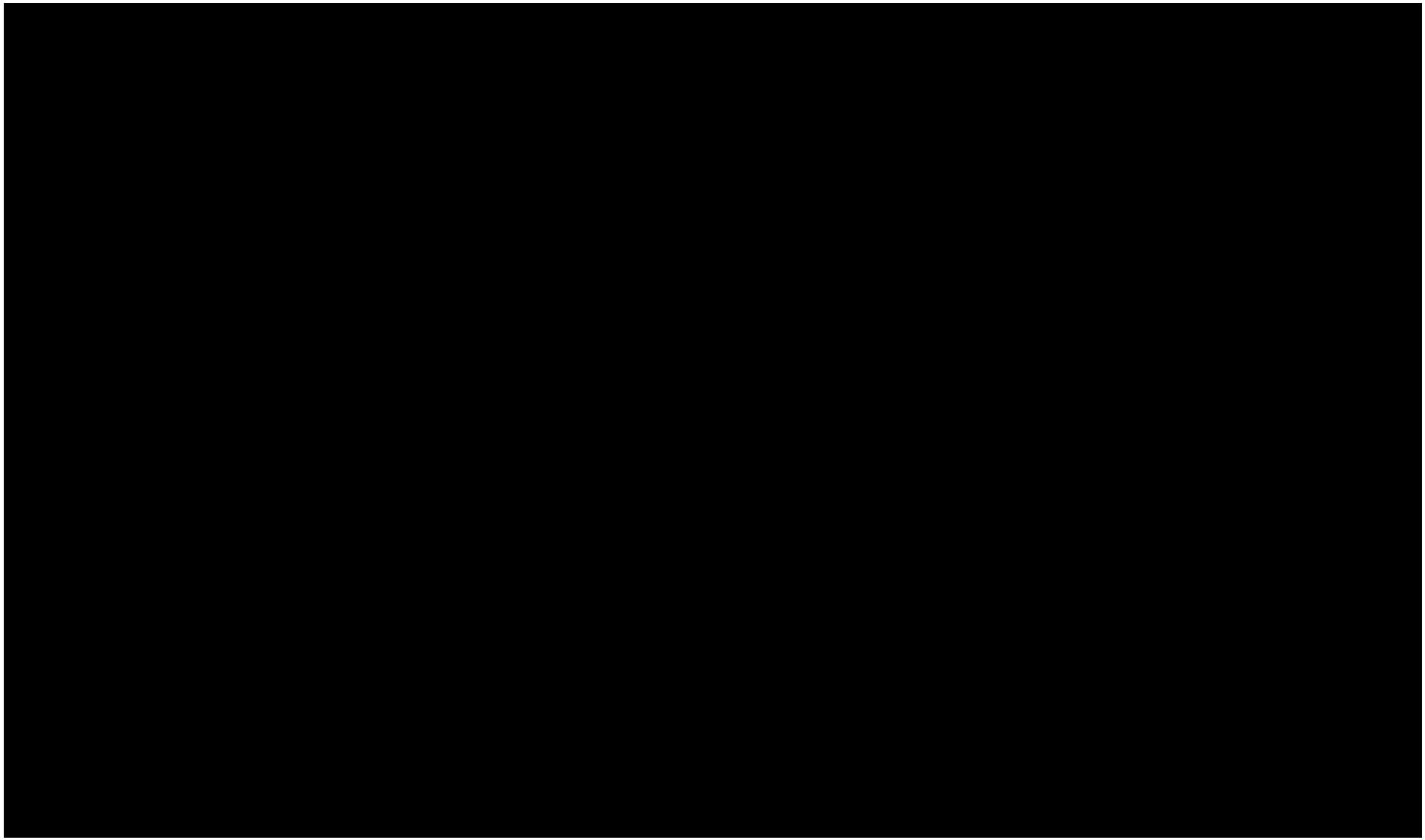

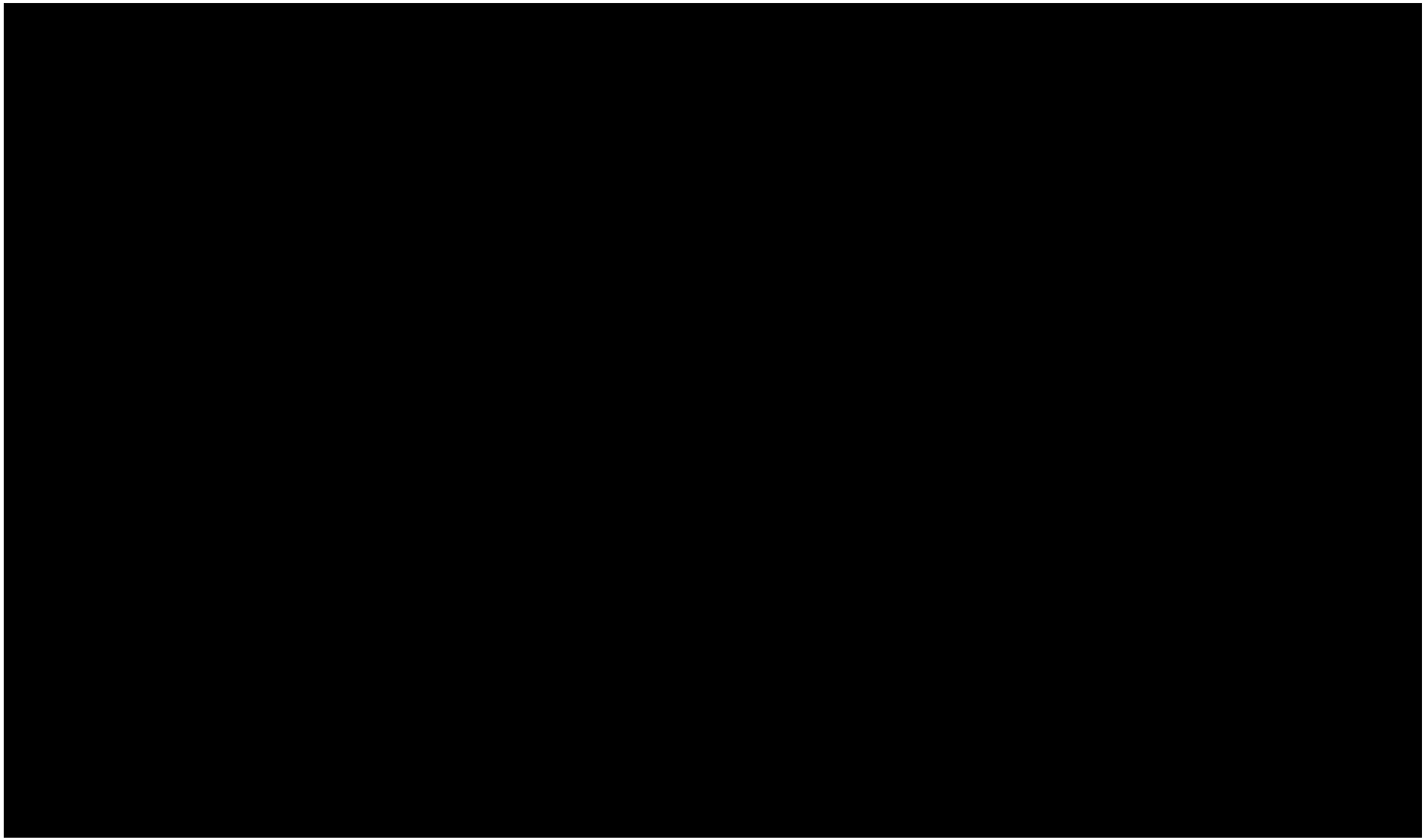

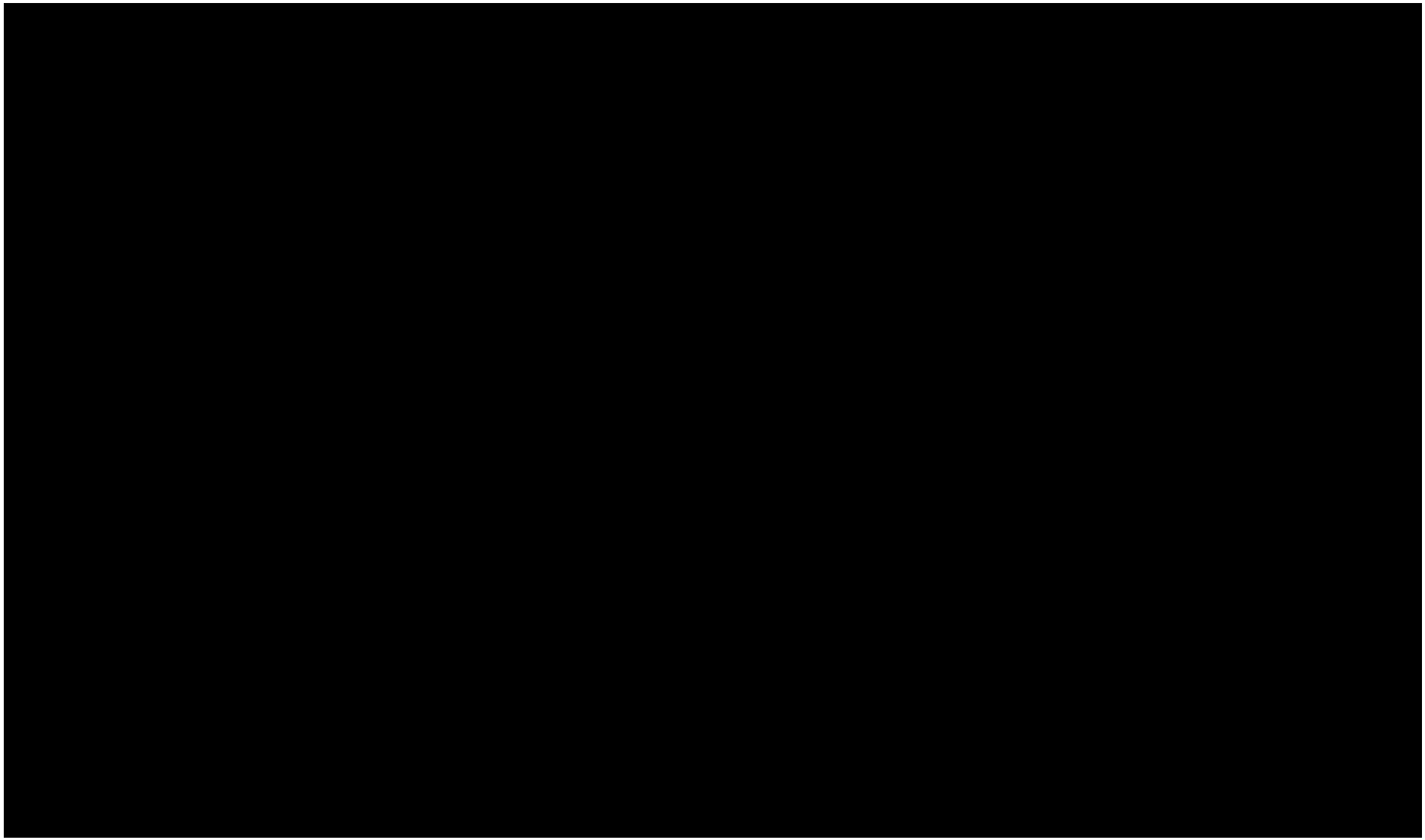

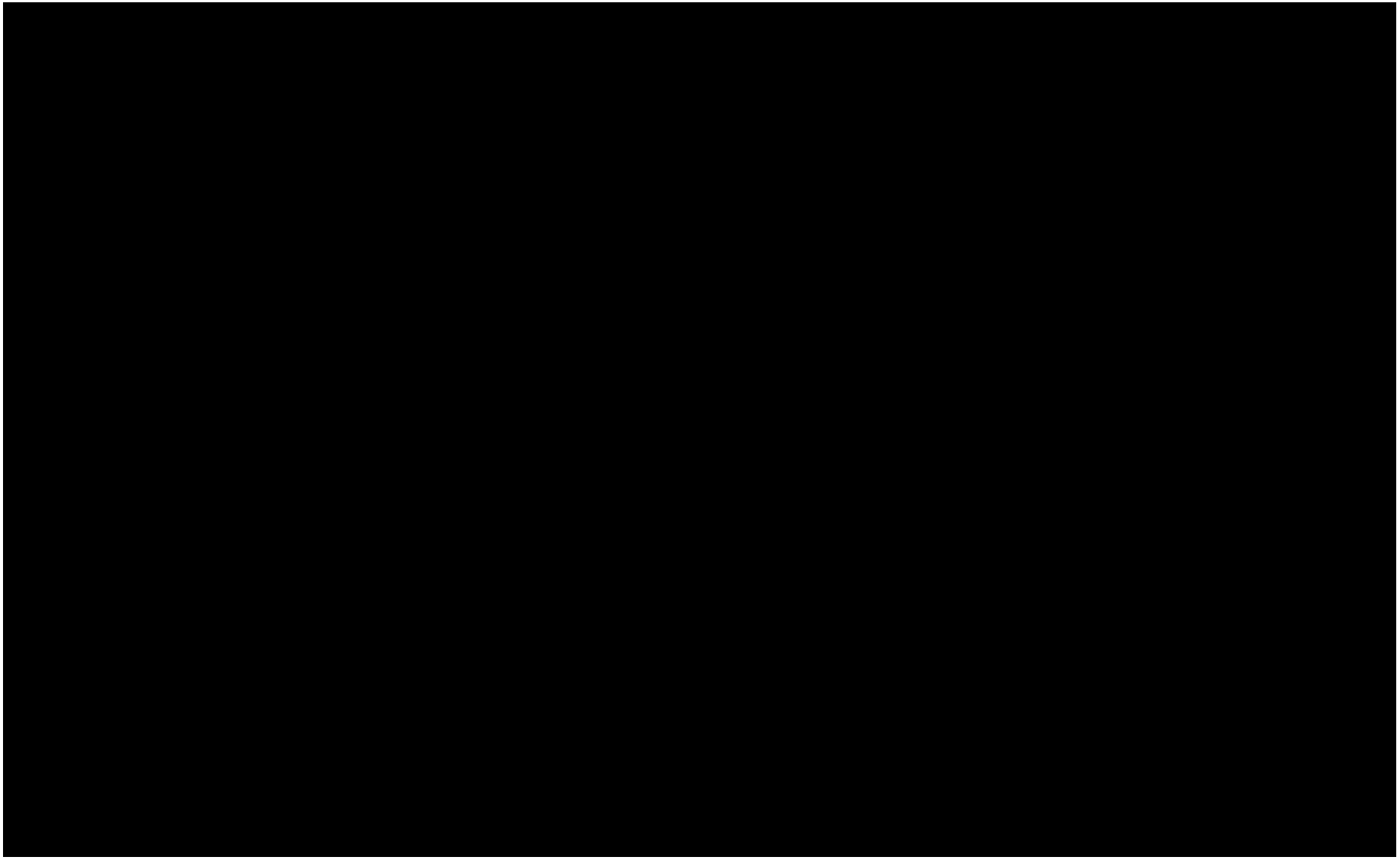

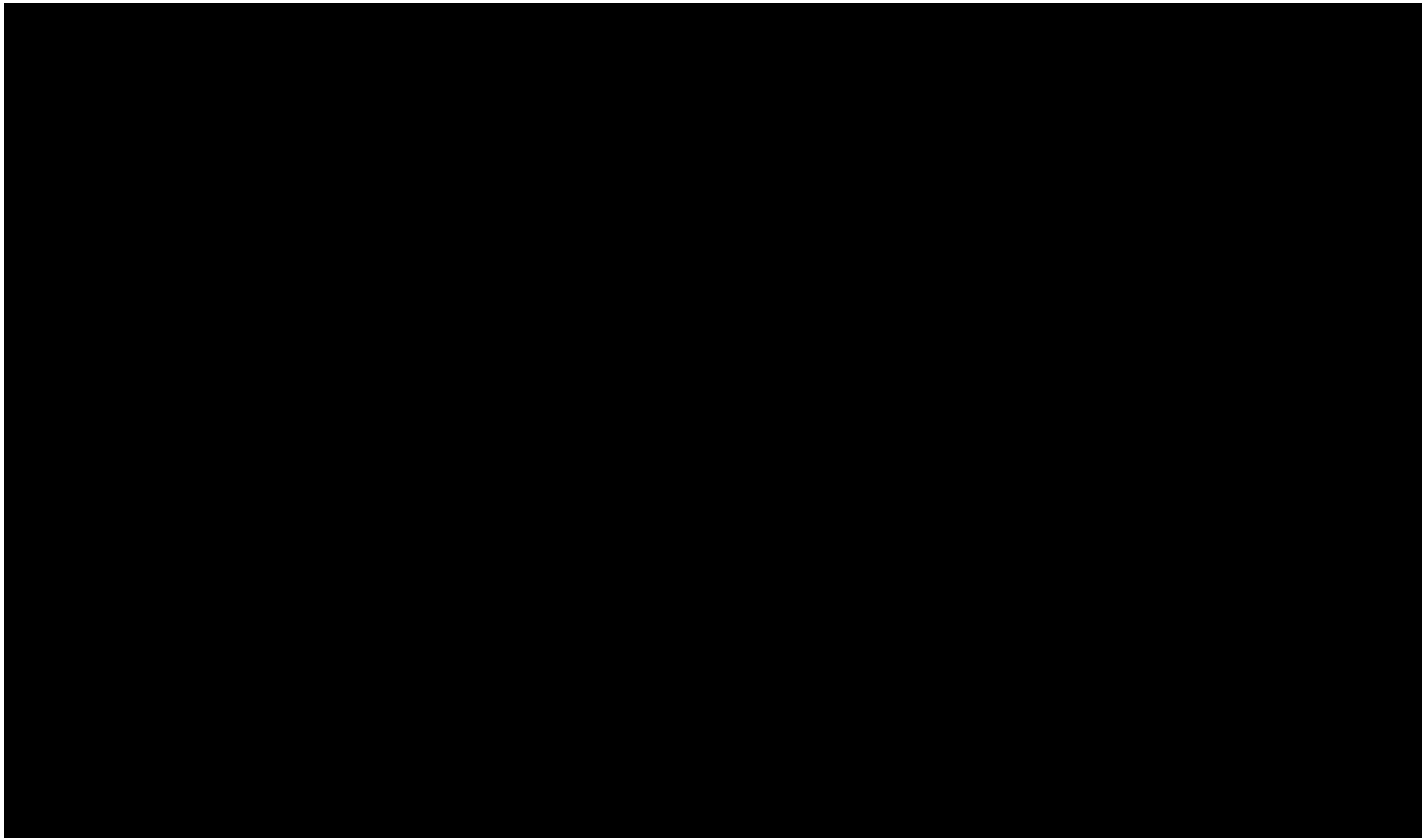

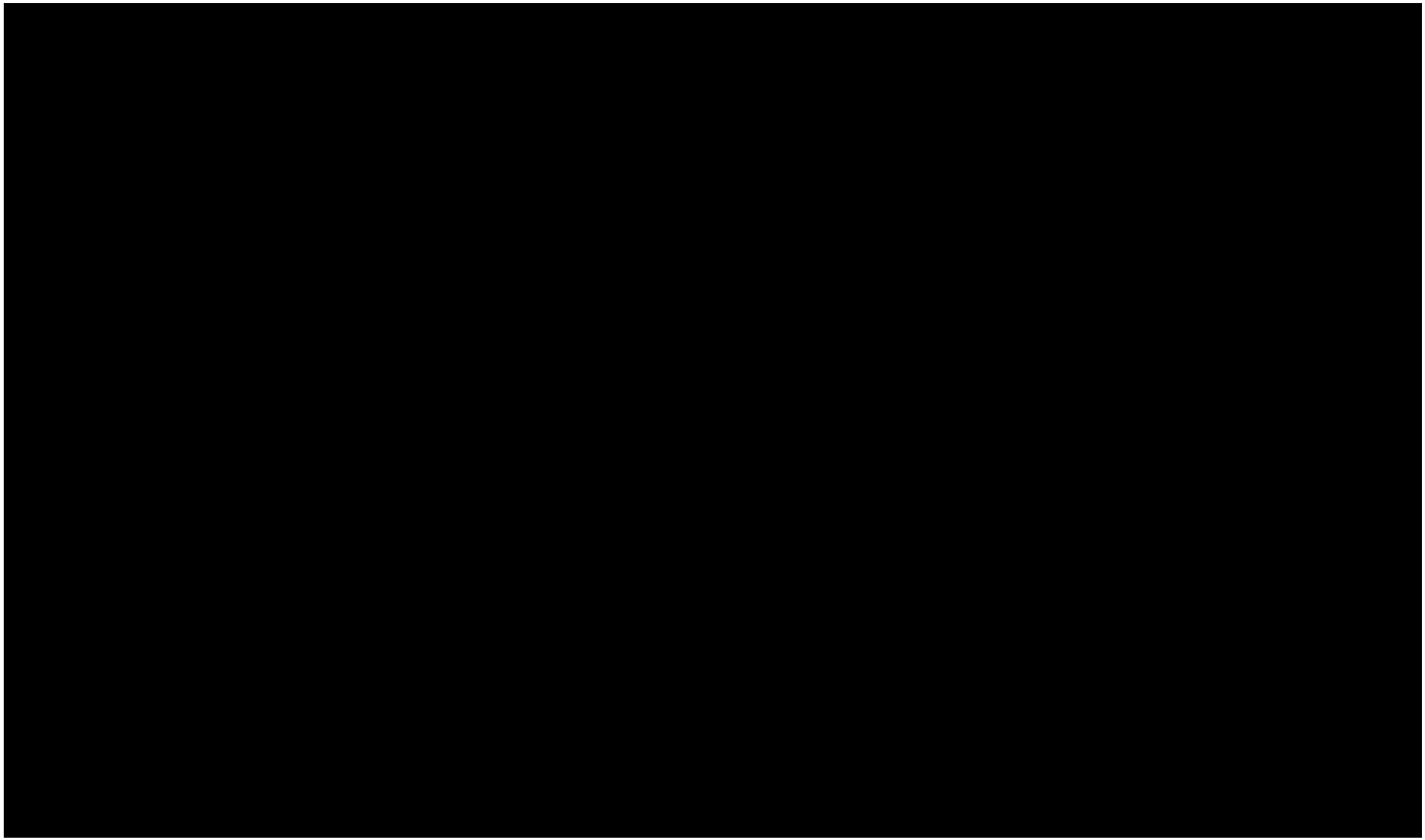

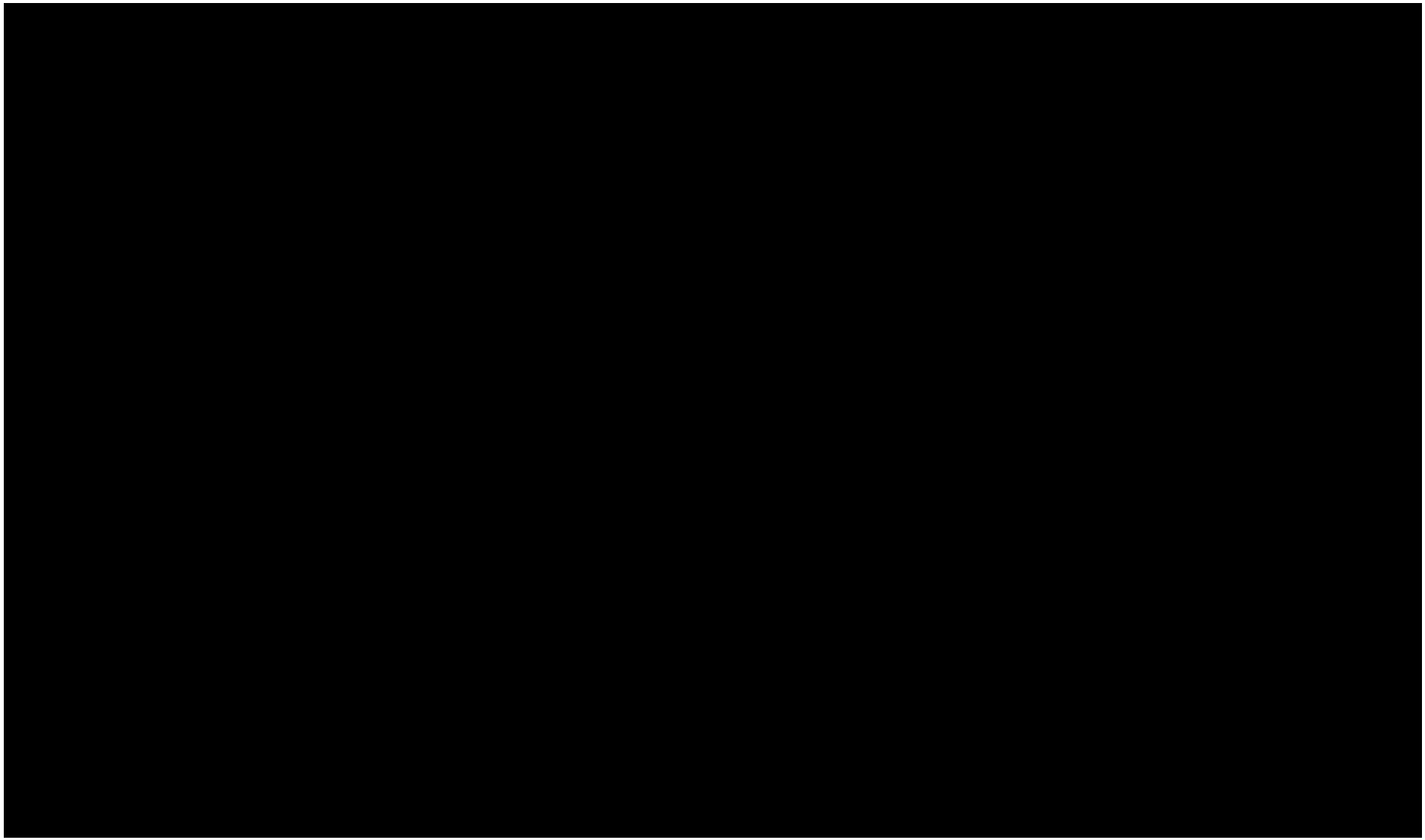

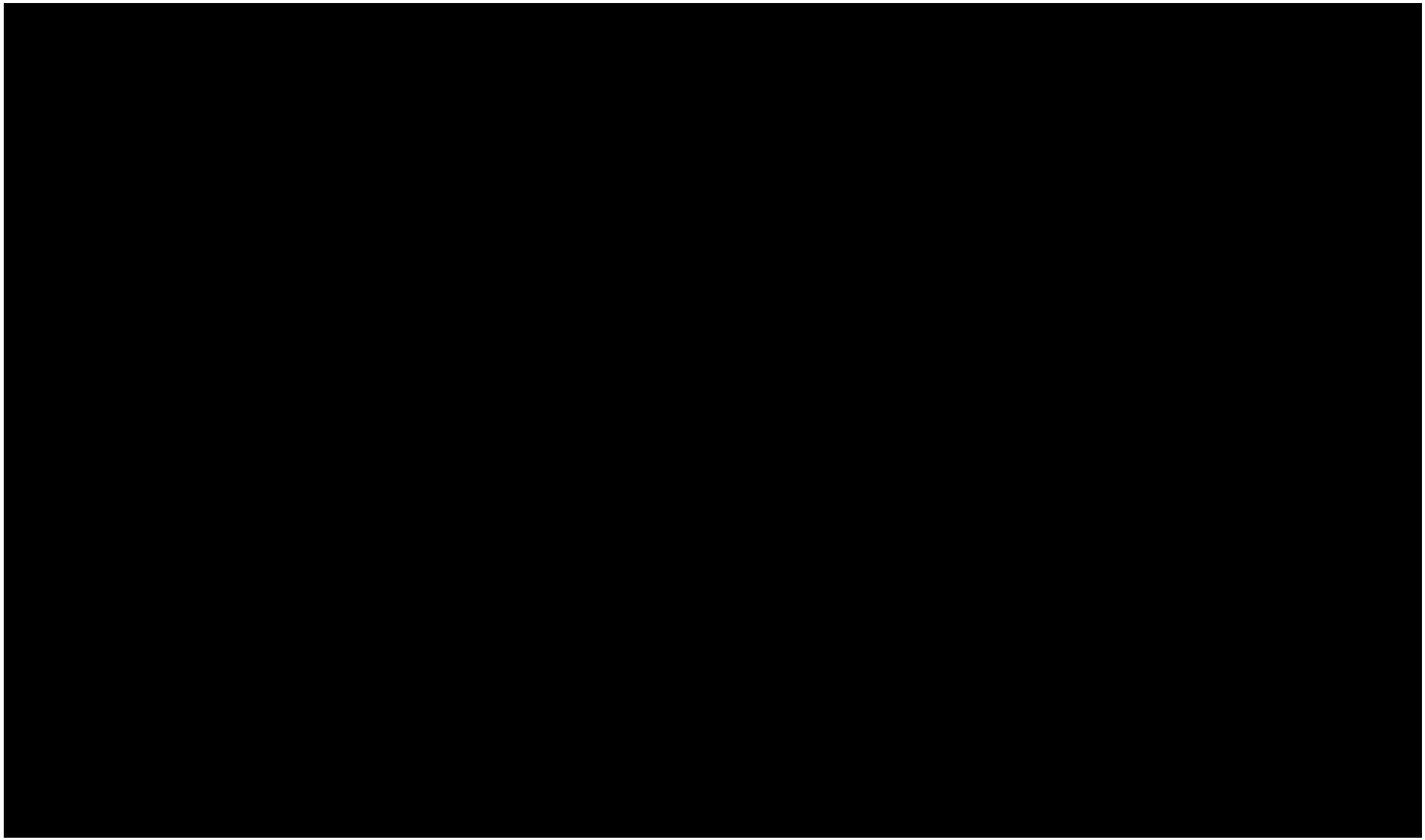

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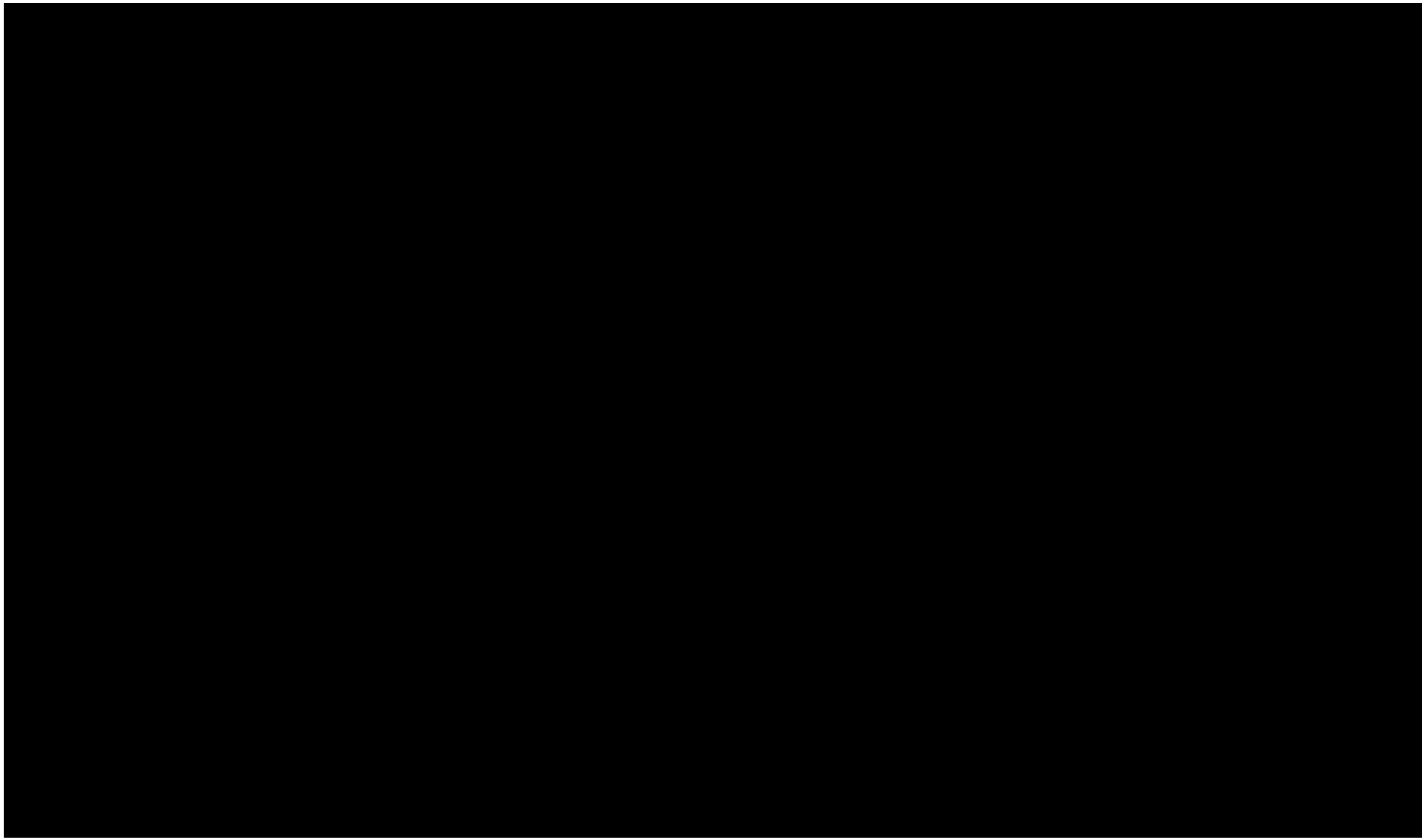

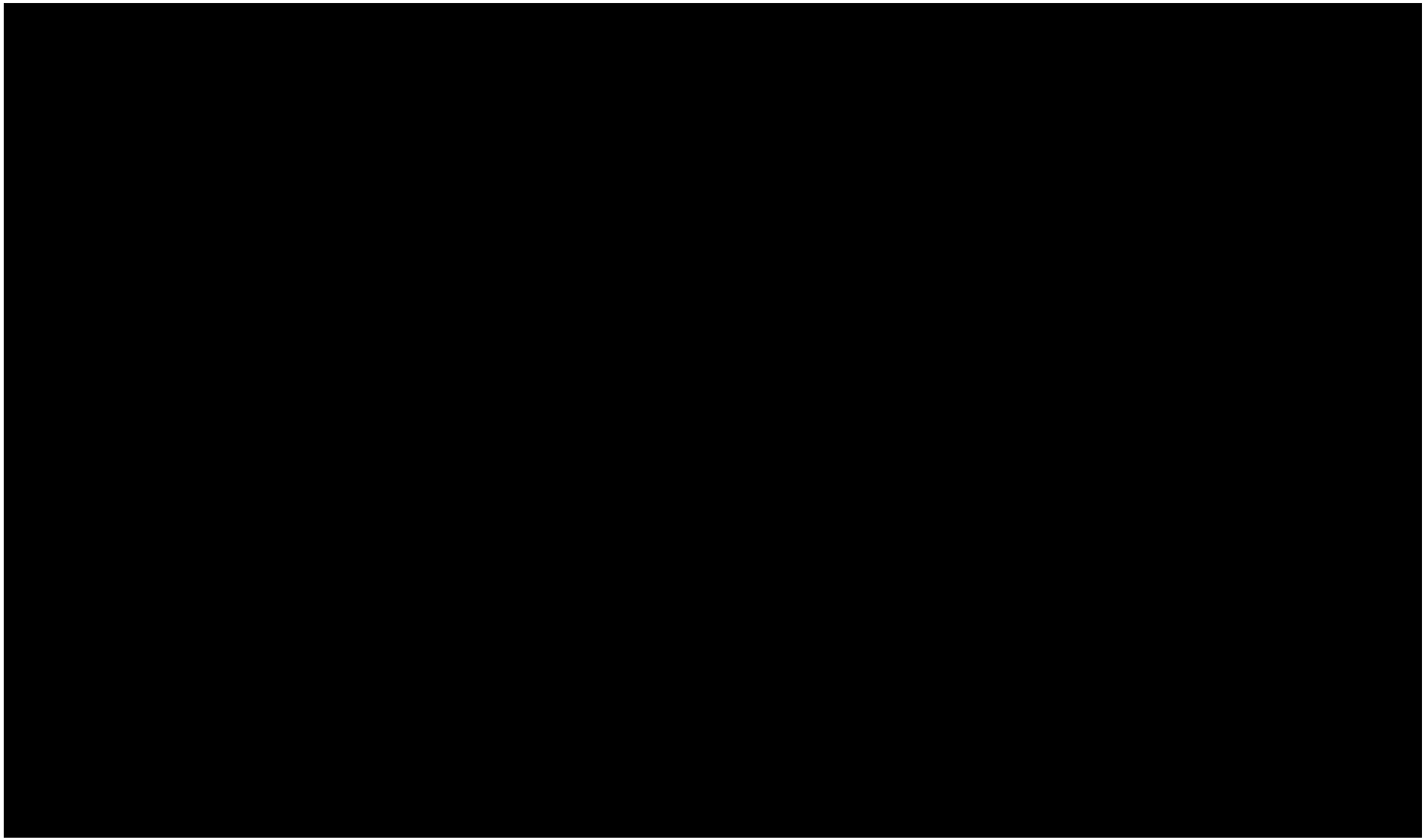

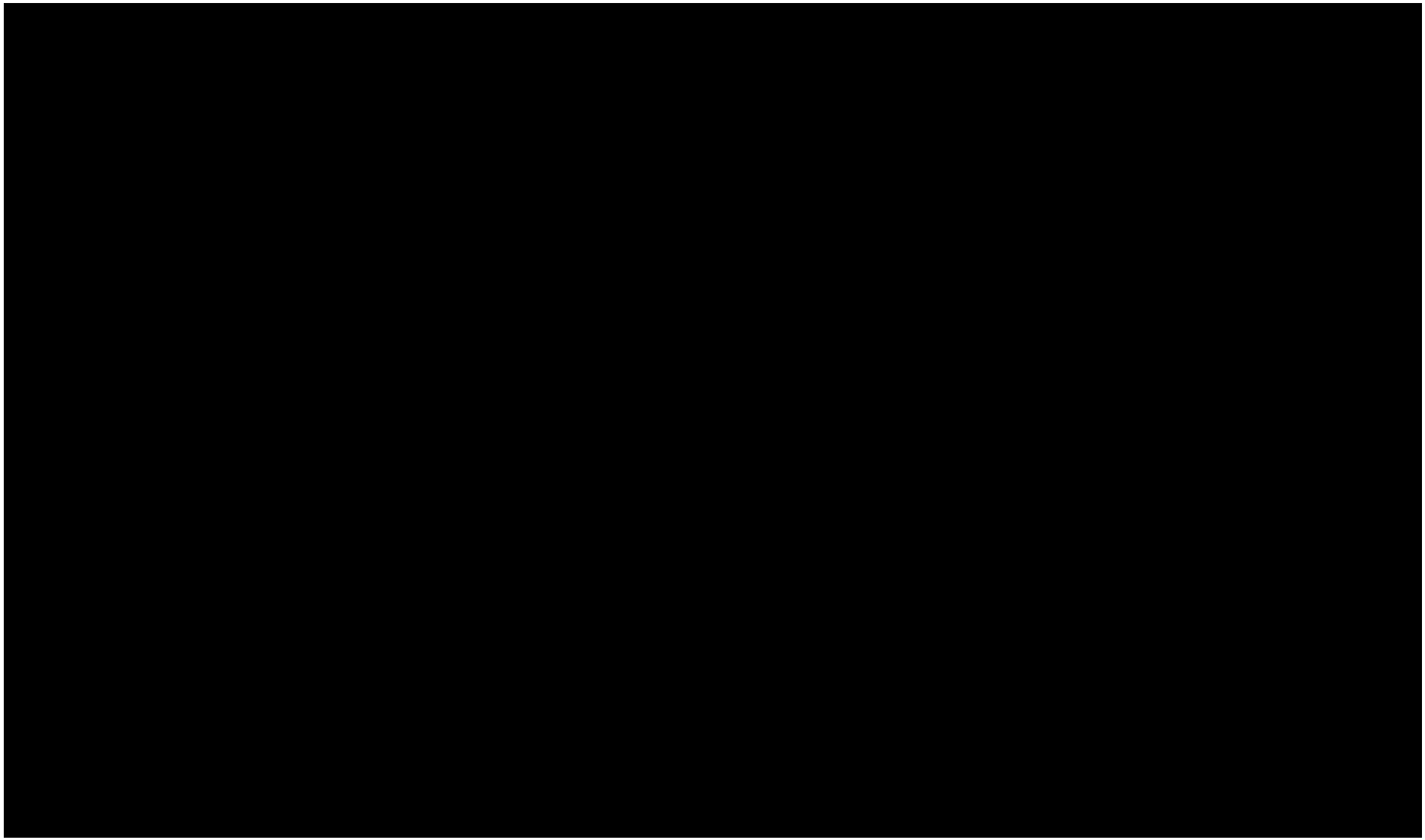

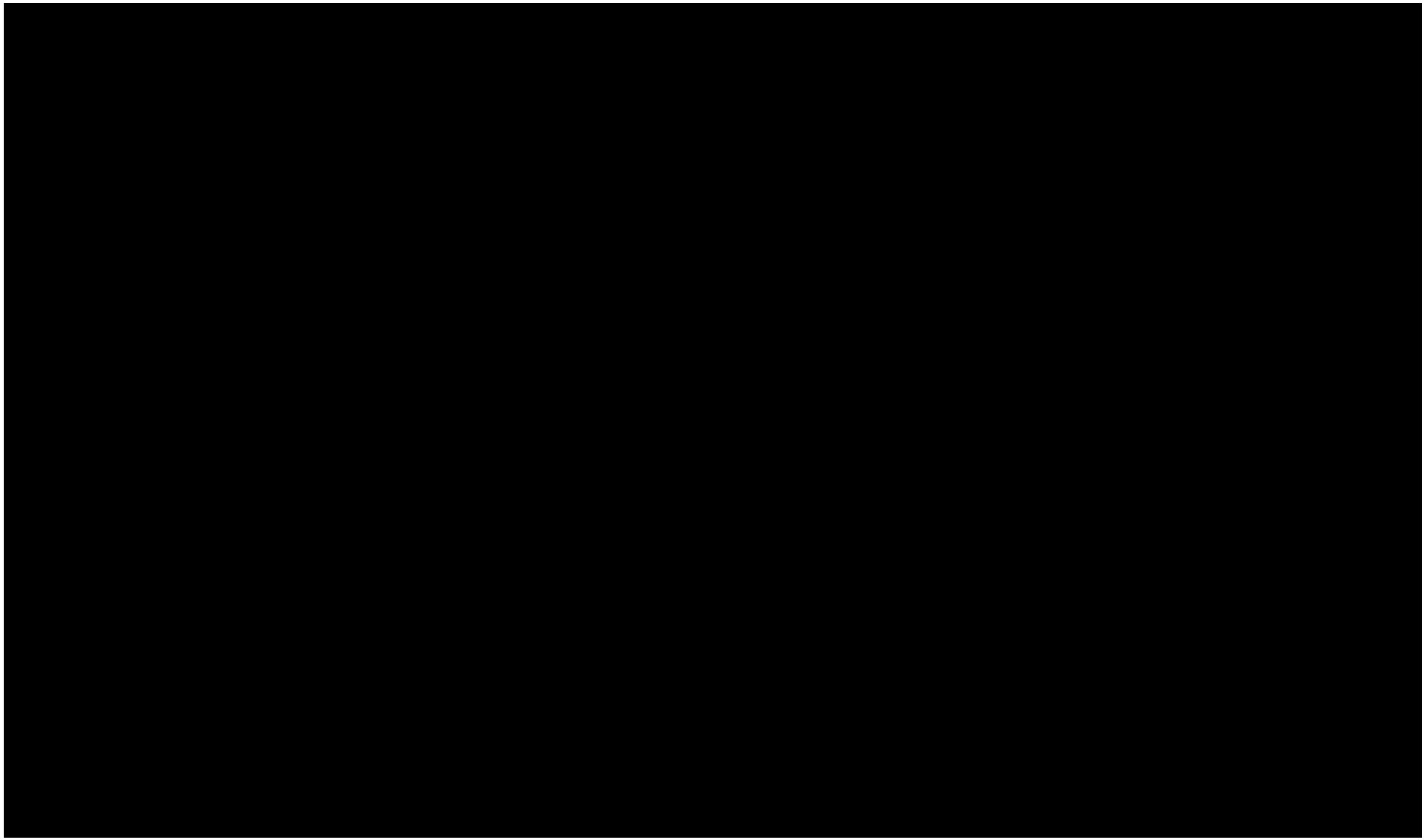

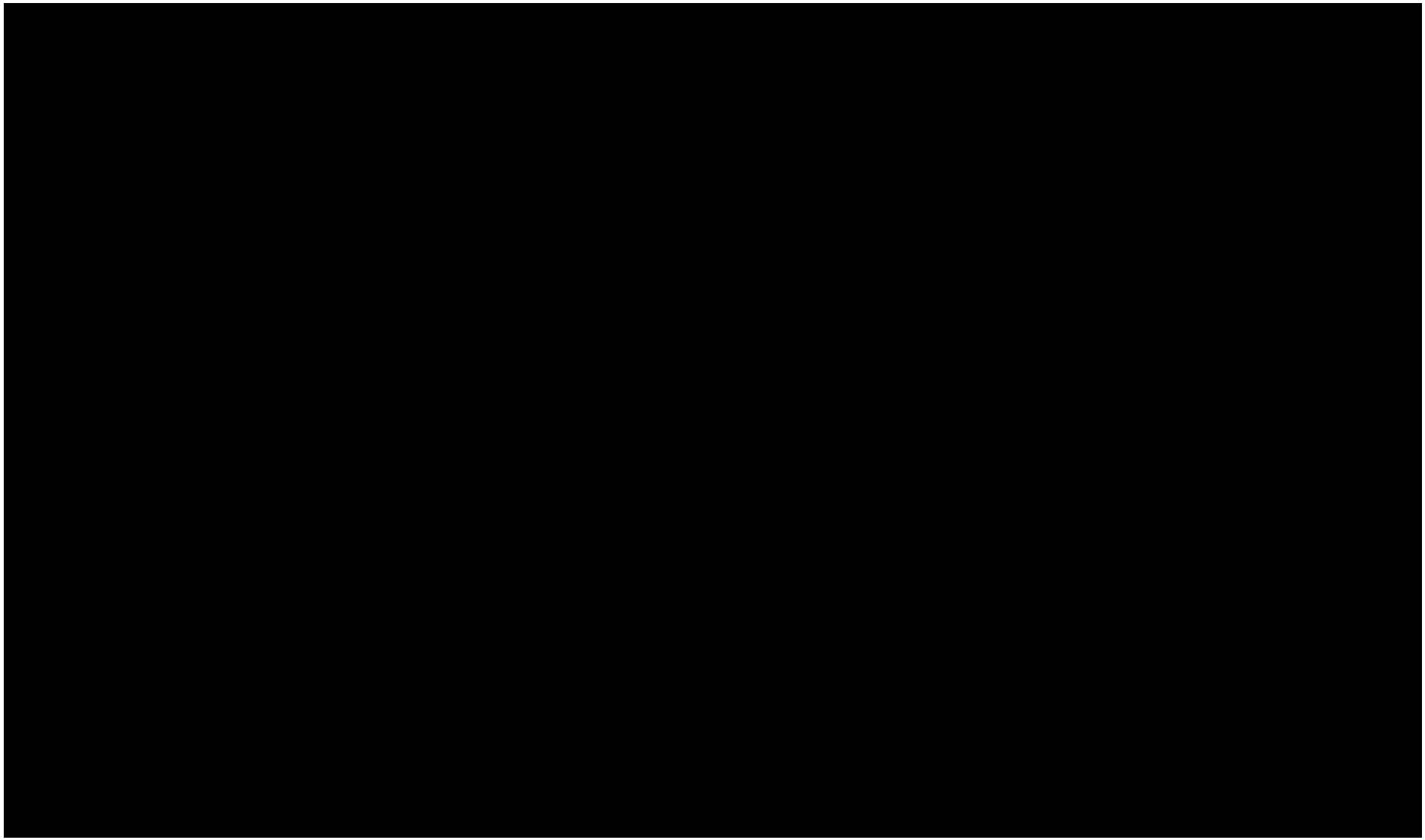

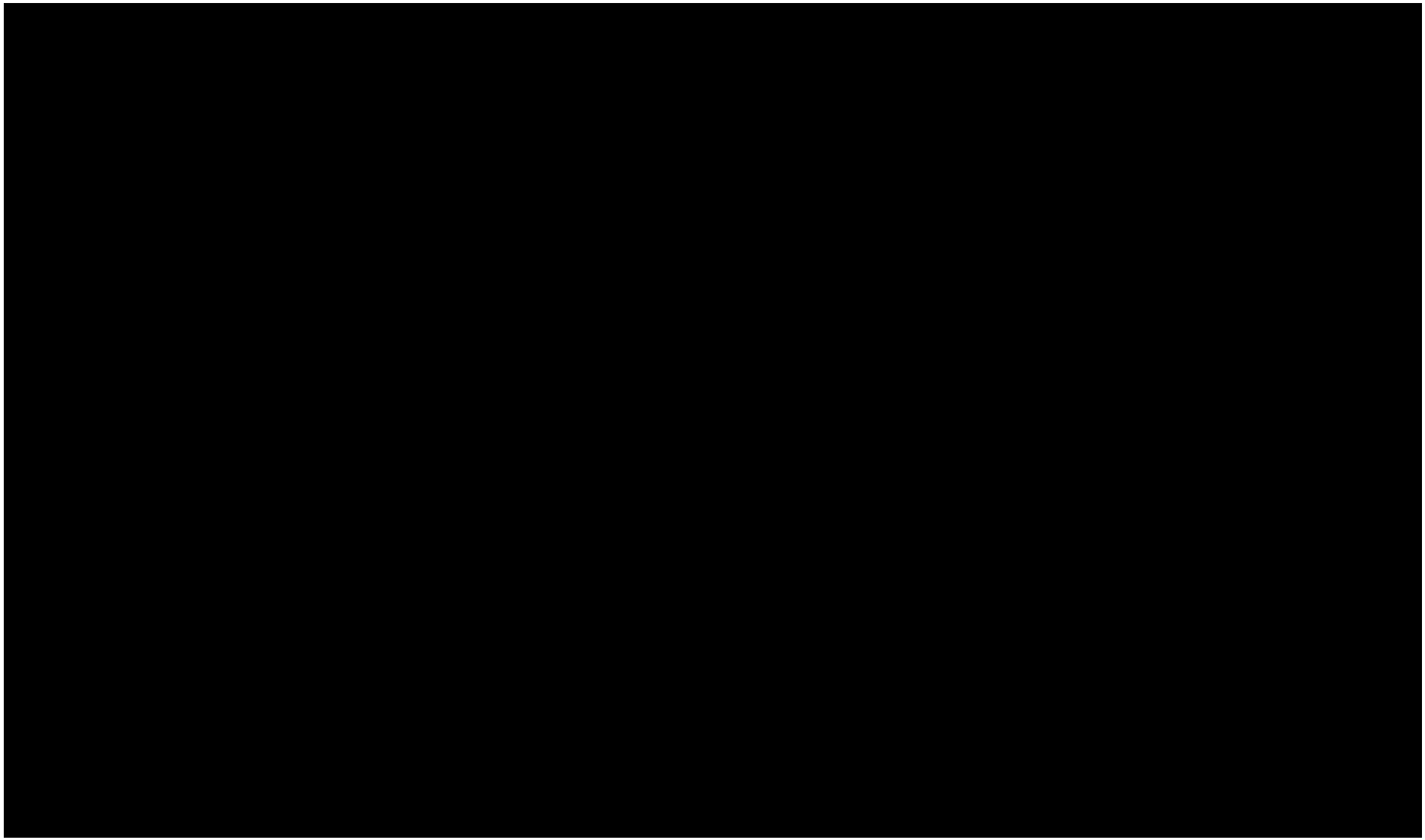

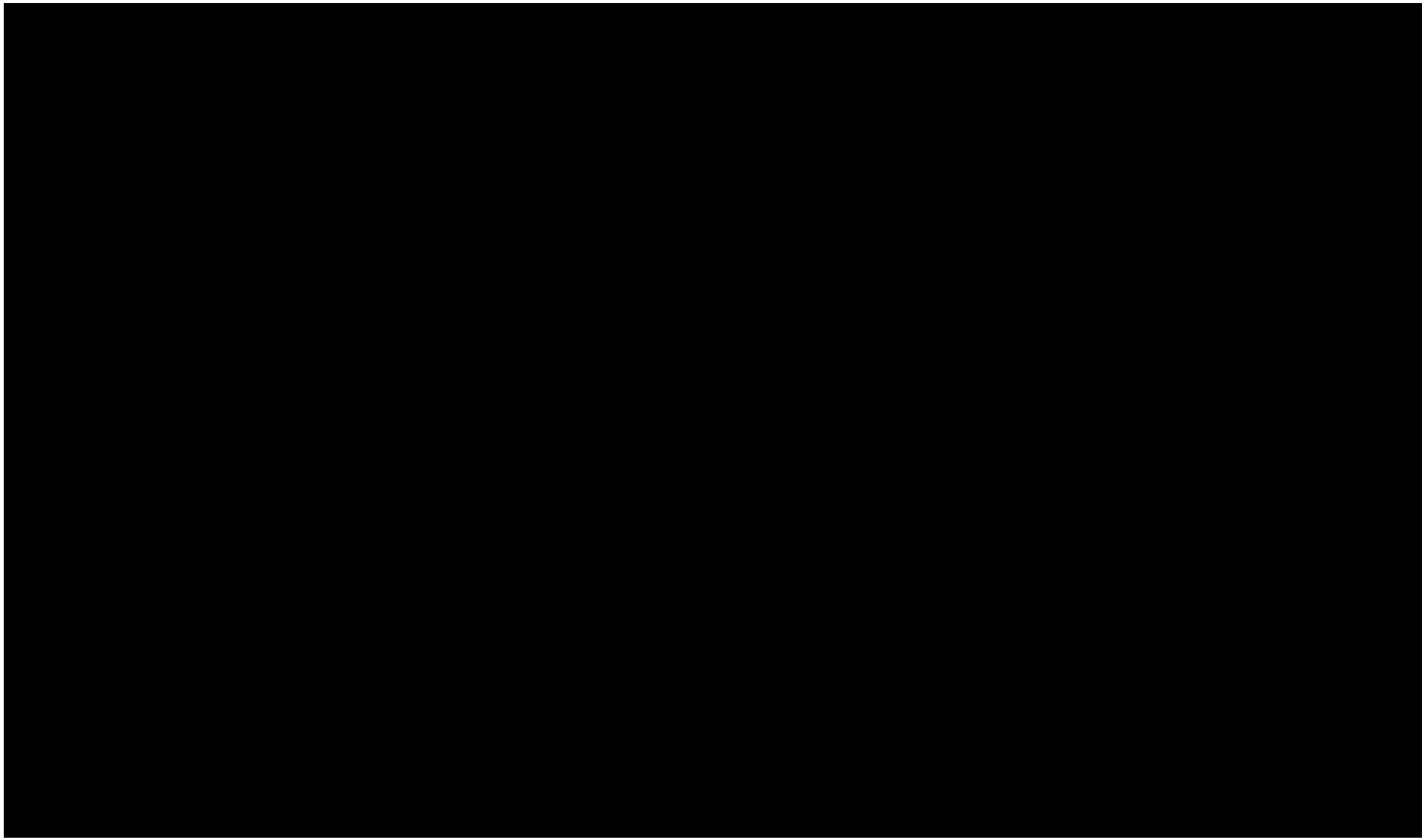

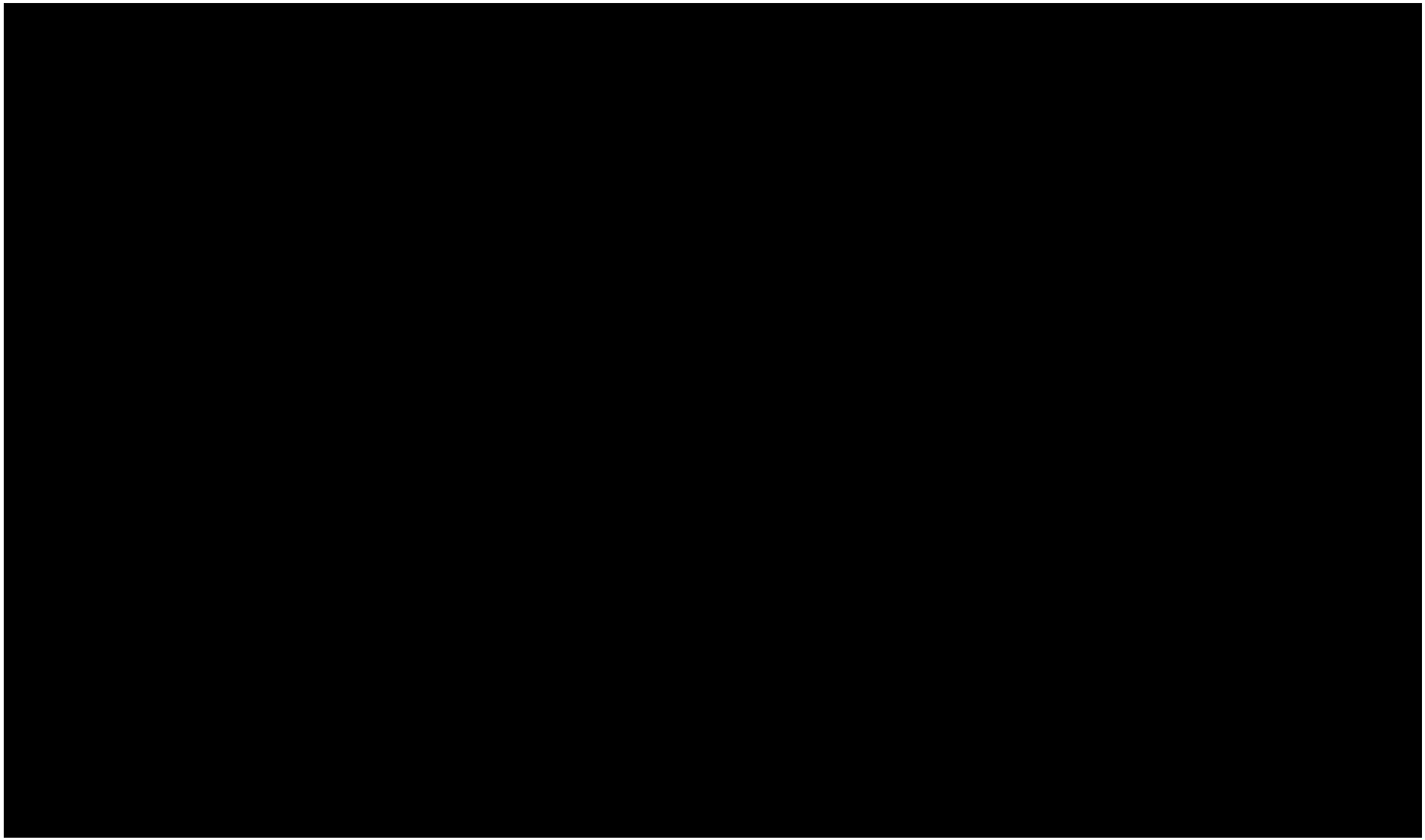

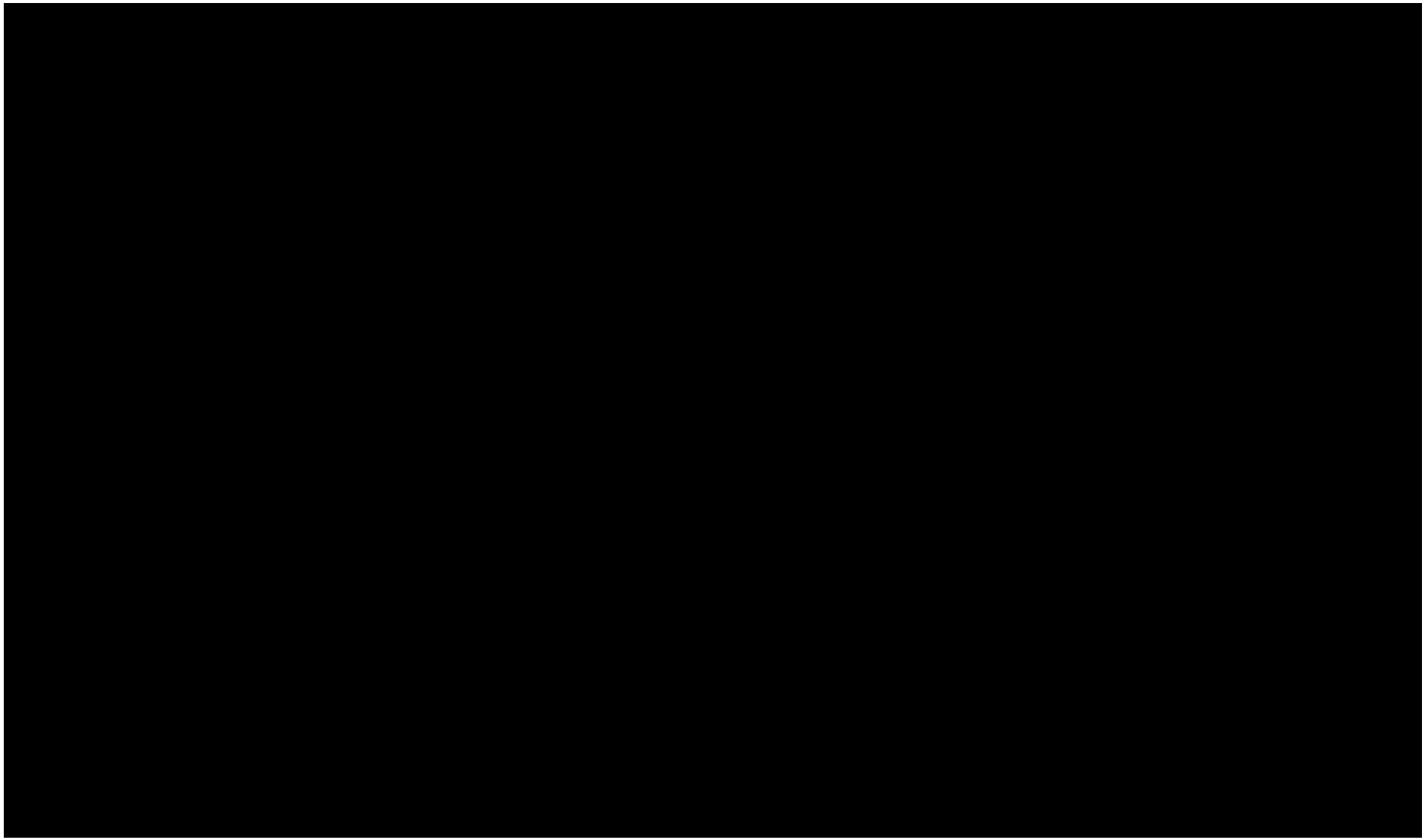

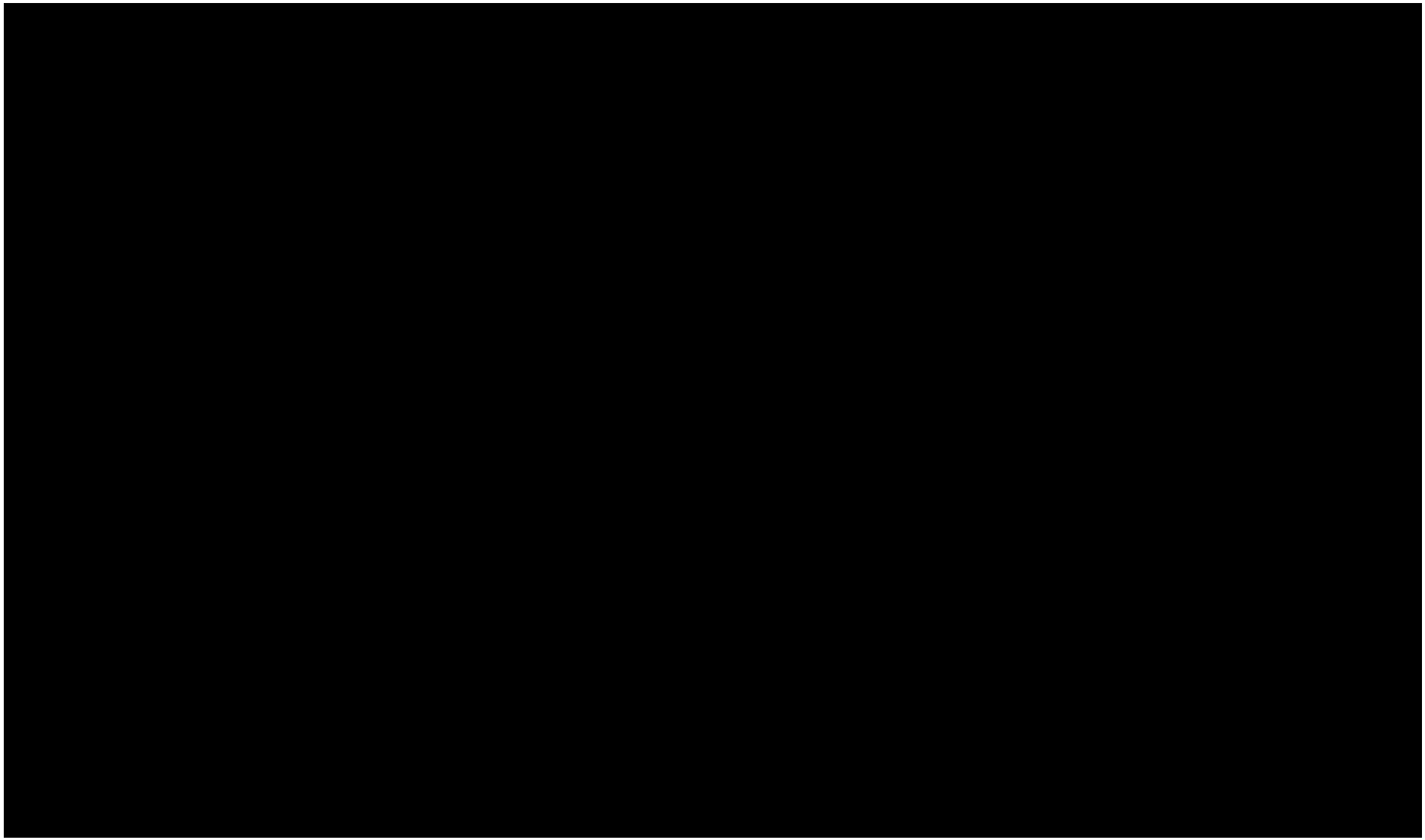

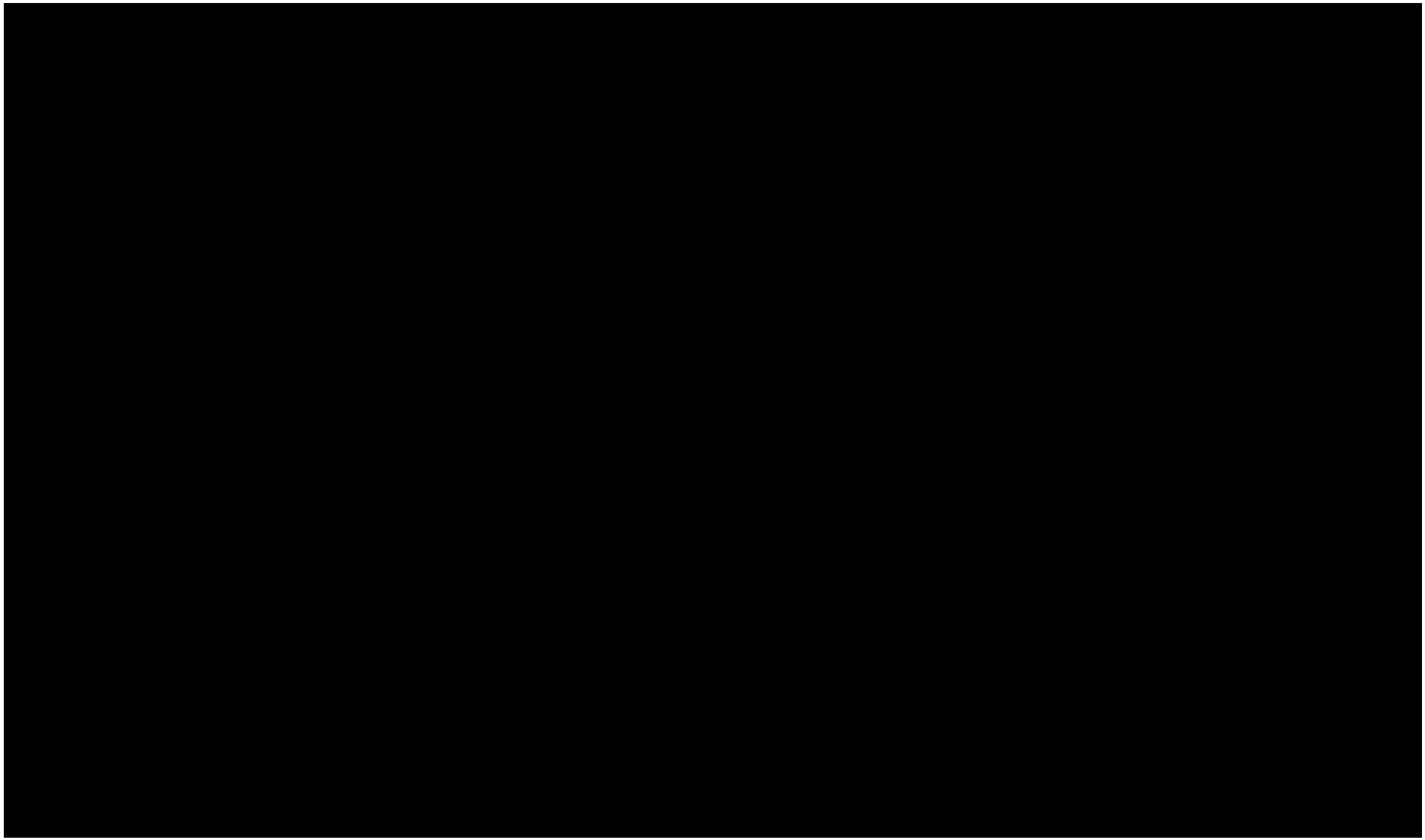

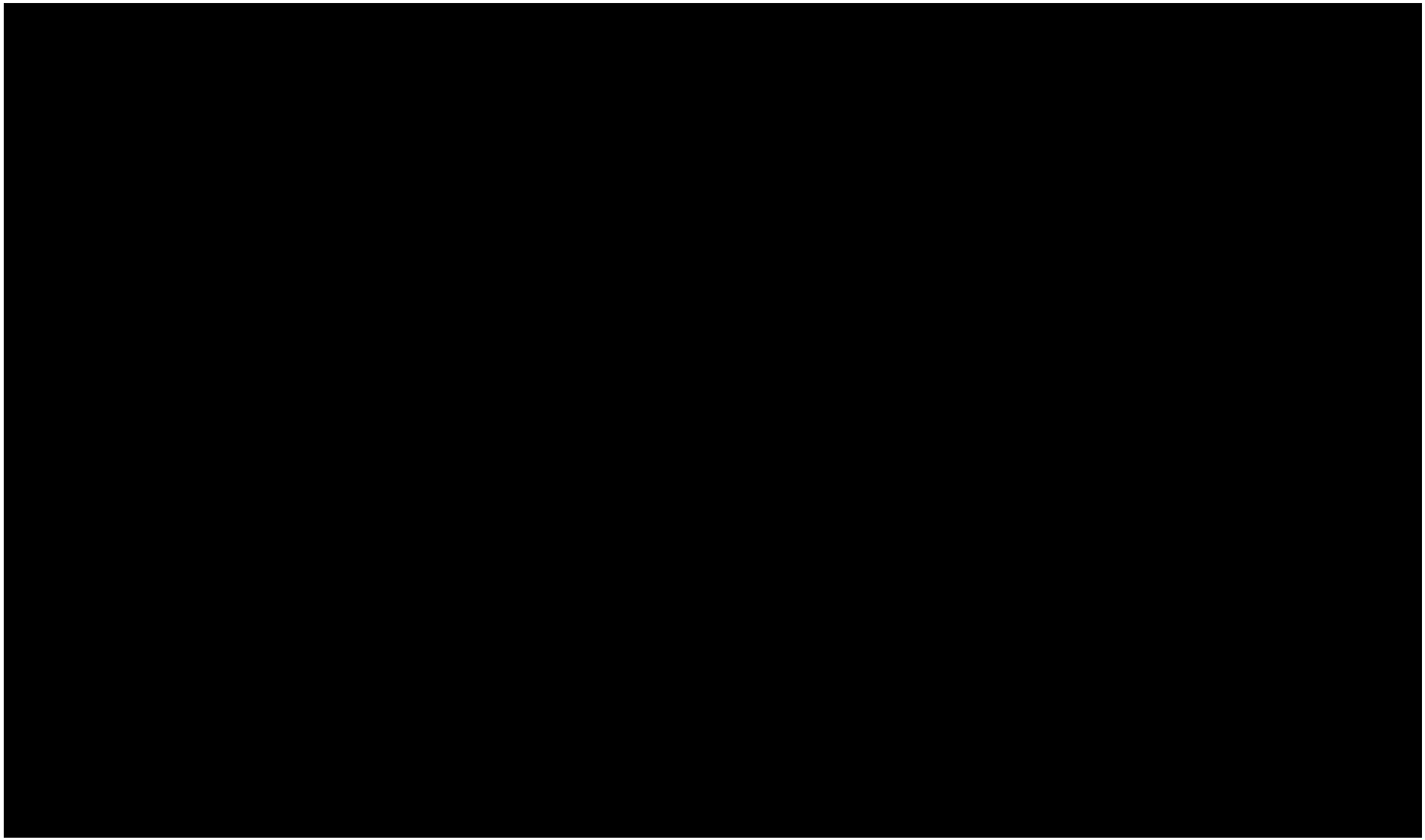

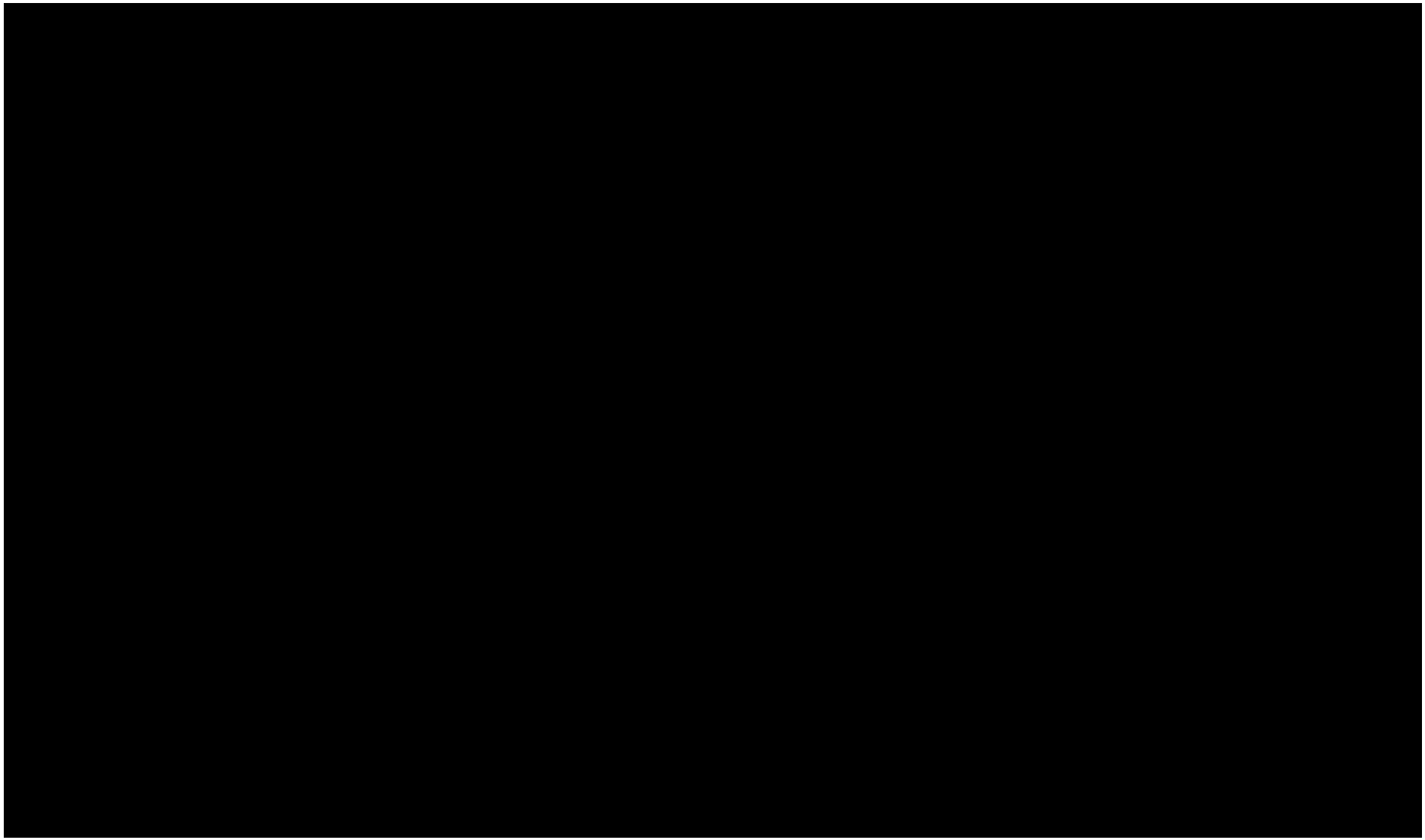

Appendix 1: [redacted]

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